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P1 A prospective study of the incidence of iatrogenic ocular damage in critically ill patients

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Crit Care 1999, **3 (suppl 1)**:P1

Introduction: Critically ill patients requiring intensive care are at risk of iatrogenic ocular damage. Studies have reported an incidence of eye problems of up to 40% in critically ill ventilated patients. We conducted this study to assess the incidence of ocular complications in our intensive care unit where all patients are cared for according to an eye care standard.

Methods: All ventilated patients over a 2 month period were included. Ophthalmic assessment was performed on admission and repeated every other day during the period of ventilation. At each assessment the average Ramsey sedation score over the previous 24 h, the presence of tracheal secretions and the presence of ventilation associated pneumonia was noted. Eye care performed was recorded.

Results: Sixty patients were included. One patient developed corneal exposure keratopathy. No patient developed conjunctivitis or corneal ulceration. Further advice on appropriate measures of eye care was given in five cases (8%). Nine patients (15%) had large amounts of respiratory secretions with positive microbiological results.

Conclusion: This study confirms that the use of an eye care standard is associated with a low incidence of ocular surface complications. The incidence of ocular complications in this group of patients is far lower than previously described.

P2 Intensive care unit procedures: cost savings and patient safety

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Crit Care 1999, **3 (suppl 1)**:P2

Introduction: Intensive Care Unit (ICU) management of critically ill patients often includes the requirement for tracheostomy and feeding access, most often a pecutaneous endoscopic gastrostomy (PEG). Although advances in ICU airway management include percutaneous tracheostomy, semi-open tracheostomy and conventional tracheostomy, the majority of critically ill surgical and injured patients still receive open tracheostomy in the Operating Room at Duke University Medical Center (DUMC). Although percutaneous tracheostomy is performed routinely in many medical ICU settings, in high risk surgical and trauma patients who often have unstable cervical spine injury and tissue edema, direct visualization of the cervical structures and trachea is imperative during tracheostomy. We have undertaken open tracheostomy and PEG in the ICU in selected patients as part of a collaborative, mulitidisciplinary ICU patient management strategy at DUMC. This initiative has been undertaken to address the risk of patient transport, the inappropriate use of OR time, and the cost to the patient as part of an effort to standardize and improve patient care.

Methods: After informed consent, utilizing DUMC conscious sedation protocol, full ICU monitoring, and sterile OR technique, 13 tracheostomies and 8 PEG placements were performed in 13 patients in the ICU since July, 1998. There were no complications. Operating Room costs include basic room fee and charge per minute for general surgery and anesthesia and the anesthesia professional fee. Surgical professional fee, tracheostomy tube cost, and gastroscope maintenance are identical and not included in the analysis. ICU costs include gowns, gloves, drapes and tracheostomy tray. For purposes of analysis, OR tracheostomy and OR PEG times were defined as 120 min and 60 min respectively; although analysis of fiscal year 1997–1998 yield widely divergent average OR times for these procedures.

Results: A table of cost comparison for individual procedure, total to date and associated cost savings are shown below.

Procedure	OR cost	ICU cost	Cost savings
Tracheostomy ($n=13$)	$37 555.05	$1323.92	$36 231.13
PEG ($n=8$)	$17 763.60	$1733.44	$16 030.16

Conclusion: Tracheostomy and PEG placement in the ICU in selected patients are safe, avoid patient travel, improve OR utilization and show a significant reduction in cost.

P3 Fiberoptic bronchoscopy of the intubated patient with life-threatening hemoptysis

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Introduction: Bleeding into the tracheobronchial tree is a potentially fatal occurrence for intubated patients. The subsequent acute respiratory failure requires an effective therapy. Fiberoptic bronchoscopy represents an easy available technique for the diagnosis and treatment of this type of hemoptysis.

Methods: We show the bronchoscopic management of endobronchial bleeding in intubated patients at our ICU. During the period 7/97–12/97 seven consecutive patients with acute endobronchial bleeding were treated with fiberoptic bronchoscopy. All patients received an endobronchial instillation of epinephrine and physiological saline solution (1:10 000–100 000).

Patient	Diagnosis	Interventions	SaO_2 [%] before treatment	Outcome
1 (74 y/f)	Goiter, large retrosternal, sternotomy	5 in 5 h	60	survived
2 (60 y/f)	Stenosis of the left internal carotid artery	20 in 10 d	90	survived
3 (71 y/m)	Ruptured abd. aortic aneurysm	5 in 5 d	90	survived
4 (65 y/f)	Axillo-bifemoral bypass-infection	3 in 2 d	50	survived
5 (63 y/m)	Aspergilloma left lung, acute myeloic leucemia	1	70	dead
6 (60 y/f)	Lung contusion, polytrauma	6 in 3 d	65	survived
7 (77 y/f)	Acute abdominal pain, urosepsis, nephrectomy	1	85	survived

Results: Control of bleeding was achieved with 1 to 20 (m ± SEM: 5.86 ± 0.93) bronchoscopic interventions. Hemostasis was accomplished in a period of 0.5 h and 10 days. Cardiocirculatory instability was observed in five patients. One patient died because of persistent bleeding caused by severe aspergillosis. Six patients survived without further interventions.

Conclusion: Endobronchial instillation of epinephrine and physiological saline solution represents an effective method in case of lifethreatening hemoptysis in intubated and mechanical ventilated patients.

P4 The compliance characteristics of the Portex Soft-Seal cuff improves seal against leakage of fluid in a pig trachea model

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Crit Care 1999, **3 (suppl 1)**:P4

A high volume low pressure (HVLP) cuff does not protect the lower airway from contamination by material leaking along longitudinal folds within the cuff wall [1]. This is a major factor in the pathogenesis of ventilator associated pneumonia [2]. The combination of shape and high compliance of the Portex Soft-Seal cuff might eliminate the folds in the cuff walls circumferentially for a portion of the cuff and prevent leakage. We have tested the Soft-Seal cuff in a pig trachea model to establish whether protection against leakage is better than that afforded by standard HVLP cuffs.

Method: The Portex Soft-Seal, Mallinckrodt Hi-Lo, Sheridan Preformed and Portex Profile size 8 mm internal diameter HVLP cuffed tracheal tubes were assessed for leakage of dye placed in the subglottic space to the trachea in a benchtop ventilation model and in six isolated pig tracheas. All cuffs were inflated at 30 cmH_2O pressure.

Results: There was no leakage in the ventilation model or in the pig tracheas with the Portex Soft-Seal group, but rapid leakage occurred in all the pig tracheas for the standard HVLP cuffs.

	Isolated pig trachea ($n=6$)	Simulated IPPV	Simulated tracheal suction	Tube motion in trachea
Mallinckrodt Hi-lo	Leak	Leak	Leak	Leak
Sheridan Preformed	Leak	Leak	Leak	Leak
Portex Profile	Leak	Leak	Leak	Leak
Portex Soft-Seal	No leak	No leak	No leak	No leak

Conclusion: This benchtop study suggests that the improved HVLP cuff compliance characteristics and shape of the Portex Soft-Seal cuff might be beneficial in the prevention of leakage of fluid to the lungs known to occur with HVLP cuffs.

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P5 Colibri coloriometric technology rapidly detects oesophagal intubations

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Crit Care 1999, **3 (suppl 1)**:P5

Introduction: Rapid verification of correct placement is extremely important [1,2]. We have tested a new coloriometric CO_2 detection indicator meant for this purpose [3].

Methods: An entdotracheal tube was placed both in the trachea and the oesophagus in otherwise healthy patients undergoing elective surgery under general anaesthesia. We compared the four first ventilations of the endotracheal and oesophageal tube using capnography and a Capno Bri indicator with four different colour

gradings. (Blue ~ 0.5%, dark green ~ 1.0%, light green ~ 3.0% and yellow ~ 4.0%)

Results: In all patients ($n = 9$), the indicator confirmed correct placement of the tube in the trachea at the first ventilation (yellow color). The indicator also verified incorrect oesophageal placement at the first ventilation in all patients (blue color).

These results were confirmed by the capnography.

Conclusion: The Colibri technology is a reliable technique for confirmation of correct endotracheal tube placement. It may be especially suitable in emergency situations where capnography is not available

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P6 Lung volume and oxygenation changes with a closed suction system (CSS) in patients undergoing volume controlled ventilation (VCV)

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Crit Care 1999, **3 (suppl 1)**:P6

We wished to measure changes in lung volume (ΔLV), airway pressures, and oxygenation during tracheal suctioning performed with a CSS and with an open suction system (OSS). We enrolled 7 adult patients, sedated and paralyzed, VCV ventilated by a SERVO 900C ventilator (Siemens, Sweden) with PEEP ≥5 cmH$_2$O and FiO$_2$ ≥ 0.4. Keeping all remaining ventilatory settings unchanged, we set trigger sensitivity at –2 cmH$_2$O, inspiratory time at 25%, inspiratory pause at 10%. We performed four suctioning manouvers at 20 min intervals using alternatively a CSS and an OSS. With both systems, we used 12 F size catheters. We performed no pre-oxygenation manouvers. Suction was applied for 20 s at a pressure of 100 cmH$_2$O. We continuously recorded signals of respiratory inductance pletismography (RIP, Respitrace Plus, NIMS, FL), arterial oxygen saturation (O$_2$Sat) by pulse oxymetry, and airway pressures. We obtained ΔLV as the change in the RIP signal measured during VCV and during suction. We measured Respiratory Rate (RR), peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), and mean airway pressure (MAP) during VCV and during suction with the CSS.

Results: variables are reported as mean ± DS.

	VCV	CSS	OSS
ΔLV (l)	–	–0.05 ± 0.13	–1.13 ± 0.27*
O$_2$Sat (%)	97.8 ± 1.8	97.3 ± 1.8	93.9 ± 4.5‡
RR (bpm)	14.9 ± 4.3	39.4 ± 6.6†	–
PIP (cmH$_2$O)	32.4 ± 8.7	26.2 ± 9.2†	–
PEEP (cmH$_2$O)	10.2 ± 4.2	7.8 ± 4.2†	–
MAP (cmH$_2$O)	15.9 ± 4.8	18.1 ± 5.3†	–

*$P < 0.01$ vs CSS, †$P < 0.05$ vs VCV, ‡$P < 0.01$ vs VCV

Comment: the use of the OSS resulted in discontinuation of ventilatory support with a loss in lung volume and in O$_2$Sat. The CSS effectively preserved lung volume and oxygenation by maintaining airway pressures during the suction manouvre. The increase in RR observed with the CSS was due to activation of the trigger mechanism.

P7 Balloon laryngoscopy reduces head extension and blade leverage in patients with potential cervical spine injury

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Crit Care 1999, **3 (suppl 1)**:P7

Background: In trauma patients, rigid cervical collar placement reduces head extension (HE) during laryngoscopy [1]. In patients with difficult airway, upper teeth or gums may be traumatized by excessive laryngoscope blade levering motion (LBLM) needed for laryngeal visualization [2]. The current study aims to compare, under stimulated spine precautions, HE and LBLM upon maximum glottic exposure (MGE) achieved with #4 conventional Macintosh blade (CMB) and #4 modified Macintosh blade (MMB) carrying two 10 Foley catheters (Fig. 1).

Methods: Anaesthesia was induced in 17 male, ASA I, Mallampati I, elective surgery patients. Spine precautions included rigid board placement under the shoulders and occiput and a rigid collar placement round the neck. Laryngoscopy was performed twice, changing between MMB and CMB. Before each laryngoscopy, the patients head was placed in the neutral position. MMB laryngoscopy technique consisted of MMB tip insertion into vallecula, right catheter balloon inflation with 2 ml air and MMB elevation until MGE achievement. The angles of laryngoscope handle axis (Fig. 2 AH) and of maxillary molars occlusal surface axis (OS) relative to horizontal (angles $\hat{a}_1$ and $\hat{a}_2$ in Fig. 2) were recorded upon MGE. Angles $\hat{a}_1$ and $\hat{a}_2$ were measured with an automatic angle finder (Fig. 1). The difference of 90°–$\hat{a}_2$ was defined as HE angle and the difference $\hat{a}_1$–$\hat{a}_2$ was defined as LBLM angle (angle $\hat{a}_3$ in Fig. 2), He and LBLM angles were compared with paired t test; $P < 0.05$ was considered statistically significant.

Results: MMB laryngoscopy resulted in significantly less HE and LBLM than CMB laryngoscopy ($P < 0.001$). Results and summarized statistics are presented in the Table. Values are shown as

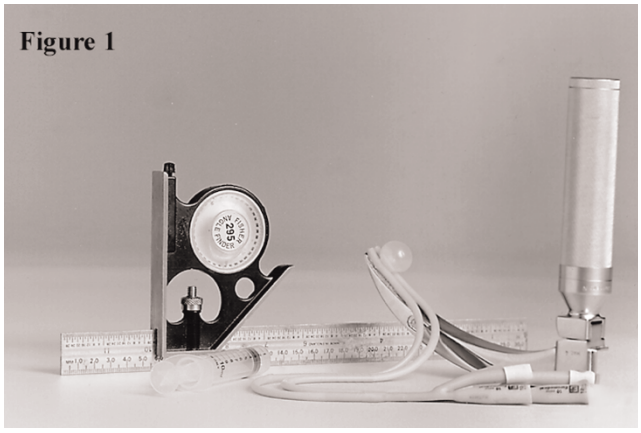

Figure 1. Modified Macintosh Blade with right catheter balloon inflated with 2 ml air and automatic angle finder.

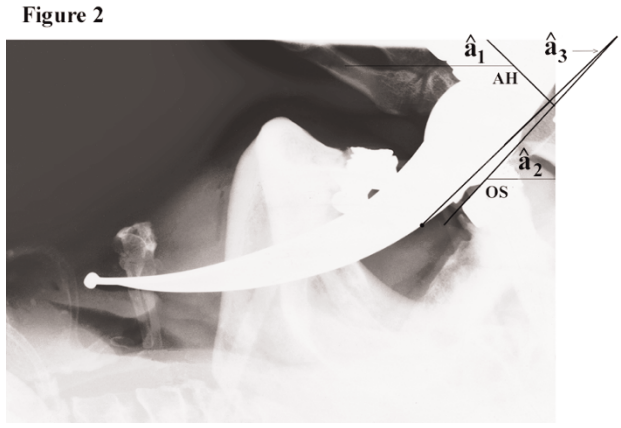

Figure 2. Lateral neck radiograph during direct laryngoscopy. AH, axis of handle; OS, axis of maxillary molars' occlusal surface; â1, angle between AH and horizontal plane; â2, angle between occlusal surface and horizontal plane, â3, angle of laryngoscope blade levering motion.

	Conventional Macintosh blade	Modified Macintosh blade	*P* value
Angle of head extension	8.29 ± 1.57	4.91 ± 1.42	<0.001
Angle of Laryngoscope-Blade-Levering-Motion	10.76 ± 1.75	5.53 ± 2.13	<0.001

means ± SD, Cormack-Lehane grade of laryngoscopic view was ≤II during all laryngoscopies.

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P8 Laboratory study of new technique using a one-pass dilator for percutaneous dilatational tracheostomy

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Crit Care 1999, **3 (suppl 1)**:P8

Background and objectives: Percutaneous dilatational tracheostomy requires the use of several dilators of increasing size. It would be a marked advantage to use only one dilator to achieve the desired 36 F. This report presents preliminary animal studies using freshly sacrificed dogs, adult pig tracheas fresh from the slaughterhouse and live piglets.

Methods: The usual technique for percutaneous dilatational tracheostomy was first followed to insert a guidewire into the trachea. A well-lubricated, one-pass, long, tapered dilator was threaded over the guidewire into the trachea. With twisting, it was inserted to the 36 F level. The one-pass dilator was removed leaving the guidewire in place and the chosen tracheostomy tube was passed over the guidewire into the trachea using the usual technique of percutaneous dilatational tracheostomy.

Results: A total of 50 dog cadavers and 25 slaughterhouse sheep tracheas were successfully tracheotomized using the one-pass dilator employing 7 and 8 mm I.D. tubes. Six live piglets were finally used successfully. No perforations or false passengers occurred.

Concusions: A one-pass technique was used successfully on fresh dog cadavers and should be evaluated on human beings.

P9 Percutaneous dilatational tracheostomy with a lightwand device

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Crit Care 1999, **3 (suppl 1)**:P9

Percutaneous dilatational tracheostomy (PDT) is a new technique which shares the same indications as surgical tracheostomy. We describe our experience with the PDT in combination with tracheal transillumination.

Patient population: Elective PDT was performed in 55 critically ill patients, mean age 54.5 ± 16 (22–72), intubation time 6.5 ± 3.2 (3–14) days.

Technique: The procedure was undertaken on the bedside using the Griggs-Portex PDT set as has been already described [1]. Before cannulation of the trachea the trachlight device (trachlight,

Leardal Medical) was inserted into the endotracheal tube with the tip at the end of the tube. By pulling back the endotracheal tube with the trach-light we examined the anatomy of the trachea and the location of the first and second tracheal rings. Besides the proper position of the end of the tube above the first tracheal ring was achieved. Afterwards we continued with the PDT technique. At the end the exact tracheotomy site and the correct placement of the tracheostomy tube was evaluated by endoscopy.

Results: The procedure lasted from 7 to 21 min (m.v. 9.5 min). The maneuver with the trachlight device lasted between 40–80 s Perioperative complications are listed below:

1) Hemorrhage minor: 2 patients
   Hemorrhage major: 0 patients
2) Premature extubation of the translaryngeal tube: 0 patients
3) Puncture of the endotracheal tube/cuff: 0 patients
4) Paramedian puncture of the trachea: 0 patients
5) Hypoxemia: 0 patients

Conclusion: PDT is a simple bedside procedure with a low complication rate. The combination with the trachlight device gives the opportunity for better identification of the anatomy of the trachea as well as the correct placement of the endotracheal tube above the first endotracheal ring. These contribute to better conditions for safe and accurate tracheal puncture and cannulation.

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P10 Percutaneous dilatational tracheostomy (PDT): a report on 103 consecutive cases of the translaryngeal tracheostomy (TLT) technique

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Introduction: We describe our experience with the TLT technique, which is a purely dilatational PDT with low inherent risks. The technique has the additional benefit of maintained ventilation and airway protection.

Technique: The TLT consists of a reinforced tracheostomy tube, with an integral dilator, which is pulled out between tracheal rings following retrograde insertion through the larynx [2]. A cuffed oral 5mm-tracheal tube inserted past the proposed stoma site maintains ventilation and airway protection. We prospectively collected data in 103 consecutive patients, 56 males and 47 females, undergoing this technique. The authors (JWF & AK) performed tracheostomies on all patients (16 to 88 years old). Pre-existent coagulopathy was not corrected. Indications for tracheostomy were mainly for term ventilation (39) and weaning difficulties (44).

Results: 102 tracheostomies were performed successfully. One was converted to a Ciaglia technique after accidental decannulation. Mean duration of operative procedure was 13.9 min. The INR ranged from 0.8–2.6, (mean 1.3), platelets ranged from 23–667 $\times 10^9$ (mean 184×10^9). There were six transient episodes of hypoxia (SpO_2<90%), three cases of hypotension, two related to the anaesthetic technique and one following traumatic intubation. There were four episodes of accidental decannulation and one case of minor subcutaneous emphysema. There was one case of moderate blood loss (100–250 ml). There was one episode of loss of airway, in a patient who was difficult to intubate (Gr. III). We had two cases of wound infection associated with pre-existent systemic bacteremia. Total duration of the tracheostomy ranged from 1–65 days. Total closure of the stoma took a mean of 4 days (range 2–9 days). The resultant scar was minimal.

Conclusion: This pure dilatational and bronchoscopically visualised method is easy to perform with training. It is worthy of consideration in patients with coagulation abnormalities. We feel it offers better control over the airway than other available techniques although there is a definite risk of decannulation while withdrawing the cannula over the obturator. The overall morbidity of this technique is low.

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P11 Independent lung ventilation using a double-lumen endobronchial tube by nasotracheal intubation

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Crit Care 1999, **3 (suppl 1)**:P11

Independent lung ventilation (ILV) is effective for the patient who is suffering from unilateral lung disease. When we ventilate the patients with ILV, they should be intubated with a double-lumen endobronchial tube. While ILV is continued for some time a number of difficulties related to the management of the double-lumen endobronchial tube (DLT) arise. Movements of the patient and routine turning of the patient threaten the DLT position and can lead to loss of lung isolation or lobe occlusion. Nasal intubation is better suited for long-term intubation than oral intubation because it is safer for equipment attachment. We have ventilated six patients (Table) with ILV using the DT by nasotracheal

Case	Age and sex	Diagnosis	Height (cm)	WB (kg)	DLT size	Durat. (h)
1	49 M	Post upper lobectomy	155.5	44	5.5	65
2	88 F	Aspiration pneumonia	145	35	5.5	120
3	59 F	Lung trauma	143	60	5.5	94
4	71 M	Aspiration pneumonia	153	59.8	6.0	100
5	85 F	Atelectasis	150	50	5.5	50
6	75 M	Atelectasis, DIC	157.8	42	6.0	25

Durat., duration.

intubation for 25 to 120 h. We intubated Portex #5.5 DT for all cases. There was no case in which DLT was required to correct its position during ILV. Although we examined the condition inside the nose, there was no severe damage by the DLT. We concluded that nasotracheal DLT intubation was done safely and could be used for ILV up to 7 days.

P12 The effect of dexamethasone on the incidence of post extubation stridor in pediatric patients

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Crit Care 1999, **3 (suppl 1)**:P12

Post extubation stridor is due to reactive subglottic laryngeal edema at the cricoid ring. Dexamethasone has been used to reduce the incidence of stridor in such patients. The evidence in the literature however is not conclusive. We conducted a prospective, randomized, double blind study of dexamethasone versus placebo to assess the efficacy of dexamethasone in reducing the incidence of post extubation stridor in children. Fifty-one patients without any known preexisting upper airway problems were studied. There were 27 patients in the treatment group and 24 in the placebo group. Both groups had similar weight, age and length of intubation. Dexamethasone was given at a dose of 0.6 mg/kg at 12 h and 1 h prior to extubation for a total of 2 doses. The control group received placebo at corresponding times.

There was no statistical difference in the incidence of post extubation stridor in the two groups. Ten of 24 children in the placebo group (41.7%) and 8 of 27 (30%) in the dexamethasone group developed stridor ($P = 0.39$). There were 3 patients in placebo group and 1 in dexamethasone group that needed reintubation, but again the difference was not statistically significant ($P = 0.33$).

This study, although with relatively small sample size, suggests that routine use of dexamethasone to prevent post extubation stridor, in children without any known upper airway abnormality, is not warranted.

P13 Evaluating the effect of steroids on the incidence of reintubation rates in children with laryngotracheobronchitis

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Crit Care 1999, **3 (suppl 1)**:P13

Introduction: Postextubation stridor is a serious problem in children with an incidence of up to 33% in electively intubated children. Our aim was to determine whether steroids decreased reintubation rates and to identify other risk factors for reintubation.

Methods: Retrospective analysis (1994–1996) of the 82 children (72 received steroids). Steroids were categorized according to the type used and the time of administration. Recognized risk factors for postextubation stridor including age (<1 and >1 year) and duration of intubation (<120 and >120 h) were analyzed.

Results: There was no significant difference in either the preintubation grade or stridor ($P = 0.67$) in both outcome groups (reintubated 22/23 grade 3 and not-reintubated 50/59 grade 3) or in the postextubation grade of stridor between both groups ($P = 0.1$). Neither type of steroid ($P = 0.32$), nor time administered ($P = 0.79$), nor age ($P = 0.22$) nor duration of intubation ($P = 0.35$) was found to significantly influence reintubation rates.

Variable	Not reintubated ($n = 59$)	Reintubated ($n = 23$)	P value
Age (months)	19.3	12.6	0.28
Weight (kg)	9.75	8.6	0.28
Intubation (2 days)	7.6	11.1	0.04 (S)
PaO_2/FiO_2	232	269	0.02 (S)
ICU stay (days)	9.6	13.3	0.05 (S)
Steroids	*52/59*	*20/23*	*0.88*
Atelectasis	10/59	9/23	0.03 (S)
Infections	23/59	10/23	0.2
Pneumonia	29/59	9/23	0.4

Conclusion: The prophylactic use of corticosteroids in routine elective extubations for laryngotracheobronchitis cannot be recommended, based on current findings. Overall, 28% of all patients needed to be reintubated. However, reintubation seems to be correlated best with atelectasis rather than the degree of postextubation stridor.

P14 Advantages of a new humidification technique

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Crit Care 1999, **3 (suppl 1)**:P14

Recently, an active HME (AHME) (Humid-Heat, Gibeck) has been developed. The AHME combines a HME with a unit which adds humidity and heat to the patient-side of the HME. The supply of humidity and heat is automatically regulated, in order to achieve 100% humidity of inspired gases at 37°C. The operation of AHME requires only the user-set input of the patient minute

ventilation. We evaluated the potential advantages of the AHME over a conventional active humidifier.

Methods: The study included seven mechanically ventilated patients. In each patient, the AHME was used for 24 h and then substituted with a conventional active humidifier (F&P) (MR730, Fisher & Paykel) with a heated wire in the inspiratory limb, for the next 24 h. AHME was preset to keep the temperature of inspired gases at 37°C. The F&P was set to 37°C in the humidifier-chamber, and to 37°C at the Y piece. The AHME and the F&P were compared in terms of: humidity and temperature output, water consumption and condensate in the water traps. The humidity output was evaluated on the basis of the condensate in the flex tube, which was scored from 0 (absent) to 3 (excessive).

Results: Minute ventilation did not differ during application of AHME and of F&P. Both devices kept the set temperatures, and provided adequate humidification, as assessed by the condensate in the flex tube. However, when the F&P was used, there was formation of condensate in the ventilator tubings, and the water traps needed to be emptied on average eight times (range: 6–9) per day.

	AHME	F&P	*P*
Minute ventilation (l/min)	11.1 ± 3.5	11.5 ± 2.4	0.64
Insp. gases temperature (°C)	36.9 ± 0.5	37.1 ± 0.2	0.33
Condensation in the flex tube (score)	2 ± 0	1.9 ± 0.1	0.42
No. of water traps emptying	0	8 ± 2	–
Quantity of H_2O in the water traps	0	100 ± 17	–
H_2O consumption (ml)	117 ± 29	667 ± 76	0.008

means ± SD; Student *t* test.

No condensation of water was found in the ventilator tubings with AHME. Compared with F&P, the AHME remarkably reduced the water usage.

Conclusion: Compared to a conventional active humidifier, the AHME provides equivalent humidification, with the advantages of both reducing the time-expenditure for handling, and of eliminating the risk caused by water condensation in the ventilator tubings.

P15 Heat and moisture exchanger PALLBB22-15F can prevent ventilator-associated pneumonia (VAP) in short term mechanically ventilated ICU patients

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Introduction: VAP is a serious infection with a mortality rate exceeding 50%. It also leads to an increase in the duration of the treatment and adds to hospital costs. Bacteria, in intubated patients, may be directly inoculated into the endotracheal tube from the hands of medical personnel or from contaminated respiratory therapy equipment (i.e. humidifiers). We tried a heat and moisture exchanger to substitute the conventional ventilator humidifiers to prevent VAP in the ICU setting.

Methods: Subjects were intubated and attached to the conventional respiratory assistance cascades in the first year of the study (July 1992–June 1993). Retrospectively, cases of VAP were calculated prospectively, during the following year (July 1993–June 1994), subjects were intubated and attached to respiratory assistance cascades; but PALL filter, a heat and moisture exchanger, was in-line and the machine humidifiers were bypassed. The cases of VAP were calculated.

Study population: Intubated ICU patients with normal CXR on admission to the unit.

Results: VAP rates decreased in the group of HMEF dramatically in comparison to the conventional humidification method (see Table below).

Humidification method	Cascade	PALLBB22-15F
Total patients in group	174	284
VAP rate, incubated 1 day	5.50%	0%
VAP rate, intubated 2–4 days	24.30%	8%
VAP rate, intubated > 5 days	46.60%	26%
VAP rate, total	28.20%	12.70%

Conclusion: We concluded that heat and moisture exchanger filters can prevent VAP in short term mechanically ventilated ICU patients, and can halve its rate in long term durations.

P16 A clinical evaluation of a new humidifier in long-term mechanical ventilation

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The adequacy of humidification of heat and moisture exchangers (HMEs) during long-term mechanical ventilation is still controversial. Recently, an active HME (AHME) (Humid-Heat, Gibeck) has been developed. This AHME combines a HME with a unit which adds water and heat between the patient and the HME. The AHME automatically regulates the water and heat supply. The only user-set input for AHME is the minute ventilation (V'e) of the patient. We evaluated the AHME efficiency for humidification during long-term mechanical ventilation.

Methods: The AHME was used for 5 days on seven patients which were mechanically ventilated in different modes. On each

day we measured the number of tracheal aspirations, the secretions characteristics, the condensate in the flex tube and in the water traps, the airway temperature, the number of changes of the V'e setting on AHME. A chest X-ray and a bronchoscopy were performed on days 1, 3 and 5. We scored the secretions characteristics and the condensate in the flex tube from 0 (insufficient) to 3 (excessive), the atelectasis at chest X-ray from 0 (absent) to 2 (evident), and the bronchial occlusions at bronchoscopy from 1 (absent) to 4 (complete).

Results and conclusion: AHME provided adequate humidification over the 5 days, as indicated by the secretions characteristics and by the absence of new atelectasis and of secretions accumulation in the bronchi. The temperature of inspired air was adequate. The value of V'e set on the AHME was changed on average twice (range: 0–8 times) per day, to maintain this setting close to the V'e of the patient. No water condensate was found in the water traps. The AHME is adequate for humidification in long-term mechanical ventilation, and eliminates the problem of condensation in the ventilator tubings. The humidification efficiency of AHME is not influenced by the mechanical ventilation mode, provided that the V'e setting of AHME is kept close to the V'e of the patient.

	Day 1	Day 2	Day 3	Day 4	Day 5	*P*
No. aspirations	12 ± 2	12 ± 1	12 ± 1	12 ± 2	13 ± 1	0.76
Quantity of secretions (score)	1.6 ± 0.4	1.4 ± 0.3	1.7 ± 0.5	1.4 ± 0.2	1.8 ± 0.5	0.34
Viscosity of secretions (score)	1.1 ± 0.1	1.2 ± 0.2	1.2 ± 0.3	1.1 ± 0.1	1 ± 0.1	0.17
Condensation in the flex tube (score)	1.9 ± 2	2 ± 0	2 ± 0.1	1.9 ± 0.2	2 ± 0	0.69
Bronchial obstruction (score)	2 ± 1.2	–	1.7 ± 0.8	–	1.7 ± 1	0.49
RX atelectasis (score)	0.3 ± 0.5	–	0.3 ± 0.5	–	0.3 ± 0.5	1
Insp. gases temperature (°C)	37 ± 0.4	36.9 ± 0.8	36.8 ± 0.5	37.2 ± 0.4	36.9 ± 0.5	0.67
Nr. of changes of V'e set on AHME	0.9 ± 1.2	2 ± 1.9	1.9 ± 1.3	1.9 ± 2.3	1.3 ± 1.6	0.66

means ± SD. ANOVA.

P17 Comparison of conventional heated humidification to a new active heat and moisture exchanger in the ICU

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Crit Care 1999, **3 (suppl 1)**:P17

Background: Heated humidification (HH) is commonly used with or without a heated wire circuit (HWC) to humidify inspired gases during mechanical ventilation (MV). We compared HH and HH with a HWC to a new active heat and moisture exchanger (AHME). The AHME (Humid Heat, Gibeck, Sweden) consists of a typical HME and a heat and water source delivered between the patient and the HME. The volume of water delivered and heat output are based on a set minute ventilation. A pre-set airway temperature of 37°C is used.

Methods: Thirty patients requiring MV for >72 h were studied. Pts received humidification via a HH, HH + HWC (Fisher & Paykel), and AHME in random sequence for 24 h each. All devices were set to deliver 37°C at the proximal airway. During each period of ventilation, the following were measured; airway temperature, min and max body temperature, number of suctioning attempts, volume of secretions, consistency of secretions, number and volume of saline instilled, water usage, condensate, ventilator settings, minute volume, number of circuit disconnections. Water usage was measured by weighing the water bag before and after 24 h use. Consistency of secretions were judged as thin, moderate, or thick as previously described (Suzukawa: *Respir Care* 1989, **34**:976). Condensate was measured by emptying fluid into a graduated container and sputum volume measured by collecting secretions in a Luken's trap. Airway temperature was measured at the ET tube using a rapid response thermistor. Resistance of the AHME was measured before and after use.

Results: There were no differences in any of the variables related to humidification efficiency (secretion volume and consistency, number of suctioning attempts, or volume of saline used). Water usage and volume of condensate were significantly different between devices, but delivered airway temperatures were not. Statistical analysis was done with ANOVA. **P* < 0.05, see Table.

Device	Water Usage (ml)	Condensate (ml)	Airway Temp. (°C)
HH	2039 ± 387	930 ± 271	36.3 ± 1.2
HH + HWC	766 ± 281	12 ± 16*	37.1 ± 1.0
AHME	135 ± 53	1 ± 3*	36.4 ± 1.7

Minute volume was similar between groups (11.6 ± 3.3 vs 11.9 ± 3.4 vs 11.8 ± 2.7 l/min) as was bias flow during flow triggering (5.8 ± 2.5 vs 5.4 ± 2.6 vs 5.9 ± 2.3). AHME resistance before and after use was unchanged (1.66 ± 0.11 vs 2.28 ± 0.82 cm H_2O/l/s).

Conclusion: In this early study, the AHME provided equivalent humidification as HH and HH + HWC with a lower water usage. This occurs because the HME portion of the AHME returns ~32 mgH_2O/l, which only requires the active portion to add ~12 mgH_2O/l to reach 44 mgH_2O/l. Additionally, by placing the AHME between the patient and ventilator circuit, continuous flow from flow triggering systems is not humidified. No other differences were noted. Disadvantages of the AHME include

deadspace (~70 ml), weight on the ET tube and the heat source near the patient. Measured external temperature of the AHME did not exceed 38°C. Further long term studies are required to define the role of the AHME.

P18 A new device for 100% humidification of inspired air

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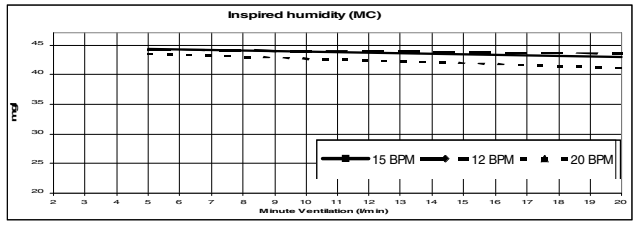
Crit Care 1999, **3 (suppl 1)**:P18

Introduction. Passive heat/moisture ex-changers (HME) which are based on a hygroscopic condensor principle usually provide adequate humidity (up to 32 mgH_2O/l air) of the inspired gas during ventilator treatment [1,2]. However, in about 5–10% of the patients with e.g. thick secretions [1,2] active humidifiers that can provide 100% humidity are needed. These devices cause free water condensation in the tubings [3] with risks of contamination and of compromising the ventilator function. To avoid this a new humidifier has been developed. It consists of a supply unit with a microprocessor and a water pump, and a humidification device, which is placed between the Y-piece and the endotracheal tube. The humidification device is based on a hygroscopic HME, which absorbs the expired heat and moisture and releases it to the inspired gas. External heat and water are then added to the patient side of the HME, so the inspired gas reaches 100% humidity at 37°C (44 mgH_2O/l air). The external water is delivered via a pump onto a porous membrane and then evaporated in the inspired air by an electrical heater. The microprocessor controls the water pump and the heater by an algorithm using the minute ventilation (which is fed into the microprocessor) and the airway temperature measured by a sensor mounted in the flex tube on the patient side of the humidification device.

The aim of this study was to test the performance of this humidifier at different ventilator settings in a lung model.

Methods: The lung model is based on the ISO 9360 International Standard with the exception of that the water-bath temperature is regulated to have a constant temperature of 35.5 ± 0.5°C. The model was ventilated with a Siemens 900 B ventilator set a minute ventilation from 5 to 25 l/min, I:E 1:2, and a rate of 12, 15 or 20/min during 90 min. The moisture content (MC) in the inspired air was calculated from the water delivered (WD) and the loss of water from the lung model (WL): MC = WL– WT + (WD–WH), where WT is the water in the tubing between the device and the lung model and WH the water trapped in the HME. WL, WT, WD, and WH were found by weighing before and after the experiment. During the experiment no condensation was found in the flex tube between the device and the lung model.

Results:



Conclusion: In a lung model, ventilated with 5–25 l/min, the new humidifier gave an absolute humidity of 39–45 g/l, with the lower level at the highest ventilation. Thus, the device had the intended performance characteristics.

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P19 Modelling the effect of ambient oxygen fraction on hypoxaemia during apnoea

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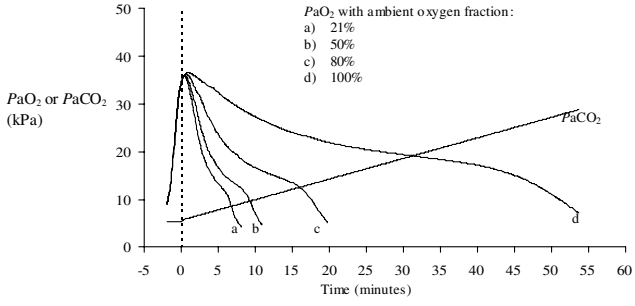
Hypoxaemia during apnoeic oxygenation complicates tests for brainstem death and exposes the patient's organs to the risk of anoxic damage. This study investigates the effect on hypoxaemia of varying the ambient oxygen fraction during apnoea.

Methods and results: The Nottingham Physiology Simulator is a validated simulation of advanced, iterative physiological models [1]. The model was set up as a 70 kg adult with normal physiological values other than: pulmonary venous admixture 20%, alveolar deadspace fraction 20% of tidal volume and functional residual capacity 2 l. The patient's lungs were ventilated with 100%



oxygen for 2 min and the patient was then apnoeic with an open airway exposed to 21, 50, 80 or 100% oxygen. Arterial oxygen and carbon dioxide tensions (PaO_2, $PaCO_2$) were recorded continuously until arterial oxygen saturation fell to 50%. The changes in PaO_2 and $PaCO_2$ are shown in the figure on the previous page.

Discussion: Provision of very high ambient oxygen fractions greatly extends the safe duration of apnoea. As oxygen fraction is increased, increasingly large effects are achieved.

Reference

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P20 Obstructive sleep apnea in acute respiratory failure

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Study objectives: Emergency medicine deals with the diagnosis and the prevention of potentially life-threatening events, as well as prevention, diagnosis and treatment of acute illnesses; one of this event is sleep apnea syndrome (SAS). The relationship between obstructive sleep apnea (OSA) and acute respiratory failure (ARF) is not well established.

The aim of the study was to evaluate the prevalence of OSA in hypercapnic ARF patients and its correlations with the severity and length of nocturnal arterial oxygen desaturation, diurnal arterial carbon dioxide ($PaCO_2$) and oxygen (PaO_2) tensions, diurnal oxygen saturation, sudden death and BMI.

Methods: 46 patients with chronic obstructive pulmonary disorder (COPD) (31 men and 15 women; M=68 years; range 36 to 83) with hypercapnic ARF underwent a full night of polysomnography.

The polysomnography consisted of continuous polygraphic recording (by Compumedic Sleep PTYLTD Abbotsford) from surface leads for electroencephalography, electrooculography, electromyography and ECG, and from noninvasive sensor for nasal airflow, tracheal sounds, body position, thoracic and abdominal respiratory efforts, and oxymyoglobin level. The number and duration of nocturnal sleep apneas and hypopneas and the consequential oxygen desaturation were evaluated; sleep apnea was defined as more than five episodes of apnea or hypopnea per hour of sleep (apnea/hypopnea index = AHI >5). Furthermore BMI, basal diurnal $PaCO_2$, PaO_2 and arterial oxygen saturation were also recorded.

Results: Overnight polysomnography was successfully performed in 39 of the 46 studied patients; 4 patients were intolerant to the study and 3 patients were awake all the sleep time. OSA was found in 13 of the 39 ARF patients (33.3%) and the mean AHI was 19.3 events per hour. We found statistically significant correlations between OSA and BMI ($P < 0.01$; M=38), PaO_2 ($P < 0.001$; M=65), diurnal oxygen saturation ($P < 0.001$; M=86) and nocturnal oxygen desaturation ($P < 0.001$; M=80).

Conclusion: The overnight polysomnography detects the possible existence of OSA in hypercapnic ARF. We also found a statistical significance positive correlation between OSA and hypoxemia. Polysomnography may be indicated to exclude sleep-induced desaturation contributing to the actual ARF, but it may also improve therapeutic and prevention strategy.

P21 Nasal continuous positive airway pressure: do mask pressures reliably reflect intratracheal pressures?

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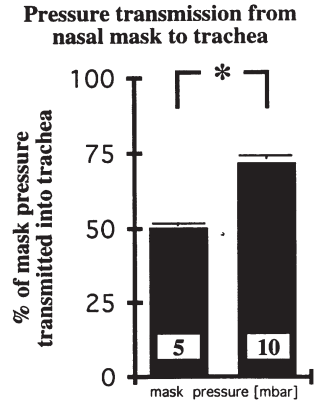
Introduction: Nasal continuous positive airway pressure (nCPAP) increases intrathoracic pressure. This way, it may increase functional residual capacity, improve pulmonary oxygen transfer, and reduce the need for endotracheal intubation in acute respiratory or cardiac failure. However, little is known about the loss of externally applied pressure on its way from mask via pharynx into the trachea. We studied the correlation between mask and intratracheal pressures in 8 surgical ICU-patients.

Patients and methods: In 8 postoperative patients after extubation, pressures were measured in nasal mask and trachea (via a catheter, o.d. 0.9 mm) during nCPAP treatment with either 5 or 10 mbar positive pressure (high-flow gas source, 65 l/min, mask-pressure adjusted with a PEEP-valve). From the area under the pressure–time curves, absolute pressures, but also the percentage of mask pressure transmitted into the trachea were calculated. Study performed with approval of the committee of medical ethics and informed consent; mean ± SD; *t*-test, $P < 0.05$.

Results: With the PEEP valve set at 5 or 10 mbar, pressures within the nasal mask were 5.6 ± 0.8 and 9.4 ± 1.0 mbar, respectively. Mean intratracheal pressures increased in all patients and were significantly higher during 10 mbar mask pressure compared to 5 mbar (6.8 ± 0.3 vs. 2.9 ± 0.5 mbar; $P < 0.007$). The relative amount of mask pressure transmitted into the trachea was significantly higher with 10 compared to 5 mbar ($P < 0.04$) (Figure). With 5 mbar of nCPAP, in 50% of the subjects, significant negative pressure swings occured during inspiration. This was not the case with 10 mbar.



Conclusion: NCPAP is an effective noninvasive means to increase airway pressure in postoperative patients after extubation. However, only with mask pressures of 9–10 mbar, but not with 5 mbar, intratracheal pressures will be maintained reliably and continuously positive during the whole respiratory cycle.

P22 Effects of mask–ventilator interface elements in a home noninvasive portable ventilator. Study in cold hypercapnic patients

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Noninvasive mechanical ventilation (NIMV) in hypercapnic COLD excacerbations with a home portable ventilator with a single ventilatory tube has some technical considerations.

Objective: We analyze influence of elements used in the mask-ventilator interface in hypercapnic COLD with a NMV: To compare differents 1). Design of filters (A, B, C, D), 2) Non-rebreathing expiratory valve: a) Swisper and b) Plateau exhalation valve 3) Rramp inspiratory time: (0.05, 0.1, 0.5 seg) affect a predetermined level inspiratory positive pressure (IPAP) (15 cmH_2O), 2) Hypercapnia (PCO_2) control and 3) Subjective responses: a) Dysnea Brog index (low: 2 to 10 high) and psychological dependence at different stages of therapy (low 2 to high 10).

Setting: ICU.

Subjects: Twelve hypercapnic COLD stable patients.

Material: BiPAP ST-D (Resp, Inc). Facial mask.

Results: See Table.

IPAP drops pressure from base line/type of filter	**A**	**B**	**C**	**D**
IPAP: 15 cmH_2O	12 ± 3	12 ± 5	10 ± 2	8 ± 2
PCO_2/pH – type of nonrebreathing valve	**Valve Swisper**		**Plateau exhalation**	
PCO_2 mmHg/pH	80/Ph: 7.23		70/pH: 7.35	
Dysnea Borg index/ramp inspiratory time	**0.05 seg**	**0.1 seg**	**0.5 seg**	
Dysnea Borg index	2	4	10	
Psychological score dependence/period	Acute	Post-acute	Weaning phase	
Ventilator	8	6	6	
Nurse	10	8	8	
Physicians	8	8	8	

Conclusion: Subjective (dysnea Brog index), objective respiratory response (hypercapnia) and level of IPAP pressure applied during NMV were influenced by a specific design of element intercalates at mask–tube–ventilator line. A specific design of these elements as we showed with a home portable single tube ventilator could affect NMV efficacy in hypercapnic COLD exacerbations.

P23 Evaluation by volunteers of respirator characteristics in modes used in non-invasive ventilation

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Introduction: We studied the medical personnel's power of distinction between various types of respirators in CPAP and CPAP+pressure support (PS) modes.

Materials and methods: Five blindfolded volunteers (2 ICU doctors and 3 nurses) performed random evaluation (5 point scale, 1 = best) of following respirators: Elema Siemens 300 (ES300), Adult Star 2000 (AS 2000) and Bird 8400 STi. All volunteers were comfortably seated and instructed to breathe freely with the

Table 1. CPAP 5 cmH_2O

Resp	BIRD	Adult Star	E 300 flow trig	E 300 Press tr
Vol 1	2	1	1	1
Vol 2	2	2	1	2
Vol 3	4	3	2	2
Vol 4	3	1	1	1
Vol 5	2	1	2	2
Mean	2.6	1.6	1.4	1.6
SD	0.8	0.8	0.49	0.49

Table 2. CPAP 5 cm H_2O+PS 10 cmH_2O

Resp	BIRD	Adult Star	E 300 flow trig	E 300 press tr
Vol 1	2	2	2	2
Vol 2	4	3	1	3
Vol 3	2	3	3	4
Vol 4	4	3	3	3
Vol 5	2	3	1	3
Mean	2.8	2.8	2	3
SD	0.98	0.4	0.89	0.63

respirator through the mouthpiece with the nostrils clipped. Pressure trigger was set at –1 cmH_2O in all respirators and in ES 900 flow trigger was also tested. After 1 min warm-up, 1 min breathing test was performed at the end of which volunteers were asked to classify their satisfaction with respirator. At first, 5 cmH_2O CPAP was tested at random in all four settings (three respirators, in ES 300 for both pressure and flow triggering) and thereafter the evaluation continued similarly with CPAP 5 cmH_2O + 10 cmH_2O pressure support. Data are presented as means ± SD, Kruskal-Wallis test was used for statistical analysis, $P < 0.05$ was considered significant.

Results: Individual scores and mean values ± SD are listed in Tables 1 and 2.

When CPAP and CPAP+PS were tested together significant differences were found within the group ($P < 0.05$). Generally, CPAP was better tolerated than CPAP+PS. ES 300 and AS 2000 yielded better results than Bird respirator.

Conclusion: ICU personnel may easily differentiate between characteristics of ICU respirators. Respirator with best characteristics may then be used for NIV and possibly also for difficult weaning.

Acknowledgement: Supported by IGA grant No. 3999-3

P24 Noninvasive positive pressure ventilation (NPPV) in critically ill patients: preliminary experience

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Study objective: To validate the efficacy of NPPV in patients with hypercapnic or hypoxemic acute respiratory failure (ARF) admitted to a Medical Intensive Care Unit.

Materials and methods: Thirty-two patients (23M, 9F, mean age 66, range 25–91) received NPPV if they met the following criteria: severe dyspnea at rest, respiratory muscle fatigue, normal mentation, normal upper airways, stable hemodynamic status and, as for hypercapnic ARF, pH <7.35, $PaCO_2$ >45 mmHg, respiratory rate (RR) >25 bpm and, as for hypoxemic ARF, PaO_2/FiO_2 <200, RR >30 bpm. Eighteen patients (12M, 6F, mean age 68,4, range 50–91) had hypercapnic ARF due to chronic obstructive lung disease (COLD); 7 (6M, 1F, mean age 75, range 73–84) had cardiogenic hypercapnic acute pulmonary edema (cAPE); 7 (5M, 2F, mean age 50, range 25–72) had severe pneumonia (SP), 2 with hypercanic ARF. End-points were the following: pH >7.35, RR <24 bpm, V_T >7 ml/kg, reduced dyspnea, diminished signs of muscle fatigue, SpO_2 >90%. NPPV was considered successful if the patient was not intubated and mechanically ventilated. NPPV was considered unsuccessful if the patient was intubated and mechanically ventilated, became intolerant of mask or died. BiPAP Respironics® ventilators (S/T-D 20, S/T-D 30, Vision), were used to administer NPPV, as pressure support ventilation, by nasal or facial masks. All patients were given standard medical therapy, as required by the underlying disease.

Results: NPPV was successful in 14 of 18 COPD patients (77.7%), in all 7 patients with cAPE (100%) and in 3 of 7 patients with SP (42.8%). Failure in 4 COLD patients was due to mask intolerance in three cases and to sudden death in one case. Four patients with SP (three seriously immunocompromised) died. COLD patients were ventilated for 3 to 62 h (mean 21.5 h), cAPE patients for 4 to 15 h (mean 7.4 h) and SP patients for 12 to 148 h (mean 59.7 h). Ventilation was longer in SP patients who obtained a therapeutic benefit (mean 112 h) than in SP patients who did not (mean 23 h).

Conclusion: With the limits of this observational study, we conclude that NPPV has been shown to be an effective support therapy for COLD patients with acute exacerbation and for hypercapnic severe cAPE patients. The use of NPPV in patients with SP was less effective and warrants ulterior study to be validated, according to literature.

P25 Noninvasive mechanical ventilation in asthma crisis: an alternative ventilatory therapy to endotracheal intubation

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Crit Care 1999, **3 (suppl 1)**:P25

Oxygen therapy by mask venturi (OMV) in asthma crisis (AC) could not be avoided,, and urgent endotracheal intubation (ETI) is the lifesave procedure recommended. Sometimes in a selected population noninvasive ventilation (NMV) may avoid ETI and his deleterious effects (barotrauma, infections, etc).

Objective: We describe our first experience in treatment of acute respiratory insufficiency in (AC). Period of study 1995-98.

Setting: Polyvalent ICU.

Subjects: MV group $n = 5$, ETI group $n = 12$, and NMV $n = 8$.

Material: Ventilators: Dragger Evita 2, and BiPAP ST-D (Resp, Inc).

Method: Inclusion criteria: Borg dysnea score: 5 ; respiratory rate: >30 rpm, PaO_2 <60 mm Hg (FIO_2 0.5%). ETI: apnoea or unstable breathing pattern, or severe dysnea. Continuous cardiorespiratory monitoring.

Results: Time of NMV: 5 ± 3 h levels of IPAP: 12 ± 3 EPAP 6 ± 3 cmH_2O; Global respiratory rate: 38 ± 10; pH: 7.36 ± 0.02; pCO_2: 45 ± 7 mmHg paO_2: 49 ± 26 mmHg. NMV intolerance (12.5%). Complications: NMV group: skin nose lesion $n = 3$; ETI group: neumothorax $n = 2$.

Groups	*n*	Success	UCI stays	Complications	Mortality
Non-invasive	8	50%	4 ± 2	Skin lesion	0
Endotracheal intubation	12	30%	12 ± 6	Neumothorax *n* = 2	20%
Venturi mask	5	70%	7 ± 3	0	0

Conclusion: NMV in asthma crisis refractory to (OMV) is a safe alternative to ETI, and could be avoided in selected patients (50%). Borg Dysnea score index and respiratory rate at 3 h: 38 ± 6 to 25 ± 6 rpm in NMV group are the best early clinical predictors.

P26 Noninvasive positive-pressure ventilation in acute respiratory distress syndrome: preliminary results

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The NIV in acute respiratory failure of a previously healthy lung is not much widespread but much discussed. We report the first data about four patients, who have been accepted in our ICU due to acute respiratory failure post-trauma and treated with ventilatory support via face mask like NIV. All patients were negative to pre-existing lung disease and got thoracic trauma with multiple costal fractures and bony fractures. We used the mechanical ventilator Adult Star (Infrasonic, Inc., San Diego USA). All the patients were co-operating and without neurological deficiency. The NIV has been applied for 2 days and alternated with spontaneous ventilation through Venturi mask after 24 h.

Results: the analyzed data show an improvement of PaO_2 in all patients, already after the first hours of treatment as well as a respiratory rate reduction.

Discussion: The NIV has to be considered as a conventional ventilation's kind also by acute hypoxemic respiratory failure. The admission's criteria of the patients to this kind of ventilation is however important. In conclusion, we can affirm that the NIV has an important advantage compared to the conventional ventilation, that is a shorter stays in the intensive care unit, associated to a reduction of pneumonia related to endotracheal intubation.

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	Basal	1 h	2 h	3 h	6 h	12 h	18 h	24 h	36 h
PaO_2	57.6 ± 11.1	126.9 ± 14.4[a]	121.7 ± 17.9[a]	121.7 ± 17.9[a]	125.4 ± 3.9[a]	125.4 ± 3.9[a]	130.7 ± 29.9[a]	116.2 ± 7.2[a]	114.7 ± 12.3[a]
$PaCO_2$	40 ± 15.7	34.3 ± 3.4	34.7 ± 3.8	34.2 ± 3.3	35.2 ± 2.8	35.4 ± 2.6	35.6 ± 2	36.2 ± 1.3	36.3 ± 1.6
RR	33.7 ± 2.5	23 ± 3.6[a]	20.5 ± 1[a]	21 ± 1.1[a]	19 ± 1.1[a]	19 ± 1.1[a]	17.7 ± 0.8[a,b]	19.5 ± 1[a]	17.7 ± 2[a,b]
PS	/	15	15	15	12	12	12	12	12
PEEP	/	5	5	5	5	5	5	5	5
FiO_2	0.5	0.4	0.4	0.4	0.3.5	0.35	0.35	0.35	0.35
Trigger	/	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
SAPS II	6 ± 2	/	/	/	/	/	/	/	/

ANOVA One Way rep. $P < 0.001$. Tukey: [a]significantly diff. vs. basal; [b]vs. 1 h.

P27 Noninvasive mechanical ventilation (NIMV) in weaning failure: could be an alternative approach?

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A trial with noninvasive ventilation (NIMV) could be a safe alternative option in some selected unweanneable patient, after a period of invasive approach of weaning with: 1) Endotracheal tube (ET) or 2) Traqueostomizated with a 'T' oxygen or Pressure Support Ventilation (PSV) trials.

Setting: Polyvalent ICU.

Subjects: We show a cases series where NIMV have been applied as an alternative weaning technique in three difference clinical situations of unweanneability: 1) Post-extubation failure $n = 12$, 2) Decanulation in traqueostomizated $n = 1$, and 3) Elective extubation $n = 3$.

Material: NIMV with BiPAP ST-D (Resp, Inc) ventilator, facial mask.

Methods: Inclusion criteria: acute respiratory insufficiency in a period (0–48 h): respiratory rate >30 rpm, increase accessory respiratory muscular activity, hypoxemia PaO_2 <60 mmHg at mask venturi (FIO_2: 0.5) after a period of 'T' piece or PSV and almost four consecutive weaning failure trials. Excluded: hemodynamic instability (SAT <90 mmHg), uncooperative patients, and excessive secretions., IPAP/EPAP cmH_2O to achieve: >10 ml/Kr and decrease in dysnea Borg score. Continuous cardiorespiratory monitoring.

Results: Unweanneable population $n = 16$. Average age: 61 ± 20, male $n = 12$; APACHE II score: 21 ± 3, time of NIMV: 72 ± 12 h.

Weaning		Success	Failure	Exclusion
Postextubation – NMV	$n=12$	8	3	1
Decanulation – NIMV	$n=1$	0	1	
Extubation – NIMV	$n=3$	1	1	1
UCI stay		4 ± 2	15 ± 5	
Mortality		2%	15 %	
Results	$n=16$	9	5	2

NIMV was effective in reduce dysnea Borg scores (4 to 2), gasometric alterations and avoid reintubation 8/12. Causes of exclusion: secretions 23%, hemodynamic instability 15%. Complications: skin lesion $n = 2$, gastric distension $n = 1$.

Conclusion: 1). A trial with a NMV as a weaning alternative technique is a safe alternative in selected patients with showed a persistent weaning failure. 2). Reduction in ICU stay, mortality, with a great comfort and few complications compare to others method.

P28 Airway pressure release ventilation (APRV) enhances cardiac performance in patients with acute lung injury (ALI)/adult respiratory distress syndrome (ARDS)

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Purpose: To determine whether APRV can safely enhance hemodynamics in patients with ALI/ARDS.

Methods: Patients with ALI/ARDS were ventilated in pressure control (PCV) with both upper and lower inflection points eliminated from the hysteresis curve; all patients had a pulmonary artery catheter. Ventilator settings achieved a pCO_2 of 35–45 torr and a pO_2 of >60 torr. Patients were then changed to APRV. Data included: age, diagnosis, ventilator settings, hemodynamic profiles, ABG, lactate, and medications. Data (means ± SD) were compared using a Student's *t*-test; significance assumed for $P < 0.05$.

Results: Mean age was 58 ± 9 years ($n = 12$) and mean Lung Injury Score was 7.6 ± 2.1. Temperature (PCV 100.8+1 v APRV 100.6+1F; $P > 0.5$) and PaO_2/FIO_2 (PCV 168 ± 24 v APRV 182 ± 18; $P > 0.05$) were similar. Diagnoses were pneumonia (22%), abdominal sepsis (45%), trauma (33%), bacteremia (18%) and transfusion related lung injury (1%). Peak airway pressures fell from 38 ± 3 (PCV) to 25 ± 3 cmH_2O (APRV, $P < 0.05$); mean pressures fell from 18 ± 3 (PCV) to 12 ± 2 cmH_2O (APRV; $P > 0.05$). Paralytic use (PCV 74% v APRV 4%; $P < 0.05$) and sedative use significantly declined (PCV 100% v. APRV 68%, $P < 0.05$). Pressor use decreased substantially (PCV 92% v ARPV 45%, $P < 0.05$). Lactate levels remained unchanged (PCV 2.2 ± 0.6 v APRV 1.8 ± 0.8 mmol/l; $P > 0.05$). Cardiac index rose from 3.2 ± 0.4 (PCV) to 4.6 ± 0.3 l/min/m² BSA (APRV; $P < 0.05$) while DO_2I increased by 36% ($P < 0.05$). CVP declined from 18 ± 4 (PCV) to 12 ± 5 cmH_2O (APRV; $P > 0.05$).

Conclusion: APRV may be used safely in patients with ALI/ARDS and decreases the need for paralysis and sedation compared to PCV. APRV increases cardiac performance with decreased pressor use and CVP in patients with ALI/ARDS. Further study of ARPV is warranted to discover its impact on resource utilization and patient outcome.

P29 Pulmonary function in children who were on long-term mechanical ventilation due to neonatal respiratory disease

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Context: Children with a history of neonatal respiratory disease that required mechanical ventilation, who develop subsequent bronchopulmonary dysplasia, often have abnormal pulmonary function. The extent to which the neonatal respiratory disease alone is involved is not clear.

Objective: To evaluate the association between neonatal respiratory disease without bronchopulmonary dysplasia on discharge and pulmonary function later in childhood.

Design: Case–control study.

Setting: Ambulatory follow-up of former intensive care patients at a university medical centre.

Table. Pulmonary function tests: mean ± standard deviation

Group	VC ($n=18$) ml	FEV_1 ($n=18$) ml	D_LCO ($n=18$) (mmol/min)/kPa	Rt ($n=16$) kPa/l/s	TGV ($n=15$) ml
Cases	2835 ± 806	2236 ± 570	6.01 ± 1.31	0.45 ± 0.19	2003 ± 491
Controls	2984 ± 572	2534 ± 435	6.36 ± 1.01	0.29 ± 0.12	1958 ± 550
Difference	−149	−299*	−0.35	0.16*	45

*Significant difference ($P<0.01$)

Participants: Eighteen children aged 11–15 years with a history of neonatal respiratory disease were randomly recruited, regardless of gestational age or cause of disease. *Inclusion criteria:* mechanical ventilation for >14 days; high inspired oxygen fraction for >2 days (FiO_2 >0.4). *Exclusion criteria:* presence of bronchopulmonary dysplasia or other acute or chronic pulmonary disease at the time of this investigation. Eighteen controls matched for age, sex and height were recruited from children of the hospital staff. All were healthy at birth and had no pulmonary disease at the time of this investigation. All parents gave informed consent.

Pulmonary function tests: Vital capacity (VC); forced expiratory volume in the first second (FEV_1) with and without challenge by the bronchoconstrictor methacholine; diffusing capacity (D_LCO); airway resistance (Rt) with and without methacholine challenge; and thoracic gas volume (TGV).

Main outcome measures: Variables of pulmonary function in the cases. Differences between the cases and controls were compared using the paired-sample *t*-test.

Results: Both FEV_1 and Rt differed significantly ($P<0.01$) between children who had had respiratory disease as neonates (cases) and controls. There were no significant differences in VC, D_LCO and TGV (Table).

Differences in VC and FEV_1 between cases and controls after methacholine challenge were not significant; however, this analysis is of limited value because only eight or nine matched pairs underwent these tests.

Conclusion: A mild degree of airway obstruction is apparent in children 11 to 15 years after neonatal respiratory disease, even in the absence of bronchopulmonary dysplasia or other pulmonary disease.

P30 Does the size of the ventilator tidal volume affect the incidence of post operative pneumonia?

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After major abdominal or thoracic surgery, the patient may develop rapid shallow ventilation because of splinting, pain or heavy sedation. This may lead to the development of post operative atelectasis and pneumonia. Hence, it seems reasonable to expect that the administration of large tidal volumes (VT) during post operative mechanical ventilation will prevent or decrease the incidence of post operative pulmonary complications including that of pneumonia. Whether or not this is true is yet to be determined. Therefore, we performed the following prospective study. We hypothesized that large VT mechanical ventilation after major operations resulted in a lower incidence of post operative pneumonia.

Adults admitted to the surgical intensive care unit for post operative mechanical ventilation after major abdominal or thoracic surgery were placed on one of two VT regimens: 9 ml/kg (group 1) or 14 ml/kg up to a maximum of 1000 ml (group 2). Patients who were not placed on the correct VT regimen and those whose tidal volumes were changed during the study were excluded. Standard ICU monitoring was instituted. In addition, ventilator performance, peak inspiratory pressures, blood gases and daily chest X-rays were monitored. The incidence of post operative pneumonia was recorded. Results were analyzed by SPSS statistical software. Results: Forty-nine patients completed the study, 29 in group 1 and 20 in group 2. Their mean age was 52.7 years. There were 28 males and 21 females. Thirteen of 49 patients (26.5%) developed post operative pneumonia. A comparison of the two groups is shown below:

	Age	Males	Females	VT (ml)	vent (h)	Pneumonia
Group 1	49	14	15	705	93	6/29 (20.7%)
Group 2	57	14	6	870	63	7/20 (35%)

Conclusion: Post operative ventilation with large tidal volumes does not reduce the incidence of pneumonia.

P31 Bronchoscopy and BAL in mechanically ventilated patients in an ICU at a university teaching hospital

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Introduction: Bronchoscopy is an important diagnostic and therapeutic tool in modern intensive care medicine. In ventilated patients it can lead to hemodynamic instability and can compromise the gas exchange .

Method: We evaluated in a prospective study from 3/1997 to 9/1998 indications, complications and side effects of bronchoscopy in a 12 bed medical ICU. The vital signs of the patients were monitored continuously by ECG, invasive blood pressure and S_aO_2 measurement. A BGA was performed 5 min before and 5/30/120 min after the examination.

Results: One hundred and fifty-one bronchoscopies were performed in 103 patients (63 male, median age 60 years, median APACHE II-Score 27.5). The indications were bacteriological examinations in 113/151 (75%), respiratory toilet in 29/151 (19%), oxygenation problems in 11/151 (7%). Less common indications were atelectasis, intubation and biopsy. A BAL was performed in 111/151 (74%) cases. The median P_aO_2/F_iO_2-ratio (PFR) was 292 mmHg 5 min before bronchoscopy and 254/182/193 mmHg 5/30/120 min afterwards. In the subgroup with BAL the median PFR was 295 mmHg 5 min before, 5/30/120 min after examination 261/181/194 mmHg. The PFR was in the critical range <80 mmHg before bronchoscopy in 5/151 (3%) and 5/30/120 min after the examination in 5/151 (3%), 9/151 (6%) and 7/151 (5%) cases. In patients with BAL the corresponding figures were 2/111 before and 3/111, 6/111, 4/111 after bronchoscopy. A decrease of the PFR between the beginning and 30 min after finishing bronchoscopy by more than 50 mmHg was observed in 59/151 (39%) cases for all patients, in 50/111 (45%) for the BAL subgroup. During 5/151 (3%) procedures serious complications were observed. An increase of the blood pressure (215/120 mmHg max.) after local application of noradrenalin and a high peak pressure during ventilation (>45 Torr) did not need therapy. A tachyarrhythmia absoluta was treated by cardioversion. A decrease of systolic arterial blood pressure (min. 67 mmHg) during sedation, could be stabilised by volume substitution and dopamine infusion. Bundle-branch block like ventricular complexes were observed on the ECG monitor in one case, which were accompanied by a blood pressure decrease. After an interruption the ECG showed sinus rhythm and the hemodynamic stabilised again. In a 24 h period after bronchoscopy the patient died because of an acute myocardial infarction.

Conclusion: Bronchoscopy is a safe procedure in critical ill mechanically ventilated patients. Even in patients with BAL, in the most cases only a slight decrease of the PFR could be observed. The lowest PFRs were observed 30 min after bronchoscopy, 90 min later the PFR was almost back to the starting level. Critical PaO_2 values were only seen in rare cases. Complications could be handled in all cases. The death of one patient in a 24 h range after bronchoscopy was probably caused by the underlying disease and is to be seen only in temporal coincidence.

P32 Clinical presentation and prognostic factors in fat embolism syndrome

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Fat embolism occurs in most of the patients following long bone fractures but 1–5% of these present clinically as fat embolism syndrome. The recorded data of 64 patients having uncomplicated long bone fractures without head and chest injuries admitted to our ICU with diagnosis of FES over a period of 3 years was evaluated to determine factors effecting management and prognosis. Forty-two patients belonged to subacute and 29 to fulminant FES group depending upon their clinical status at the time of ICU admission.

Majority of FES patient had fracture femur and presented with respiratory distress as initial symptom. Lung injury score was 1.34 ± 0.64 in subacute and 3.36 ± 0.44 in fulminant group ($P < 0.01$). Patients with fulminant FES had more number of abnormal laboratory parameters. Eighteen patients (43%) in subacute and all patients in fulminant group required ventilation. There was significant delay from FES presentation to ICU admission for subacute FES patients requiring ventilatory support than the patients improving with conservative therapy alone ($P < 0.05$). One patient in subacute (2.3%) and 10 patients in fulminant FES group (45.5%) died. The compliance of respiratory system (C_{rs}) at the start of intermittent positive pressure ventilation was significantly less in fulminant as compared to subacute FES patients ($P < 0.05$). Most of the ventilated patients had initial improvement in C_{rs} with ventilation but only those patients who made continuous improvement in C_{rs} beyond 48 h of ventilation ultimately maintained oxygenation and survived in both the groups. We conclude that early ICU admission and supportive therapy is important determinant of morbidity in FES. Patients with more number of abnormal laboratory parameters and those in whom C_{rs} and oygenation index does not improve even after 48 h of adequate ventilatory support are unlikely to improve by conventional ventilatory support alone and need to be shifted to other modalities of maintaining oxygenation.

P33 Acute respiratory distress syndrome in a University Hospital ICU in Japan

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Objective: To determine prognostic factors for and the outcome of acute respiratory distress syndrome (ARDS) in our ICU.

Method: The American–European consensus conference definition [1] was used for ARDS diagnosis. Thirty-three (2.1%) of 1588 patients admitted to the ICU met the criteria for ARDS. Mechanical ventilation with PEEP was performed for all patients with ARDS. Steroid pulse therapy (60%), nitric oxide inhalation (21%), surfactant replacement (9%), and neutrophil elastase inhibitor administration (24%) were also used. For determination of prognostic factors of ARDS, mean pulmonary arterial pressure (mPAP), pulmonary vascular resistance (PVR), and multiple organ dysfunction score (MODS) [2] excluding the Glasgow Coma Score were measured and compared with outcome.

Results: There were 22 men and 11 women aged 61 ± 12 years. The mortality rate of ARDS was 73%. Sepsis was the main cause of ARDS accounting for 73% of cases. All ARDS patients with septic shock ($n = 9$) and with sterile shock [3] ($n = 4$) died. The patients with shock had higher MODS compared to those without shock with mortality rate 55%. There were no significant differences in mPAP and PVR between survivor and nonsurvivors. ARDS patients who had high MODS, especially those with low PaO_2/FIO_2 and high pressure-adjusted heart rate, 5 days after the onset of ARDS had a poor prognosis.

Conclusion: Shock and MODS, but not pulmonary hypertension, are important as prognostic factors for ARDS.

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P34 High-frequency oscillatory ventilation (HFOV) in bronchiolitis patients

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Respiratory syncytial virus (RSV) is nowadays the leading cause of bronchiolitis and viral pneumonia in children. Although the course is often benign, some children need prolonged hospitalisation and mechanical ventilation or even ECMO if conventional mechanical ventilation (CMV) fails.

HFOV is currently considered to be contraindicated in obstructive airway disease with prolonged time constants due to the risk of dynamic airtrapping. This could give rise to circulatory and ventilatory compromise and barotrauma. Nevertheless, bronchiolitis patients are sometimes put on HFOV after deterioration on CMV.

We report 9 patients with RSV bronchiolitis and pulmonary overdistention (small airway disease) successfully treated with HFOV after deterioration on CMV. Although marked hyperinflation was present in all our patients prior to transition, no airleaks developed during HFOV. In one patient the oxygenation index (OI) increased after start of HFOV. Nitric oxide was added and oxygenation improved immediately. All patients survived without residual lung disease.

In distinct to current opinion, we showed that small airway disease can safely and successfully be managed with HFOV. Ventilatory strategy should be directed to open up the small airways and keep them open with sufficiently high mean airway pressures ('the open airway strategy' similar to the 'open lung strategy' in diffuse alveolar disease). Permissive hypercapnia may be used to reduce pressure swings as much as possible, leading to less shear stress on lung tissue, without influencing airway recruitment. Further dynamic airtrapping can be prevented with the use of longer expiratory than inspiratory times and with prevention of spontaneous breathing. An increasing OI at 48 h may be an indicator of failure of HFOV and alternative treatments should be considered. NO might be such an option to avoid ECMO.

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P35 The importance of prone position ventilation in ARDS for the improvement of oxygenation index

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Introduction: In acute respiratory distress syndrome (ARDS) change from supine (SP) to prone position can improve gas exchange by recruiting alveoli situated in dorsal dependent regions and by alteration of ventilation/perfusion ratio. The aim of this study was to investigate the effect of prone position (PP) after application of high fractional inspired oxygen ($hFiO_2$), inverse ratio ventilation (IRV), positive end exspiratory pressure (PEEP)

as well as kinetic therapy (KT) and hemofiltration (HF) did not lead to a breakthrough in treatment of severe ARDS.

Methods: We studied 22 consecutive patients with severe ARDS (mean age 64 ± 11.16 [SE] years) in a clinical follow-up design. All patients received $hFiO_2$, IRV and PEEP before starting prone position, while 15 obtained HF (Prisma®, Hospal) and 3 KT (Rotorest®). Prone position was commenced 82 h median time (range 6 to 417 h) after onset of severe ARDS at a mean PaO_2/FiO_2 ratio of 98.02 ± 6.11 (SEM) mmHg. We compared individual oxygenation index (PaO_2/FiO_2) before and after start of prone position with linear regression analysis (Excel® regression-procedure; SPSS® T-test).

Results: In the stage of supine position neither treatment with $hFiO_2$, IRV, PEEP nor HF and KT led to an improvement of oxygenation index. After starting prone position ventilation 20 of 22 patients showed a significant increase of the oxygenation index (responder: $Y_{[SP]} = [-46.11 \pm 3.41] \times X + [194.03 \pm 3.78]$; $Y_{[PP]} = [25.00 \pm 3.05] \times X + [170.36 \pm 2.68]$; [mean ± SEM]; $P < 0.05$), while 2 patients showed no improvement of oxygenation index (slope of regression SP/PP: 42.96/–22.70 and –11.63/–19.33). Renal failure of these two non-responders was not treated by HF. Improvement of oxygenation index was independent of duration in supine before the begin prone position (range 6 to 417 h). In one patient PP was started actually after 417 h of treatment at our Intensive Care Unit.

Conclusion: Starting prone position seems to mark a U-turn for oxygenation for the majority of patients with severe ARDS, while application of high fractional inspired oxygen, inverse ratio ventilation, positive end exspiratory pressure as well as kinetic therapy and hemofiltration do not necessarily improve oxygenation. The timing of this non invasive technique primarily depends on the decision to turn the patient from supine to prone. We recommend prone position in ARDS as soon as possible to reduce lung injury and complications resulting of mechanical ventilation.

P36 The effect of the pulmonary time constant on the cough peak flow rate at two different inflation pressures: a bench test model

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Supramaximal flow is characteristic of the cough manoeuvre and is thought to be the result of dynamic compression of collapsible airways. We investigated the effect of changing the pulmonary time constant on the peak flow rate produced by an *in vitro* cough manoeuvre. We used a prototype artificial cough generator and a simplified lung-airway model. The model consisted of a compliant bag with a resistor (internal diameter 3 mm to 7 mm) that emptied through a collapsible tube. The resulting range of emptying time constants (420 to 2800 ms) included those found *in vivo* (500 to 2000 ms). The lung-airway model was inflated to one of two pressures (31 cmH_2O or 55 cmH_2O) and then compressed within a glass container to a pressure of 45 cmH_2O. A mechanically-operated glottis opened rapidly and the resultant flow was measured by a pneumotachograph. The cough peak flow rate (CPFR) was recorded for 20 cough manoeuvres for each configuration and the values of the mean and standard deviation are shown in the Table.

Time constant (ms)	420	1078	1850	2800
CPFR l/min Inflation to 31 cmH_2O	419 SD 44.6	185 SD 25.3	108.7 SD 17.1	67.6 SD11.7
CPFR l/min Inflation to 45 cmH_2O	544 SD 70.8	353 SD 56.6	225 SD 29.4	112 SD 29.0

The results from this bench-test model suggest that the pulmonary time constant has a profound effect on the magnitude of the cough peak flow rate.

P37 Computer simulation: a guideline in ventilator setting in severe lung disease

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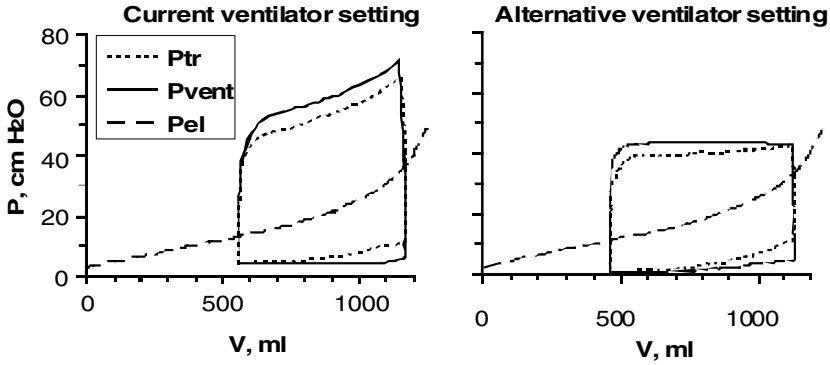
Mechanics and gas exchange can in be studied with a computer-controlled ventilator. The physiological profile obtained describes the Pel/V diagram, inspiratory and expiratory resistance versus volume and the expired volume of CO_2 versus tidal volume. When setting PEEP, frequency, I:E ratio, and minute ventilation or inspiratory pressure the physician needs to assimilate the information of the physiological profile and all clinical information to assure an adequate gas exchange at a non-traumatic ventilation. In ALI/ARDS harm can be caused both by ventilation at too low lung volumes and by ventilation at high volumes. In COPD the task is to ventilate at the lowest possible volume and airway pressure.

The complexity of the physiology and ventilator settings makes it impossible to figure out what is the ideal pattern of ventilation in order to reach the immediate therapeutic goals defined by the physician. However, on the basis of an adequate mathematical physiological profile, a computer can by simulation prognosticate what would be the consequences of alternative modes of ventilation. Through repeated simulations the physician can search a mode of ventilation that leads to his goals.

Computer simulation can be used to: a) increase the understanding of various patterns of ventilation in disease. b) predict the consequences of alternative settings in a particular patient.

In left diagram the total pressure in the ventilator (Pvent), the tracheal pressure (Ptr) and the alveolar, i.e. the elastic pressure, Pel,



is shown for a patient with critical obstructive lung disease. Under current setting (volume control 10 l/min, Ti = 25%, Tpause = 10%, RR = 16, PEEP = 4 cmH_2O) the $PaCO_2$ of 9.2 kPa was deemed acceptable. The pressures were, however, very high. By repeated simulations it was possible to identify a setting which dramatically would reduce the pressures without changing $PaCO_2$.

P38 Clinical evaluation of a new closed loop ventilation mode: adaptive supportive ventilation (ASV)

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Introduction: ASV (Galileo, Hamilton Medical, Inc.) is a mode of mechanical ventilation (MV) with a closed loop algorithm to determine and adjust ventilator settings. ASV may adjust mandatory breath rate, I:E ratio, and inspiratory pressure of mandatory breaths. Target minute ventilation (V_E) is determined by ideal body weight (IBW) and clinician selected Percent Vent (% Min Vol). Galileo assesses the pt by measuring dynamic compliance and expiratory time constant. With IBW and %Min Vol settings, optimal settings for rate, T_i, V_T, and V_E are determined. We compared MV with ASV to MV with physician determined vent settings during the initiation of MV.

Methods: Ninteen post-operative pts requiring MV were studied. Vent settings by physician were noted and each pt was placed on those settings or ASV randomly. IBW was determined from standardized tables and %MinVol was set to 100%. PEEP and FiO_2 were determined by staff and held constant. ABG's and cardiopulmonary variables (f, V_T, V_E, T_i, PIP, P_{aw}, HR, MAP, and VCO_2) were measured and recorded after 30 min on each mode. Data were compared using student's *t*-test.

Results: 19 pts (14 male) were studied. Initial 'test breaths' during ASV were well tolerated. Mean IBW was 88.8 Kg. Mean age was 54.3 years. Table 1 reveals set and measured ventilator parameters for both study periods. PIP and V_T were lower during ASV. Respiratory rate was higher during ASV. V_E, T_I, and P_{aw} were unchanged between study periods. Mean values for PEEP and FiO_2 were 7.3 and 0.48, respectively. Table 2 reveals ABG measurements, CO_2 production, and V_D/V_T ratio. There were no clinically relevant differences in ABG's or VCO_2 between study periods. V_D/V_T was lower during ASV. No pt suffered any adverse events from derangements in ventilation or acid-base balance. One pt with ARDS receiving 17 cmH_2O PEEP was hypoxemic during ASV (PaO_2 57.2). Table 3 reveals heart rate and mean arterial pressure during each study period. There were no clinical changes to any measured vital sign between the two study periods.

Table 1.

	Conventional	ASV
Rate (bpm)	10.1 ± 2	14.4 ± 3
V_T (ml)	863 ± 133	690 ± 121
V_E (l/min)	9.5 ± 2	9.6 ± 2
PIP (cmH_2O)	31.9 ± 9	25.2 ± 8
P_{aw} (cmH_2O)	11.5 ± 2.4	12.0 ± 2.8
T_I (s)	1.5 ± 0.5	1.43 ± 0.3

Table 2.

	Conventional	ASV
PH	7.39 ± 0.06	7.40 ± 0.07
$PaCO_2$ (mmHg)	38.6 ± 5	37.6 ± 5
PaO_2 (mmHg)	106.1 ± 33	100.0 ± 31
SaO_2 (%)	99.3 ± 1	99.1 ± 1
V_D/V_T (%)	51.3 ± 6	57.4 ± 8
VCO_2 (ml/min)	265 ± 56	262 ± 48

Table 3.

	Conventional	ASV
HR	89 ± 16	87 ± 16
MAP	72 ± 19	73 ± 15

Discussion/conclusion: Upon initiation of mechanical ventilation, the precise V_E requirement of the pt may not be known. Clinicians use rough estimates and clinical experience to determine V_E, respiratory rate, V_T, and T_i. Determination of vent settings made by the machine have been suggested (*Intern Care Med* 1996, **22**:199). Our results suggest that ASV as startup mode of ventilation is acceptable and comparable to physician determined ventilator settings. Gas exchange during ASV is equivalent to physician determined ventilation. V_T during ASV is more consistent with 'lung protective' strategy (7.8 ml/kg) than was conventional V_T (9.7 ml/kg). Mechanical ventilation with ASV is more efficient as evidenced by lower V_D/V_T and may be safer as a result of lower V_T and PIP.

P39 Relationship of body mass index (BMI), lactate and intra-abdominal pressure (IAP) to subsequent mortality in ICU patients

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Introduction: Excess body weight increases the risk of death from any cause and from cardiovascular disease in adults [1]. In the majority of population studies, the relationship of BMI to mortality is a U-shaped curve, with increased risk in the lowest and highest percentiles of the distribution. In acutely ill patients however BMI below the 15th percentile remains an independent predictor of mortality whereas a high BMI (>85th percentile) was not significantly related to risk of mortality [2]. We wanted to study in a prospective clinical trial the relationship between IAP and lactate and BMI and their relationship to subsequent mortality in ICU patients. The results of an interim analysis are presented in this abstract.

Methods: Over a 12 month period 405 patients, hospitalised in a seven bed mixed ICU, were screened for increased IAP >12 mmHg (normal 0–5 mmHg) with the standardised intravesical pressure recording method. Data collected within the first 24 h of ICU admission were: age, gender, MODScore, APACHE-II and SAPS-II score and BMI. Maximal IAP and lactate levels were recorded within the first 72 h. Study endpoints were: duration of ICU and hospital stay, ICU and hospital mortality and cost of ICU and hospital stay. Statistical analysis was done with Fisher exact and two-tailed unpaired Student's *t*-test, values are mean ± SD.

Results: The percentage of female patients was 55.3, age 66 ± 17.4, MODScore 3.4 ± 3.3, APACHE-II score 16.4 ± 6.2, SAPS-II score 35.1 ± 17.5, BMI 25.1 ± 4.8, IAP 8.3 ± 4.7 mmHg, lactate 3.3 ± 4.2 mEq/l, ICU-stay 6.3 ± 9.5 and hospital stay 22.4 ± 22.9 days. Raised IAP was present in 71 patients (17.5%). The incidence of IAP ≥ 12 and the mean IAP values were higher in patients who underwent emergency surgery: 39.4% (mean 11.5 ± 5.3) versus 19.8% (8.6 ± 4.9) in medical versus 6.1% (6.9 ± 3.5) in scheduled surgical patients. The ICU and hospital mortality were respectively 18% and 27.2%. The IAP was significantly higher in patients who died in the ICU: 13.2 ± 5.2 versus 7 ± 3.6 ($P < 0.0001$) as well as in patients who died in the hospital: 11.5 ± 5.3 versus 6.9 ± 3.6 ($P < 0.0001$). The Table lists the parameters studied in patients with high and normal IAP. The ICU and hospital mortality was significantly higher in patients with high IAP; respectively 64.8% versus 8.1% ($P < 0.0001$, OR 20.9, 95% CI 11.2–39) and 70.4% versus 18% ($P < 0.0001$, OR 10.9, 95% CI 6.1–19.5). With a cut-off at 12 IAP had 64.8% sensitivity, 78.6% specificity, 75.8% accuracy, 38.7% positive predictive value and 91.3% negative predictive value for ICU mortality. There was a poor but significant correlation between BMI and IAP: BMI = 0.2106 × IAP + 23.268 ($R^2 = 0.0413$, $P < 0.0001$) and between lactate and IAP; lactate = 0.4851 × IAP–0.3885 ($R^2 = 0.2847$, $P < 0.0001$). There was a trend towards lower ICU mortality with higher BMI but none of this reached statistical significance: 25.8% in the first, 15% in the second, 16.3% in the third, and 16.2% in the fourth BMI quartile. In patients within the first BMI quartile (<22) ICU mortality was significantly higher when compared to the total group of other BMI quartiles: 25.8% versus 15.8% ($P = 0.04$, OR 1.9, 95% CI 1.1–3.3).

	IAP≥12 ($n=71$)	IAP<12 ($n=334$)	*P*-value
IAP (mmHg)	15.8 ± 3.6	6.4 ± 2.6	<0.0001
BMI	26.3 ± 5	24.8 ± 4.7	0.15
Lactate (mEq/l)	6.7 ± 6.3	2.4 ± 2.9	<0.0001
MODS	6.9 ± 3.5	2.6 ± 2.7	<0.0001
SAPS-II	52.4 ± 16.1	31.3 ± 15.4	<0.0001
APACHE-II	23.3 ± 9	14.3 ± 7.8	<0.0001
Age (years)	69.1 ± 11.9	65.3 ± 18.3	NS
ICU-stay (days)	16.2 ± 15.2	4.2 ± 5.9	<0.0001
Hospital stay (days)	27 ± 23.3	21.5 ± 22.7	0.06
ICU cost (US$)	11980 ± 10230	2651 ± 3490	<0.0001
Hospital cost (US$)	15600 ± 11590	8388 ± 8226	<0.0001

Conclusion: The interim results of an ongoing prospective clinical trial show that increased IAP can be expected in about 17.5% of cases. It seems to be a predictor of mortality and causes a considerable extra-cost and prolonged ICU-stay. High IAP does not correlate well with high BMI or lactate. There is no U-shaped (concave) mortality curve associated with BMI, on the contrary, patients with higher BMI had lower mortality compared to patients within the first BMI quartile, and this is in accordance with the results from others [2]. We suggest that IAP should be used as part of routine monitoring in the ICU and that future studies examining variables predictive of ICU-mortality should include IAP and BMI.

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P40 The search for optimal PEEP in acute lung injury (ALI): correlation between intra-abdominal pressure (IAP) and the lower inflection point (Pflex). Results of a pilot study

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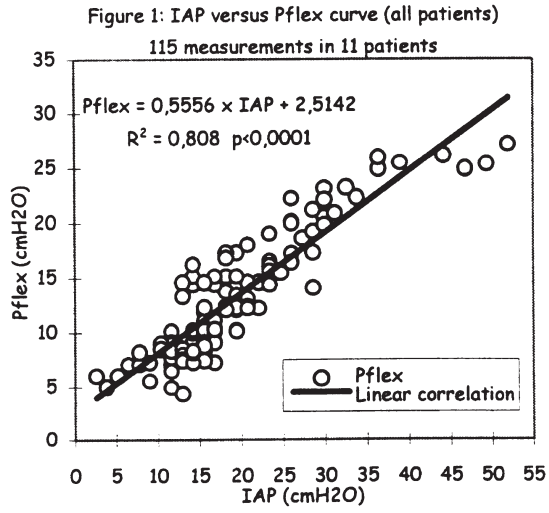
Introduction: It is well known that IAPs above 15–20 mmHg increase peak and plateau alveolar pressures. The rise in pressure on the diaphragm causes a pattern of restrictive lung disease with a drop in functional residual capacity and all other lung volumes. Finally this results in diminished chest wall compliance causing difficult ventilation and weaning. The respiratory system can be

divided into the chest wall and the lung. Since the diaphragm is coupled to the abdominal wall any increase in IAP may therefore affect chest wall and lung compliance [1]. By calculation of static V–P curves it has been shown in animal and human studies that abdominal and subsequently chest wall compliance goes up after abdominal decompression and this correlates well with the volume recruited [1]. Recent studies looking at compliance in primary and secondary ARDS found that the latter presents with preserved lung but decreased chest wall compliance and PEEP allows to recruit lung units markedly [1,2]. In a previous study we found that in patients with secondary ARDS and raised IAP, PEEP-adjustment for IAP calculated at zero PEEP (ZEEP) resulted in significant better oxygenation at the expense of a significant increase in peak and plateau alveolar pressures but without the risk for early barotrauma [3]. In this pilot study we wanted to sort out if there is a correlation between IAP and Pflex.

Methods: Over a 2 month period 115 measurements were performed in 11 patients. The IAP was calculated at ZEEP with the standardised intravesicle pressure recording method and Pflex with the super-syringe method. The M/F ratio was 6/5, age 67.1 ± 9.4, MODScore 6.5 ± 3.3, APACHE-II score 25.2 ± 8.5, SAPS-II score 54.4 ± 15.7, ICU-stay 11.3 ± 6.3 days. The number of measurements in each patient was 10.5 ± 7.5. There were three patients with primary and three with secondary ARDS, and three patients had secondary ALI according to the definitions given by the American–European consensus conference. Calculation of correlation was done with the Prism GraphPad™ software (version 2.00 October 31 1995), values are mean ± SD.

Results: The values for IAP (mmHg), IAP (cmH_2O) and Pflex (cmH_2O) were 14.9 ± 6.8, 19.4 ± 8.9 and 13.3 ± 5.5, respectively for the whole group of patients; 15.8 ± 7.6, 20.6 ± 9.8 and 13.2 ± 6.0, respectively in secondary ALI/ARDS and 12.6 ± 3.4, 16.4 ± 4.4 and 13.6 ± 3.9 respectively in primary ARDS. There was a very good correlation between IAP (cmH_2O) and Pflex (cmH_2O) for the whole group of patients (Fig. 1): Pflex = 0.552 × IAP + 2.5146 ($R^2 = 0.808$, $P < 0.0001$) and this correlation was even better in the patients with secondary ALI/ARDS; Pflex = 0.5745 × IAP + 1.3227 ($R^2 = 0.888$, $P < 0.0001$). As suspected the correlation was worse in patients with primary ARDS: Pflex = 0.7622 × IAP + 1.1624 ($R^2 = 0.7428$, $P < 0.0001$).



Conclusion: We found a very good correlation between IAP and Pflex. Calculation of IAP can easily be done at the bedside of every ICU patient who has a Foley catheter in place. We propose this simple strategy for determination of best PEEP in ALI instead of the more time consuming, not generally accepted and not without risk calculation of Pflex with the super syringe method. Before being used for clinical purposes, the results of this pilot study need to be validated in a multicentre trial.

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P41 Determination of the best volume of perfluorocarbone to ensure partial liquid ventilation in the pig with ARDS

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Introduction: Partial liquid ventilation consists of filling the residual functional capacity with perfluorocarbon (PFC), while providing tidal volume by conventional ventilation. Several studies have shown that smaller volumes of PFC allow significant improvement in ventilation parameters during experimental ARDS. To date no study has compared several small volumes of PFC. The purpose of this study was to make a comparison with the minimum doses of PFC in a pig model presenting ARDS.

Method: 16 pigs, average weight 24 ± 5 kg, under general anesthesia and myorelaxation were prepared with installation of a central venous catheter and an arterial catheter with continuous oxygen saturation monitoring The animals were then ventilated (Evita 4, Dräger) with intermittent positive pressure ventilation (FiO_2:1) in order to obtain $PaCO_2$ at 35 ± 1 mmHg. At this point ARDS was induced by intravenous injection over half an hour of 0.3 ml/kg oleic acid. ARDS was confirmed by a PaO_2/FiO_2 <150 taken over two successive arterial samples. A pressure–volume curve was established and used to identify the lower inflection point (LIP) and the level of the 'best PEEP'. The animals were then split into four groups of four, with a control group being given continuous positive pressure ventilation (CPPV) without PFC. The second group was administered 5 ml/kg intra tracheal perfluorocarbon (Rimar 101, Mitsubishi Milano) then given CPPV ventilation. The third group was administered 10 ml/kg PFC and the last group 15 ml/kg. In all four groups CPPV ventilation was maintained with the 'best PEEP'. Arterial pressure, central venous pressure, heart rate, SaO_2 and $PETCO_2$ were recorded continuously. Blood gases and ventilation parameters: peak inspiratory pressure, tidal volume and pulmonary compliance were recorded every 15 min. The three groups were compared using an ANOVA, a Friedman test and a Mann and Whitney U-test ($P < 0.05$ significant).

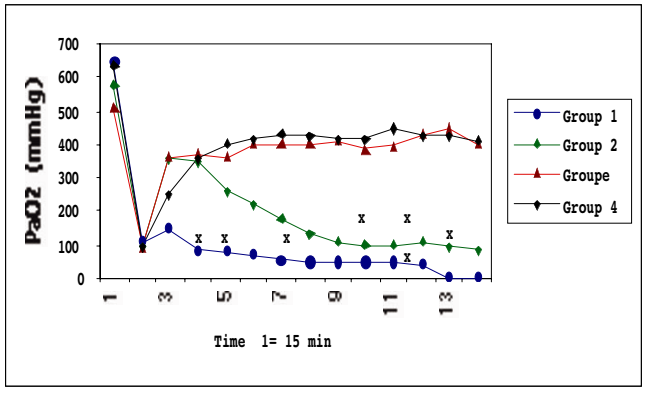

Figure 1. Evolution of the PaO_2 in the four groups. x: times when the pigs died.

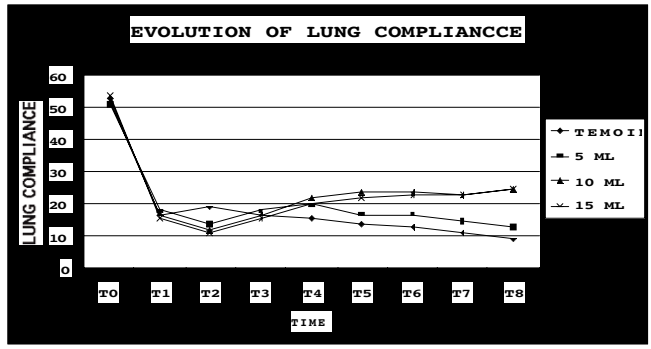

Figure 2. Evolution of lung compliance.

Results: In the control group lung compliance and PaO_2 continued to drop for all the animals; in PLV groups, lung compliance decrease after administration of PFC. After a few minutes, the compliance increase significatly. In the 5 ml/kg group lung compliance and PaO_2 rose to an average of 354 ± 197 mmHg and 15.4. In the 10 and 15 ml/kg group PaO_2 was restored to its initial level of 448 ± 74 and 445 ± 86 mmHg. Lung compliance increase to satifactorys values (21.4 ± 3.1; 21.48 ± 2.4). All the animals in the control group died in a mean time of 109 ± 25 min, the animals in the 5 ml/kg group survived on average 158 ± 17 min, the animals in the 10 ml/kg and 15 ml/kg groups survived for the whole 3 h the experiment lasted ($P < 0.05$).

Discussion: It would thus appear that in pigs a dose of 5 ml/kg PFC enables satisfactory ventilation parameters to be restored, but the level remains lower than that obtained with 10 ml/kg. The fact that a low dose does not have long-lasting effects might be due to faster evaporation of the product and a drop in its efficiency. There is no beneficial effect with larger dose than 10 ml/kg.

P42 Cardiorespiratory effects of inhaled nitric oxide during acute hypercapnia with and without correction of blood pH in acute respiratory failure in piglets

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Objective: To evaluate the effects of inhaled nitric oxide on gas exchange and hemodynamic data during acute hypercapnia with uncorrected and corrected blood-pH.

Design: Prospective, randomized, experimental study.

Setting: University research laboratory.

Subjects: Ten piglets weighing 9 to 13 kg.

Interventions: After induction of anesthesia, tracheostomy and controlled mechanical ventilation animals were instrumented with two central venous catheters, a pulmonary artery and two arterial catheters, and an ultrasonic flow probe around the pulmonary artery. Acute respiratory failure was induced by the infusion of oleic acid (0.08 ml/kg) and repeated lung lavages with 0.9% NaCl (20 ml/kg). The protocol consisted of randomly assigned periods with different $PaCO_2$ levels (Normocapnia = $PaCO_2$ 40 torr, Hypercapnia I = $PaCO_2$ 65 torr, Hypercapnia Ic = $PaCO_2$ 65 torr-pH corrected, Hypercapnia II = $PaCO_2$ 85 torr, Hypercapnia Iic = Hypercapnia 85 torr-pH corrected). Tidal volume was reduced to

	BL	NC	HC-I	HC-Ic	HC-II	HC-IIc
PAP (torr)NO-0	21.8 ± 1.4	28.1 ± 0.6	32 ± 1.7	29.2 ± 1.2	35.1 ± 1.8	30.8 ± 1.6#
PAP (torr)NO-10	19 ± 1.1	25.8 ± 1.2	27 ± 3**	26 ± 1	28.5 ± 1.1**	26.3 ± 1.3*
MAP (torr)NO-0	83 ± 1.7	79.3 ± 2.9	72.6 ± 2.5	78.4 ± 3.7	74.2 ± 3.0	76.7 ± 4.1
MAP (torr)NO-10	82 ± 1.8	81 ± 2.4	79 ± 3.8	82 ± 5	74 ± 4	77 ± 4
CO (l/min)NO-0	2.6 ± 0.39	1.9 ± 0.19	1.72 ± 0.15	1.77 ± 0.1	1.90 ± 0.17	1.90 ± 0.2
CO(l/min)NO-10	2.5 ± 0.4	2.0 ± 0.2	1.77 ± 0.11	1.72 ± 0.14	1.91 ± 0.16	2.16 ± 0.21
PVR (dyne.s.cm^{-5})NO-0	362 ± 53	684 ± 85	928 ± 157	694 ± 97	956 ± 142	823 ± 197
PVR (dyne.s.cm^{-5})NO-10	275 ± 41	582 ± 99	642 ± 69*	611 ± 123	685 ± 124*	469 ± 107*
PaO_2/FiO_2 (torr)NO-0	454 ± 37	98 ± 12	101 ± 5.2	109 ± 12	95 ± 5	106 ± 13
PaO_2/FiO_2 (torr)NO-10	469 ± 35	148 ± 11**	151 ± 13**	146 ± 17*	154 ± 25**	148 ± 21*

*$P < 0.05$ vs iNO 10ppm, **$P < 0.01$ vs iNO 10ppm, #$P < 0.05$ vs pH-correction, BL, baseline; NC, normocapnia; HC-I, hypercapnia 65 torr; HC-II, hypercapnia 85 torr; C, pH-correction

induce hypercapnia, inspiratory time was prolonged to achieve constant mean airway pressures (Paw). Tham infusion was used to correct pH. At each $PaCO_2$-period the animals were ventilated with and without inhaled nitric oxide (10 ppm).

Measurements and results: Continuous hemodynamic monitoring included right atrial, mean pulmonary artery and mean systemic arterial pressures, and continuous flow recording at the pulmonary artery. In addition, airway pressures, tidal volumes, lung compliance and airway resistance, arterial and mixed venous blood gases were measured. Data were obtained with and without inhalation of nitric oxide at baseline, normocapnia and 2 levels of hypercapnia with and without pH correction and are given in the Table.

Conclusion: Acute hypercapnia resulted in a significant increase in pulmonary artery pressure and pulmonary vascular resistance without significantly influencing oxygenation and cardiac output. pH-correction at hypercapnic episodes decreased pulmonary artery pressure and pulmonary vascular resistance associated with a slight increase in cardiac output and oxygenation. Inhaled nitric oxide significantly reduced pulmonary hypertension induced by acute hypercapnia and significantly improved oxygenation during normocapnia and acute hypercapnia with and without acidosis.

P43 Cardiorespiratory effects of inhaled nitric oxide and moderate hypercapnia in an experimental model of single ventricle

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Objective: To evaluate the effects of inhaled nitric oxide and moderate hypercapnia on hemodynamics and gas exchange in an experimental model of single ventricle.

Design: Prospective, randomized, experimental study.

Setting: University research laboratory.

Subjects: Nine piglets weighing 10 to 14 kg.

Interventions: After induction of anesthesia, tracheostomy and controlled mechanical ventilation animals were instrumented with two central venous catheters and two arterial catheters. After a midline sternotomy the animals were placed on cardiopulmonary bypass and subjected to atrial septectomy, patch closure of the tricuspid valve, and creation of a 4 mm systemic to pulmonary arterial shunt. Before weaning from cardiopulmonary bypass ultrasonic flow probes were placed around the pulmonary artery and the descending aorta. In addition a pulmonary artery catheter was inserted into the pulmonary artery via the right ventricle. The protocol consisted of randomly assigned periods with different $PaCO_2$ levels (Normocapnia = $PaCO_2$ 40 torr, Hypercapnia I = $PaCO_2$ 50 torr, Hypercapnia II = $PaCO_2$ 60 torr,) and a period of inhaling nitric oxide (10 ppm) at normocapnia. Tidal volume was reduced to induce hypercapnia, inspiratory time and PEEP were adjusted to achieve constant mean airway pressures (Paw).

Measurements and results: Continuous hemodynamic monitoring included right atrial, mean pulmonary artery and mean systemic arterial pressures, and continuous flow recordings at the pulmonary artery and the descending aorta. In addition, arterial and central venous blood gases were measured. Data were obtained at baseline, normocapnia with and without NO-inhalation and 2 levels of hypercapnia and are given in the Table.

Conclusion: The creation of this experimental model of single ventricle resulted in a significant decrease in oxygen saturations and mean arterial pressure. Moderate hypercapnia resulted only in minimal changes in pulmonary artery pressure, pulmonary vascular resistance, and oxygen saturations. Inhaled nitric oxide decreased pulmonary artery pressure and resistance associated a slight increase in oxygen saturations.

	BL	NC	NC-iNO	HC-I	HC-II
RAP (mmHg)	8.9 ± 0.9	10.6 ± 1.5	10.7 ± 1.4	11 ± 1.4	11.3 ± 1.5
PAP (mmHg)		23.1 ± 1.8	20.4 ± 1.5	23.6 ± 1.8	25.2 ± 2.1*
MAP (mmHg)	88 ± 5.9	53 ± 3.7#	51.5 ± 3.4#	48.6 ± 3#	46.4 ± 3.3#
Qp/Qs		0.94 ± 0.1	1.17 ± 0.1	0.89 ± 0.1*	0.98 ± 0.1
CO (l/min)		1.95 ± 0.1	1.89 ± 0.1	1.81 ± 0.1	1.63 ± 0.1
PVR (dyne.s.cm^{-5})		1504 ± 331	967 ± 148	1514 ± 246	1661 ± 188*
SaO_2 (%)	99.6 ± 0.1	77 ± 3.6#	79.7 ± 2.3#	74 ± 4.4#	74 ± 3.4#
SvO_2 (%)	89 ± 1.2	45 ± 3.5#	47 ± 2.4#	42 ± 3.2#	40 ± 2.1#*

RAP, right atrial pressure; PAP, pulmonary artery pressure; MAP, mean arterial pressure; Qp, pulmonary artery flow; Qs, systemic flow; PVR, pulmonary vascular resistance; BL, baseline; NC, normocapnia; HC-I, hypercapnia 50 torr; HC-II, hypercapnia 60 torr; iNO, inhaled nitric oxide
*$P < 0.05$ vs NC-iNO, #$P < 0.01$ vs BL

P44 Impact of inhaled nitric oxide on pulmonary capillary pressure in ARDS patients

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Introduction: Inhaled nitric oxide (NO) causes selective pulmonary vasodilation. In experiment, pulmonary arteries were shown to be primary site of NO effect. Our aim was to study the effect of inhaled NO on pulmonary vasculature in ARDS patients.

Materials and methods: Inhaled NO was tested in 8 ARDS patients (PaO_2/FiO_2 = 71 ± 26 mmHg, LIS >2.5). One hour test of 20 ppm NO was performed and in 3 patients NO was additionally increased to 40 ppm with the primary aim to improve oxygenation. Positive pressure response was defined as a decrease of mean pulmonary artery pressure (mPAP) >2 mmHg. Pressure curves during pulmonary artery occlusion were recorded in duplicate before and with NO and the more representative one was used for pulmonary capillary pressure (PCP) estimation [1]. Positive response in oxygenation was defined as PaO_2/FiO_2 increase >20%. Statistics: nonparametrical Wilcoxon test for two related samples and simple correlation when appropriate. Data are presented as means ± SD. $P < 0.05$ was considered significant.

Results: In 1 patient a marked decrease in mPAP was measured (15 mmHg), in other 4 patients the drop was marginal (3–4 mmHg). Three patients did not respond to NO inhalation by any significant change in mPAP. In five responders PCP and PCWP pressure did not change before and after the NO test (25.0 ± 4.5 and 24.2 ± 5.3 mmHg for PCP; $P = 0.18$ and 18.0 ± 3.3 and 17.8 ± 3.9 mmHg for PCWP; $P = 0.59$). Transpulmonary pressure difference (dPAP–PCWP) decreased significantly (14.6 ± 1.4 and 11.0 ± 3.7 mmHg, respectively; $P = 0.04$) which corresponded with trend to decrease the arterial component of the transpulmonary pressure difference (dPAP–PCP) (7.6 ± 3.0 and 4.5 ± 2.6 mmHg, respectively; $P = 0.11$ i.e. decrease in 4 cases).

Conclusion: When effective in lowering pulmonary pressures, inhaled NO seems to act primarily on the arterial component of transpulmonal vascular resistance.

Acknowledgement: Supported by IGA grant No. 3999-3

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P45 Correlation of lung mechanics with saturated phosphatidylcholine ratios and surfactant protein A in bronchoalveolar lavage fluid from infants with RSV induced respiratory failure

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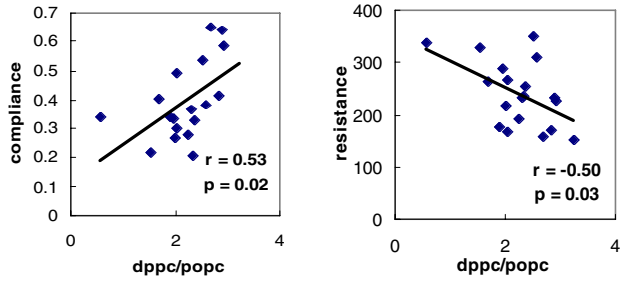
Aim: Infants with respiratory syncytial virus (RSV) induced respiratory failure have been shown to be deficient in surfactant, both in quantity and ability to reduce surface tension. Theoretical evidence suggests that surfactant may have a role in maintaining patency of small airways, which has implications for RSV bronchiolitis. In addition, a minimum ratio of surfactant protein A (SPA) to fully saturated dipalmitoylphosphatidylcholine (DPPC) must be present for surfactant to be fully functional. We wished to investigate the relationship between (a) lung mechanics and SPA/DPPC ratios, and (b) lung mechanics and the ratio of DPPC to the monounsaturated palmitoyloleoylphosphatidylcholine (POPC) in bronchoalveolar lavage (BAL) fluid from ventilated RSV positive infants.

Methods: Nineteen infants were studied, median age 7 weeks (range 3–25 weeks), median weight 4 kg (range 2–6 kg). BALs were taken within 24 h of commencing mechanical ventilation. BAL surfactant phospholipid composition was detected by electrospray ionization mass spectrometry, and SPA levels by enzyme-linked immunosorbent assay. Static respiratory system compliance and resistance were measured using the single breath occlusion technique with a commercially available device (PEDS® 4.1, Medical Associated Services, USA).



Results: The median (interquartile range) values for compliance were 0.36 (0.31–0.47) ml/cmH_2O/kg, and resistance 234 (184–277) cmH_2O/l/s. The DPPC/POPC ratio correlated significantly with both compliance and resistance (see Figure). There was no correlation (neither linear nor exponential) between SPA/DPPC ratio and lung mechanics (compliance: $r = 0.1$, resistance $r = 0.24$).

Conclusion: Surfactant containing higher ratios of saturated phosphatidylcholine has a role in maintaining compliance and small airway patency in RSV infected infants. Although a certain minimal level of SPA is necessary for surfactant function, additional benefit is not seen with increasing SPA/DPPC ratios. These findings have implications for exogenous surfactant supplementation in this disease.

P46 Experimental study on prevention of simulated high altitude ALI by tetramethylpyrazine in dogs

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Twenty-one hybird dogs were randomly divided into acute lung injury (ALI) treated and control groups at simulated high altitude environment of 4000 m. All animals were sacrificed after 6 h. The tetramethylpyrazine (TMP) treated group showed that the WBC count was significantly higher at 15 min after fat tissue extract was given ($P < 0.05$), the edema of both capillary endothelial cells and alveolar epithelial cells was less serious, the number of leukocytes accumulated in the lungs was less. The increase in production of leukotriene B (LTB) by polymorphonuclear neutrophil (PMN), alveolar macrophage (AM), and the activity of platelet-activating factor (PAF) by PMN were partially inhibited ($P < 0.01$). Although the ratio of the pulmonary extravascular water volume/blood free dry lung weight (PEWV/BFDL) of TMP group was significantly elevated as compared with that of control group, no significant difference was seen ($P > 0.05$). However, the level of PaO_2, the PMN and AM count, and the albumin level of the BALF in both groups had no significant difference. These results demonstrated that the early treatment with TMP could inhibit the decrease in the WBC count, and reduce the accumulation of leukocytes in the lungs.

P47 Effects of C1-inhibitor and rSP-C surfactant on oxygenation and histology in rats with lavage-induced acute lung injury

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Introduction: The acute respiratory distress syndrome (ARDS) is characterized by diffuse injury to the endothelial and epithelial surfaces of the lung leading to severe respiratory failure. Alterations in the surfactant system and activation of the contact system of coagulation are major contributors to the pathophysiology of ARDS. C1-inhibitor (C1-INH) is the main inhibitor of contact activation and the only known inhibitor of classical pathway complement activation. The aim of this study was to investigate the effects of C1-inhibitor administration and rSP-C surfactant application on oxygenation and lung histology in an ARDS-model.

Methods: Thirty-six male Sprague Dawley rats were subjected to repetitive lung lavage with isotonic saline solution. Three experimental groups and two control groups were studied: Group 1 and 2 served as controls without any treatment. Animals of group 1 were sacrificed 60 min after the last lavage procedure (p.l.). Animals of group 3–5 received 200 U/kg body weight (b.w.) C1-INH (Centeon, Germany) intravenously (group 3), 25 mg/kg b.w. rSP-C Surfactant (Byk Gulden, Germany) intratracheally (group 4) or both (group 5) at 60 min p.l. Blood gases were determined 120, 150, 180 and 210 min p.l. All animals of group 2–5 were sacrificed at 210 min p.l. and the lungs were excised for histological examination. Hyaline membrane formation, distribution and severity of intraalveolar neutrophil (PMN) accumulation and the severity of intraalveolar and perivascular hemorrhage were graded semiquantitatively using a scale from 0 to 4+.

Results: At 210 min p.l. pO_2 values of group 4 (456 ± 74 mmHg) and group 5 (387 ± 155 mmHg) were significantly higher than in group 3 (120 ± 103 mmHg) or in controls (63 ± 12 mmHg). Hyaline membrane formation was significantly reduced in group 4 and 5. The grading for PMN infiltration was significantly lower in animals who received C1-INH (group 3 = 2.0, group 5 = 2.3) than in controls (group 2 = 2.7) or in animals treated with surfactant only (group 4 = 3.3). The severity of intraalveolar hemorrhage and edema were significantly reduced in group 3 and highest in group 4.

Conclusion: Surfactant application was effective in improving pO_2 which was related to the reduction of hyaline membrane formation. C1-INH administration had no significant effect on pO_2 and hyaline membrane formation but was effective in reducing PMN infiltration, intraalveolar hemorrhage and edema formation.

P48 Inhibition of pulmonary microvascular chemokine production by human Laktoferrin and Phosphatidylethanolamine

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Chemokines, a large family of structurally related chemotactic cytokines, are essential for the migration of leukocytes during inflammatory processes. The release of neutrophil attractant chemokines such as MCP-1, Groα, ENA-78, GCP-2 and NAP-2 as well as fractalkine by lung microvascular endothelial cells (LMVEC) is dramatically increased upon stimulation with LPS. The present study was performed to investigate, whether human Lactoferrin (hLf) or Phospholipase A2-inhibitor Phosphatidylethanolamine (PE) can intervene with the release of these chemokines by LMVEC under LPS stimulation.

LMVEC were pretreated with hLf for various time intervals prior to stimulation with LPS or with LPS in the presence of hLf. In other experiments, cell impermeable PE, Cyclooxygenase-

inhibitors (CoI) (indomethacine, acetyl-salicylic acid) and a platelet activating factor (PAF)-antagonist, were added to LPS stimulated LMVEC. Chemokine release was measured by ELISA and detection of chemokine mRNA by means of RT-PCR.

HLf added to LMVEC at the time of stimulation did not influence chemokine production. However, when hLf was added prior to LPS stimulation, a significant inhibition of MCP-1 ($P < 0.001$) and ENA-78 ($P < 0.01$) but not of Groα production was observed. In order to investigate if LPS induced chemokine production was dependent on PAF, Arachidonic acid (AA) or its metabolites, LMVEC were treated with PE, CoI and PAF-antagonist either after or at the time of LPS stimulation. Treatment of LMVEC with PE completely inhibited the LPS induced chemokine production of MCP-1, ENA-78 and Groα in a time and dose dependent fashion. This was still observed, when LMVEC were pretreated with LPS. CoI and PAF-antagonist could partly reduce LPS induced chemokine production. Furthermore mRNA expression of ENA-78, Groα, GCP-2 and fractalkine was decreased after LPS stimulation in the presence of PE. Our data demonstrate, that hLf and PE are potent agents to counteract LPS induced chemokine produktion by LMVEC. These findings may have clinical implications in the treatment of acute lung injury during sepsis.

P49 Lipid peroxidation, antioxidant status and selenium levels in patients requiring prolonged ventilatory support

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Introduction: Recently free oxygen radicals have been implicated as possible mediators of respiratory muscle dysfunction, particularly diaphragm fatigue. The aim of the study was to evaluate lipid peroxidation, antioxidant status and selenium levels in patients with sepsis requiring ventilatory support and during weaning.

Methods: After institutional approval 40 critically ill patients were prospectively studied during ventilatory support and weaning, three patients due to death were excluded. All patients were weaned according to standard weaning protocol. Blood samples were drawn daily and collected until analysis. Malondialdehyde (MDA) serum levels, total glutathion (GSH), glutathion-peroxidase (GPX) and superoxid-dismutase (SOD) activity in erythrocytes and serum selenium levels were estimated at the time of admission to ICU (T1), on the last day of full ventilatory support (T2), on the day when weaning was started (T3) and on the first day of spontaneous ventilation (T4). After successful weaning patients were divided in two groups according to the length of weaning (W): group S (W ≤ 3 days, $n = 15$), group L (W > 3 days, $n = 22$). *t*-test or Mann Whitney Rank Sum test were used for statistical analysis (SigmaStat, Jandel Co., USA), values are expressed as mean (SD) or median (25%–75% percentiles), $P < 0.05$ was considered statistically significant.

Results: Summarized selenium values (μmol/l) were 0.63 (0.28) in Group S and 0.57 (0.16) in Group L.

	T1	T2	T3	T4
MDA – S	0.72 (0.55–1)	0.94 (0.72–1.39)	0.89 (0.82–1.25)	1.02 (0.82–1.2)
MDA – L	1.14 (0.94–1.89)*	1.07 (0.67–1.43)	0.96 (0.74–1.32)	0.94 (0.67–1.31)
GPX – S	31.5 (8.2)	39 (8.0)	34.9 (8.6)	39.1 (7.8)
GPX – L	34.6 (10.2)	35.5 (4.2)	27.2 (11)	31.3 (6.2)**
SOD – S	1320 (279)	1320 (310)	1090 (256)	1270 (350)
SOD – L	1270 (439)	1120 (107)	1360 (107)***	1290 (275)

MDA pg/ml – median (25–75%), GPX U/g Hb – mean (SD), SOD %inhib – mean (SD), * $P = 0.006$, ** $P = 0.009$, *** $P = 0.013$

Discussion: Prolonged ventilatory support and weaning longer than 3 days were associated with higher MDA levels and lower GPX levels, also selenium levels were insignificantly lower in patients with prolonged ventilatory support. The clinical importance of these findings needs to be further studied.

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P50 Primary endogenous pneumonia in severe burn patients

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The study has been approved by the Institutional Board for Clinical Research

Objective: To determine primary endogenous pneumonia effect on severe burn patient mortality and to establish the associated factors with primary endogenous pneumonia.

Design: Prospective observational.

Setting: A six-bed burn intensive care unit.

Patients: All patients of ≥14 years admitted between January 1995 and January 1996 with a total body surface burn area of ≥20%. Exclusion criteria included immunosuppression, pregnancy, and length of stay less than 5 days or admission ≥48 h following burn trauma.

Intervention: Collection of data on surveillance samples from throat and rectum on admission and afterwards twice weekly, and primary endogenous pneumonia during the intensive care unit stay.

Statistical analysis: The variables potentially related to mortality were age, sex, total body surface burn area, full-thickness burn

area, inhalation injury, primary endogenous pneumonia, bloodstream infection, burn wound infection and urinary tract infection. Comparison between groups was performed using Wilcoxon test or Fisher's exact test when appropriate.

Results: Thirty-one patients fulfilled the criteria of analysis. Mean age was 43 years (36–50), total body surface burn area 43% (36–50), full-thickness burn area 24% (17–31). Inhalation injury was identified on 13 patients. Mean stay was 28 days (21–35). Mortality was 29% (nine patients).

Fourteen patients developed 19 pneumonias: 12 primary endogenous, six secondary endogenous and one exogenous. The causative microorganisms were 14 *Staphylococcus aureus*, three *Haemophilus influenzae*, two *Streptococcus pneumoniae*, one *Pseudomona aeruginosa* and one *Acinetobacter* spp.

In the univariate and multivariate analysis the factors associated ($P < 0.05$) with mortality were primary endogenous pneumonia and full-thickness burn area. The risk factors associated ($P < 0.05$) with primary endogenous pneumonia were full-thickness burn area and inhalation injury. Increasing the number of cases (56 patients), both variables were statistically significant in the univariate analysis, but were not statistically significant in the multivariate analysis. At present we are continuing the study to know the factors associated with morbidity and mortality in severe burn patients.

Conclusion: Half the patients developed a pneumonia (63% primary endogenous pneumonia). The isolated pathogens were predominantly *Staphylococcus aureus*. Primary endogenous pneumonia in severe burn patients may be associated with mortality, but is necessary collecting more cases to show it.

P51 Outbreak of nosocomial infection/colonisation caused by *Stenotrophomonas maltophilia* with mucoid phenotype

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The Gram-negative bacillus *Stenotrophomonas maltophilia* (SM) has emerged as an important pathogen associated with significant case/fatality ratio [1,2]. SM is a potentially dangerous organism because of its resistance to many antibiotics. We present here an outbreak of mucoid phenotype SM pneumonia (four cases) and respiratory tract colonisation (three cases). Our review of literature revealed only one case report of pneumonia characterised as mucoid phenotype [2]. The outbreak was caused following admission of a 65-year-old male patient with respiratory distress, fever, leukocytosis (24000/µl) in the ICU. Chest X-ray showed an infiltrative shadow in the right lower lobe and bilateral pleural effusion was detected on CT. Sputum cultures obtained before admission to ICU and subsequent days yielded mucoid phenotype SM. Treatment with ticarcilline plus clavulonic acid to which the isolates was susceptible was initiated. One-day later chest X-ray showed diffuse bilateral pneumonic infiltrates and the patient's condition rapidly deteriorated. Ciprofloxacine was added to the treatment. Subsequent SM isolates rapidly developed antimicrobial resistance to antibiotics. Four patients in the ICU were lost with SM pneumonia within 7–10 days. SM isolates were identified by standard Analytical Profile Index procedure (API 20E and API 20 NE). A significant number of both infected and colonised patients had severe systemic diseases and tracheotomy, they were mechanically ventilated and receiving broad spectrum antibiotics before isolation of SM. SM is emerging as an important nosocomial pathogen in critically ill ICU patients and should no longer be regarded as a harmless bacillus in ICU.

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P52 Selective decontamination of the digestive tract influences the acquisition of *Helicobacter pylori* among intensive care nurses

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Introduction: *H. pylori* prevalence is increased in health care workers and in intensive care nurses. Exposure to *H. pylori* by gastric secretions and faeces are the main sources of transmission of *H. pylori* infection to health care workers. The routine use of selective decontamination of the digestive tract (SDD) at an intensive care unit suppresses *H. pylori* in critically ill patients. It was questioned whether as a consequence, a decreased exposure of *H. pylori* to intensive care nurses would lead to a lower prevalence of *H. pylori* infection in these nurses.

Methods: The *H. pylori* infection prevalence of intensive care nurses from a unit using SDD routinely (group I) was compared to that of intensive care nurses from a unit not using SDD (group II). Health care workers from other departments where no SDD was used (group III) served as a control group. Both the intensive care nurses and controls were included on a voluntary basis. Persons using proton pump inhibitors were excluded. *H. pylori* was detected by Laser Assisted Ratio Analyser-^{13}C-urea breath test (UBT).

Results: Three UBTs were unable to be processed in group I ($n = 64$), five in group II ($n = 55$) and five in group III ($n = 50$). The prevalence of *H. pylori* infection was 11% (7/61) in group I and 25.5% (14/50) in group II ($P = 0.027$, Pearson Chi-Square). In group III the prevalence of *H. pylori* infection was 16% (8/45) which is not significantly different from both group I and II. The mean age in the three groups was 35.9, 37.8 and 36.6 years respectively (NS).

Conclusion: The prevalence of *H. pylori* infection among intensive care nurses is lower in nurses from units using SDD compared to the ones from a unit not using SDD. Acquisition of *H. pylori* by transmission from critically ill patients appears to be diminished once SDD is used.

P53 Factors predicting the etiologic pathogens in intensive care patients with early-onset pneumonia

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Objective: National surveillance data of nosocomial infections in Intensive Care Units (ICUs) in Belgium show that in early-onset pneumonia cases (i.e. within 48 h after ICU-admission) microbiology results are more likely to be lacking than in late-onset pneumonia cases. The aim was to examine whether the etiologic pathogen in ICU-patients with early-onset pneumonia could be predicted by specific patient characteristics.

Material and methods: Data provided by the ICUs participating in the national surveillance programme for nososcomial infections in ICUs between January 1996 and June 1998 were examined. For the most frequently isolated pathogens in early-onset pneumonia, associated patient characteristics at admission were identified. Independence of association was verified by multivariate analysis using logistic regression.

Results: Seventy hospitals reported 472 cases of early-onset pneumonia, 366 (77.5%) of which were microbiologically documented. The most frequently isolated pathogens were *S. aureus* (17.2%), *E. coli* (13.7%), *P. aeruginosa* (13.4%) and *S. pneumoniae* (12.8%). In univariate analysis, *S. aureus* infection was associated with a high Simplified Acute Physiology Score (SAPS II) (55 or more: OR 4.0, $P < 0.001$; P for trend = 0.001), *P. aeruginosa* infection with prolonged prior hospital stay (1–7 days: OR 2.9, $P = 0.02$; >7 days: OR 4.3, $P < 0.001$; P for trend = 0.002). Factors associated with *S. pneumoniae* infection were younger age (<70 years: OR 2.2, $P = 0.01$), community origin (OR 4.8, $P < 0.0001$), no use of antibiotics in the last 48 h (OR 3.4, $P < 0.001$) and no prior surgery in the 30 days preceding diagnosis of pneumonia (OR 3.1, $P = 0.002$). No patient characteristics were found to be predictive for infection with *E. coli*. After multivariate analysis, *S. aureus* and *P. aeruginosa* infection remained significantly associated with respectively a high SAPS II score and prolonged prior hospital stay. For *S. pneumoniae* infection, only community origin and no use of antibiotics in the last 48 h remained independently associated.

Conclusion: Empirical antimicrobial treatment for early-onset pneumonia in Belgian ICUs is common. Patient characteristics at admission, such as duration of prior hospital stay, prior antibiotic use and patient severity score, are important factors in predicting the most probable etiologic pathogen and may be helpful in decision-making with regard to empirical antimicrobial therapy for early-onset pneumonia in ICUs.

P54 Nosocomial infection: main cause in development of septic complications in surgical postoperative patients

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Introduction: In this first attempt to prove the main cause of septic complications in postoperative ICU patients in Bulgaria's biggest hospital (more than 1000 beds) we analyzed all patient admitted in general ICU during 5 year period (1993–1997).

Methods: We provided a standard bacterial monitoring of all body media (tracheal tubes, urinary tract, blood, central venous lines, sputum and surgical wounds). According to bacterial growth we divided patients into three groups. The Group 1 included patiens without any bacterial growth. Group 2 included patients with nosocomial infection. Group 3 included patients with secondary surgical endogenous infections.

Results: Of all patients during these 5 years, we include those 913 (62.9%) who stayed for more than 72 h in ICU. Group 1 included 256 patients(28%). From Group 2 we obtained following positive cultures: 457 from tracheal tubes (88.8%), 376 from urinary tract (41.9%), 282 from blood (47.2%), 164 from central venous lines (15%) and 66 from sputum (8.8%). The dominating pathogens in cultures were: from tracheal tubes: Acinetobacter spp. (27.4%); from blood: *Acinetobacter* spp. (21%), *Serratia* spp. (16.4%), *S. epidermidis* (21%); from urine: till 5 day *E. coli* (18%), *Acinetobacter* spp. and *Citrobacter* spp. (13.8%); and after 5 days: *Candida* spp. (25%) and *Pseudomonas aeruginosa* and *S. aureus*. In Group 3 we obtained samples from surgical wounds and drainage tubes. The dominating pathogens were the same as in other body media (*Acinetobacter* spp., *Serratia* spp.).

Conclusion: The nosocomial infection remains the main cause of septic complications in postoperative ICU patients and its emergence in ICU further rises There is also increase in secondary endogenous surgical infection. We noted *P. aeruginosa* moved to third-second place as a cause of nosocomial infection. The importance of Gram-positive flora nearly equalised that of Gram-negative in ICU.

P55 Nosocomial pneumonia and bacteremia in intensive care: results from the Belgian national surveillance, 1996–1998

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In 1996 the Scientific Institute of Public Health – Louis Pasteur (IPH), in collaboration with the Belgian Society of Intensive Medicine and Emergency Medicine, started a multicentre surveillance of intensive care units (ICU) acquired pneumonias and bacteremia. From January 1996 to June 1998, 60% of Belgian acute-care hospitals ($n = 101$) participated during at least one surveillance period (3 months), and 64% of those participated more than one period. A total of 31 374 patients were included for the analysis.

In 4.7% (95% CI 4.5–5.0) of the patients a pneumonia with onset later than 48 h of ICU stay and matching CDC criteria for nosocomial pneumonia was registered. In 89% of those at least one ventilation-day had preceded the onset of the infection (RR 10.4%; 8.9–12.2). The number of ventilator-associated pneumonias per 1000 ventilation-days was 19.0/1000 ventilation-days, varying from 11.9 in coronary surgery patients to more than 25 in patients having undergone neurosurgery, non-cardiac thoracic surgery, vascular surgery and transplantation. The predominant micro-organisms were *Pseudomonas aeruginosa* (recovered in 18.0% of the episodes), *Staphylococcus aureus* (17.7%), *Escherichia coli* (12.6%), *Candida* spp. (12.1%) and *Enterobacter* spp. (9.5%).

Bacteremia was reported in 2.4% of the patients. Five percent of bacteremia occurred within the first 48 h. Forty percent ($n = 301$) were secondary to another infection site and 55% (1.3% of the patients and 2.3 BSIs per 1000 patient-days) matched the CDC case definition of laboratory-confirmed primary bacteremia. The device-adjusted primary bacteremia rate was 3.1/1000 catheter-days and varied between 1.5 in coronary surgery to 4.8 in patients with multiple trauma and 6.0 in neurosurgical patients. The five predominant micro-organisms in primary bacteremia were *Staphylococcus epidermidis* (in 33.3% of the episodes), *Staphylococcus aureus* (12.8%), *Enterococcus faecalis* (7.1%), *Pseudomonas aeruginosa* (6.1%) and *Enterobacter aerogenes* (5.7%).

The frequent participation to the national surveillance led to an important national database that allows to study the risk factors of ICU-acquired infections, to identify areas for prevention and to improve the inter-ICU comparability of infection rates according to the risk profile of the different ICU populations. International comparisons remain a delicate matter by lack of internationally standardised surveillance methods.

P56 Protected specimen brush bronchoscopically directed versus unprotected tracheal aspirate in patients with ventilator associated pneumonia

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Objectives: Bacterial resistance to antimicrobial treatment is actually one of the most debated issue in medical field. Therefore, it is important to dispose a diagnostic procedure to allow an aimed antimicrobial treatment. Unprotected tracheal aspirate (UTA) is the most widely used sampling technique to assess pulmonary infection even though known to have a high sensivity and a low specificity [1]. Protected specimen brush bronchoscopically directed (PSB) is a procedure that purpose a higher specificity [2]. The aim of the study is to compare both methods for the diagnosis of pneumonia in ICU.

Materials and methods: 70 consecutive patients admitted to an 8-bed general ICU over a period of 18 months, intubated and mechanically ventilated [3]. When patients met clinical and radiological criteria for suspicion of pneumonia both UTA and PSB were performed.

Results: Data collected from the two methods pointed out significative differences.

PSB vs UTA revealed complete negativeness or growth of different microorganisms in 29 patients (41.5%); this result had statistically significance ($P < 0.01$).

Above all it is to underline that microorganism most frequently represented in UTA and not detected by PSB were in sequence: *Candida* spp, *Pseudomonas aeruginosas*, *Staphylococcus aureus*. No complications were reported during the procedures.

Antimicrobial therapy based on PSB data was started, leading to a good clinical response and favourable outcome.

Conclusion: PSB is a reliable and safe method useful to investigate pulmonary infections. High specificity of the technique allows to aim antibiotic therapy, so reducing the risk of inducing resistance to molecule still effective with a consequent optimization of expenses. UTA and corrispective PSB were both negative in *X* case (*y*%) VPN = 1. In consideration of UTA elevated vpn, this method could represent a first diagnostic step followed in case of positiveness by PSB

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P57 Incidence and pathogenesis on severe burns patients infection

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The study has been approved by the Institutional Board for Clinical Research

Objective: To know infection incidence, pathogenesis and microorganisms on severe burns patients.

Design: Prospective observational.

Setting: A six-bed burn intensive care unit.

Patients: All patients of ≥14 years admitted between January 1995 and January 1996 with a total body surface burn area of ≥20%. Exclusion criteria included immunosuppression, pregnancy and length of stay less than 5 days or admission ≥48 h following burn trauma.

Intervention: Collection of data on surveillance samples from throat and rectum on admission and afterwards twice weekly, and infections during the intensive care unit stay. The infections were diagnosed according to the CDC criteria.

Results: Thirty-one patients fulfilled the criteria of analysis. Mean age was 43 years (36–50), total body surface burn area 43% (36–50), full-thickness burn area 24% (17–31). Inhalation injury was identified on 13 patients. Mean stay was 28 days (21–35). Mortality was 29% (nine patients).

Twenty-two patients developed 59 infections: 28 primary endogenous, 27 secondary endogenous and four exogenous.

Fourteen patients developed 19 pneumonias: 12 primary endogenous, six secondary endogenous and one exogenous. The causative microorganisms were: 14 *Staphylococcus aureus*, three *Haemophilus influenzae*, two *Streptococcus pneumoniae*, one *Pseudomona aeruginosa* and one *Acinetobacter* spp. Eight patients had nine urinary tract infections: eight primary endogenous and one secondary endogenous. The pathogens were: six *Escherichia coli*, three *Streptococcus faecalis* and one *Serratia*.

Nine patients developed 10 burn wound infections: one primary endogenous, eight secondary endogenous and one exogenous. The causative microorganisms were: six *Staphylococcus aureus*, three *Pseudomona aeruginosa*, one *Escherichia coli*, one *Acinetobacter* spp, one *Proteus* and one *Klebsiella*.

Fourteen patients had 21 bloodstream infections: seven primary endogenous, 12 secondary endogenous and two exogenous. The pathogens were: nine *Staphylococcus aureus*, four coagulase-negative staphylococcus, two *Streptococcus faecalis*, one *Streptococcus faecium*, three *Escherichia coli*, two *Pseudmona aeruginosa*, and one *Candida* spp.

Conclusion: Burns patients infections are similar to trauma patients, with 50% primary endogenous infections. The isolated pathogens were predominantly gram positive coccus, except in urinary tract infections.

P58 Evaluation of the infections due to central venous catheters in intensive care unit patients

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Introduction: Central venous catheters (CVC) are responsible for a part of the infections seen in intensive care units (ICU). In our ICU routinely we use CVC for fluid and drug administration as well as CVP measurement. On the ather hand, infection, one of the most important complications of CVC must always be thought. Infections due to CVC are attributed to colonization of microorganisms at the tip of CVC and then their migration to the circulation. In our study , we planned to determine the colonization ratio of microorganisms at the tip of CVC and analyse the agents of infection.

Method: We evaluated the data obtained from 40 CVC that we could send to the laboratory in a year. The insetion sites of CVC were V. basilica ($n = 25$), V. subclavia ($n = 5$), V. jugularis interna ($n = 4$) and V. femoralis ($n = 6$). CVC were inserted under sterile condition by using sterile gloves and surgical drapes. The duration of catheterization was 8.4 ± 5.1 days (2–23 days). Central venous pressure measurements and fluid administrations were made by the nurses under sterile conditions. Fluid administration sets were changed two times a week. Cannulation sites were cleaned with povidone-iodine (Betadine®) every day and sterile deesings (Tegaderm®) were applied. Approximately 2 cm to the tip of each with drawn CVC is sended to the laboratory of microbiology in a sterile tube for culture-antibiogram analysis.

Findings: We determined an agent of infection in 6 of 40 catheters tips that we evaluated (1%5). The agents were: *Acinetobacter* spp. ($n = 2$), Coagulase (–) staphylococci ($n = 2$), Fungi ($n = 1$), Oxacilline resistant Staphylococci aureus ($n = 1$). We determined no agent of infection in the others 34 catheters.

Discussion: Infection rate was less compared to previous reports and was similar to the results of the study by Nahidh *et al.* in which povidine iodine was used in the control group. Then we concluded that the ratio of infections due to colonization at the tip of CVC may be decreased by daily care of catheters made under sterile conditions.

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P59 A.V.A.: a novel approach to venous access

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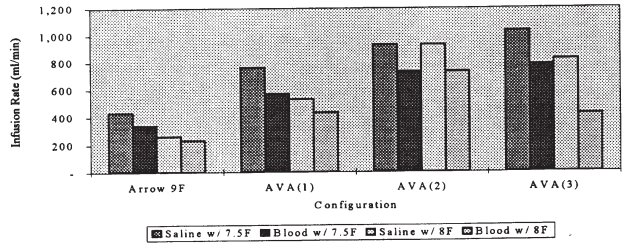
Introduction: Central venous access is an integral part of patient care. The dilemma was whether to insert an introducer or multi-lumen catheter for access. However, the Advanced Venous Access device (A.V.A.) from Baxter now offers the option of a single device to accomplish multiple functions with one stick. The object of this study was to compare maximal flow rates of this new device with other introducers utilizing the Haemonetics Rapid Infusion System (R.I.S.) and the more traditional pressurized I.V. system

Test methods: Devices tested with the traditional system were: Baxter A.V.A., which incorporates a 9F PA access with one distal (D) and two proximal lumens (P1&P2); Arrow 9F; Argon 9F. The test system has been described previously. Devices tested with the RIS were the Baxter A.V.A. and the Arrow 9F introducer. Fluids measure were saline and a blood/plasma mixture. The RIS was set up in a manner to continually infuse fluids through the device using a cut-off pressure of 300 mmHg to judge maximum flow. Devices were tested with PA catheters (7.5F & 8F). Results for the A.V.A. are shown in various configurations: AVA(1)=D+P1; AVA(2)=P1+P2; AVA(3)=D+P1+P2 (Fig. 1).

Results: In the traditional I.V. system, the A.V.A. delivered higher flows than all other introducers. Figure 1 below shows flow rate results for the RIS system.



Discussion: In all categories, the Advanced venous Access device delivered higher flows than the other introducers. Therefore, the A.V.A. device offers a new dimension in central access for trauma, critical care, and high blood loss surgeries (i.e. liver transplants). It now gives us the ability to monitor the circulation and infuse fluids with fewer venous punctures.

P60 Biochemical and haematologic predictors of fungemia in previous colonised ICU patients

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Introduction: In last years the nosocomial ICU fungal infections are assuming a greater impact with increasing morbidity, mortality and cost. A better outcome is correlated with an earlier treatment.

Objectives: The aim of the study was to assess the accuracy of simple not expensive biochemical and haematologic parameters to predict the change of fungal colonisation to a status of fungemia.

Materials and methods: Three-year retrospective study with 806 ICU medical and surgical non-neutropenic patients. The study group consisted of 90 patients with fungal documentation, 37 patients were excluded for insufficient data. We considered two groups.

Group 1 – colonisation 73 patients (fungal documentation in biological products except blood)

Group 2 – fungemia 17 patients (at least one positive blood culture)

	Group I			Group II		
	24 h	48 h	72 h	24 h	48 h	72 h
Age		63 ± 13.78			54.87 ± 13.43	
SAPS II		40.87 ± 12.58			40.87 ± 13.43	
Alkaline phosph.	120.6 ± 110.91	110.06 ± 98.2	154.4 ± 130.13	117.5 ± 73.86	136.5 ± 70.6	178.27 ± 87
Lactate dehyd.	772.5 ± 591.6	735.74 ± 575.52	705.4 ± 598.8	773 ± 335.6	650 ± 311.3	717.13 ± 370.9
Leukocytes	13.7 ± 6.3	13.28 ± 6.37	12.9 ± 5.71	13.85 ± 4.86	14 ± 5.24	12.55 ± 5.78
Platelets	195.26 ± 139.8	183.6 ± 140	195.2 ± 150.3	332.4 ± 193.3	317.2 ± 188.3	288.1 ± 171
pH	7.4 ± 0.11	7.42 ± 0.09	7.42 ± 0.1	7.4 ± 0.09	7.4 ± 0.07	7.42 ± 0.08
Bicarbonate	28.87 ± 9.56	30 ± 8.92	31.6 ± 9.2	26.6 ± 7.28	26 ± 6.07	27.77 ± 7.26
Blood lactate	33.6 ± 20.5	33.35 ± 21.7	28.5 ± 20.83	27.23 ± 8.4	24.42 ± 8	27.66 ± 12.11

Age, SAPSII in first 24 h, alkaline phosphatase, lactate dehydrogenase, blood lactate, pH, bicarbonate, leukocytes, and platelets were evaluated in all patients the 3 days preceding fungal documentation. We compared biochemical and haematologic results in group 1 and group 2 trying to identify a different profile and evaluated the predictive value of the different parameters. Results are presented as media and standard deviation. We applied *t* student test comparing the two groups and we considered a $P < 0.05$ to be significant.

Results: (See Table). We found significant statistical difference with bicarbonate, and platelet count when comparing the two groups. We also observed an increasing blood level on alkaline phosphate in fungemic patients.

Conclusion: In our study, variations on bicarbonate, platelet count and alkaline phosphatase are predictive of fungemia in previous colonised patients. However, further observations, analyses, are needed and perhaps involving larger patient numbers to evaluate the clinical utility of these findings.

P61 Fluconazole prophylaxis of systemic candida infection in non-neutropenic critically ill patients: a prospective randomized study

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Introduction: Systemic candida infection has been associated with increased morbidity and mortality in patients requiring intensive care. Fluconazole (F) is the preferred therapy in *Candida albicans* infection. The aim of the study was to evaluate effect of daily prophylactic fluconazole administration on the incidence of systemic candida infection.

Methods: After institutional approval 38 critically ill patients were prospectively studied. In 18 patients (group F) presumptive fluconazole therapy after admission was started in daily dose 100 mg intravenously until discharge or evidence of systemic candida infection, which was treated using standard dosage. Control group (C) consisted of 20 patients. Apache II, candida colonization, selected risk factors for candidemia (central venous and urinary catheters, parenteral nutrition, corticosteroids therapy, broad-spectrum antibiotics, H_2-receptor antagonists), length of ICU and hospital stay, ventilatory days, incidence of candida albicans and non albicans candida species were recorded. The cultures from nasopharynx, trachea, urine, stool and blood stream were taken. Values are expressed as a mean (SD), *t*-test, Mann Whitney Rank Sum test, z-test were used for statistical analysis, $P < 0.05$ was considered significant.

Results: Selected results are presented in the Table.

	Group F	Group C
APACHE II	23.6 (3.8)	22.6 (4.7)
ICU stay (days)	17.6 (8.9)	11.5 (4.1)
Hospital stay (days)	21 (9)	15.7 (6.2)
Ventilatory days	17.6 (11.9)	11.9 (4.9)
Candida colonization	27%	33%
Candida albicans	10 (66%)	13 (81%)
Non *albicans* species	5 (33%)	3 (19%)

Conclusion: There were no significant differences in incidence of candida colonization and proportion of albicans v. non albicans species between both groups. Hospital and ICU stay and length of ventilatory support were nonsignificantly longer in group F. Clinical usefulness of early fluconazole prophylaxis needs to be further evaluated.

P62 Nosocomial candidemia in an Italian tertiary care hospital

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In a retrospective ongoing study, the incidence of nosocomial candidemia among patients (pts) admitted to a tertiary-care teaching hospital (bed capacity 2400; 78 beds for intensive care units, ICUs) was evaluated together with causative pathogens, potential risk factors, antifungal treatment, and crude mortality. During the primary study period (November 1991–October 1994) there were 136 episodes of candidemia occurring in 136 pts (median age 62 years, range 4–96). The overall incidence of candidemia was 11.3 episodes per 10 000 hospital admissions. The underlying diseases were the following: solid or hematological malignancies (43 pts), major abdominal surgery (30 pts), cardiovascular diseases (18 pts), trauma (17 pts), other diseases (28 pts). At the onset of candidemia 67 pts (49%) were located in ICUs, 48 and 21 pts respectively in surgical and medical wards. *C. albicans* (83 strains) accounted for 53% of all blood culture Candida isolates. Fifty-three pts (39%) received adequate antifungal treatment: 16 pts amphotericin-B and 37 pts fluconazole. The overall crude mortality was 54%. The number of positive fungal blood cultures (1 culture versus >1 culture) did not influence crude mortality (54% versus 63%). In addition, the mortality of pts infected by *C. albicans* (55%) was similar to that of pts infected by *C. non-albicans* species (45%). The mortality of pts located in ICUs (79%) was significantly higher ($P < 0.001$) than that of pts in surgical (29%) and medical wards (33%). Finally, the mortality of pts who did not receive adequate antifungal therapy (70%) was significantly higher ($P < 0.001$) than that of treated pts (30%). In conclusion, the incidence of nosocomial candidemia was high during the primary phase of the study; most of our pts with candidemia had severe underlying diseases and were hospitalized in ICUs. The number of fungal positive blood cultures did not influence the crude mortality, confirming that a single bood culture shuld not be dismissed as benign transient candidemia. On the contrary, about two-third of our pts did not receive an adequate antifungal treatment and the majority of them died.

P63 Herpes simplex and intensive care medicine: an underestimated problem?

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Herpes Simplex Virus (HSV) infection may cause different disorders in patients hospitalized in intensive care. Bronchoalveolar lavage (BAL) is a procedure performed almost as a routine in patients with unexplained respiratory insufficiency in our department. During the last 10 years, HSV has been isolated frequently from the respiratory tract at our 30 beds intensive care unit. The objectives of this retrospective study were to define risk factors of the population in whom HSV virus was isolated.

The study concerned patients with an isolation of HSV from either bronchial aspiration (BA) or BAL in the past 5 years (1992–1997). HSV was isolated by culture on shell vials and identified by immunofluorescence after staining with monoclonal antibodies or by the conventional culture and cytopathogenic effect on Vero-cells. From the 64 cases observed, 47 HSV isolations originated from BA, 13 from BAL (of which 9 with simultaneously negative BA) and 4 from both BA and BAL. The mean age of the patients was 62 years (range from 16 to 82). Only 50% of the patients had fever at the time of the investigation. The majority of the patients (94.9%) was intubated before the isolation. The role of immunosuppression, previously recognized as a risk factor for herpes infection, was not confirmed in this study: only 20.4% had received either corticosteroids or immunosuppressive agents. Striking is that 73.4% had undergone a surgical procedure before the isolation, mainly coronary bypass grafting or other thoracic operations. Daily chest X-rays from 2 days before till 2 days after virus isolation were reviewed blindly by the same radiologist. There was no pathognomonic image at the chest X-ray: a localized infiltrate resembling pneumonia, diffuse alveolar infiltrates or an interstitial pattern were observed and 14% of the chest X-rays were even defined as normal. Lung injury was severe: almost 60% had a PaO_2/FiO_2 less than 200. 28 patients received aciclovir therapy once herpes was isolated, without an effect on the outcome: 48.4% of all patients and 42.8% of those receiving aciclovir therapy (28) died.

Isolation of HSV in respiratory samples from critically ill patients is therefore more frequent than previously known. Whether these isolates contribute to illness and its evolution remains to be determined.

P64 Preliminary validation of new prognostic scoring system in patients with invasive meningococcal disease

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Introduction: Invasive meningococcal disease (IMD) caused by an invasive strain of Neisseria meningitidis group C:2a:P1,2,P1,5 and lately by an invasive strain group B:2a:P1,2 as well appeared in the Czech republic in 1993 and completely changed severity of the disease. Incidence and severity of the disease in the West Bohemian region is the highest in our country. We have published preliminary results of our several studies of prediction factors of this disease. Haemocoagulopathy seemed to be of great and reliable prediction value. Fibrinogen, Quick, platelets and AT III. were found as the most reliable factors in patients treated in the interdisciplinary ICU.

Purpose of the study: Prospectively to develop and preliminarily validate a model for the probability of hospital death in patients with meningococcal invasive disease.

Methods: Defined continuous variables (fibrinogen, Quick, platelets and AT III) and categorical variable (survival) were collected. A preliminary model was developed on the base of 82 patients data. Logistic regression was used for the development of the model, which was evaluated by the receiver operating characteristic (ROC) analysis. The mortality rate preliminary validation as the outcome was studied.

Studied group characteristics: Unlike previous studies we studied now the group of patients with IMD treated in the whole West Bohemian region. Six patients from total number of 88 patients were excluded from the study due to incomplete data ($n = 82$).

Age-median	12 years	Fibrinogen-median	2.6 g/l
Male:female ratio	39:43	Quick-median	50%
Niklasson-median	3	Platelets-median	139×10^{12}/l
Mortality rate	14.6% (12)	AT III-median	60.5%

Results:
(1) Logistic regression model has validity coefficient = 0.469: $P(Death=1) = 1/(1+EXP(\Sigma\beta_0 + \beta_i X_i))$

(2) Receiver operating characteristic for logistic model – ROC report: (see Table overleaf).

Set up of optimal value of P(Death=1) by logistic regression model was based on minimal number of the false death predictions (C) along with maximum correct death predictions (A), (D=survival prediction, B=false death prediction). We looked up in ROC report the value of P(Death=1) with maximum ratio between sensitivity and false positivity. The value P(Death=1) ≥0.256 increased the percentage of correctly classified patients on the level of 91.46%. The area under the ROC curve is 0.869. By the substitution to the next equation enables simply calculate the preliminary validated prediction. Result ≥0.256 means the prediction of the death probability 91.46%.

$$P(Death=1) = 1/(1+EXP(1.200–0.020\times TROMBO–0.448\times QUICK–0.592\times ATIII+0.228\times FBG))$$

Reference

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Response: DEATH					Sens.		False+ Spec.		
X: LOG MODEL	A	B	C	D	A/A+C	C/A+C	B/B+D	D/B+C	Cum Area
2.198709E-04	12	69	0	1	1.0000	0.0000	0.9857	0.0143	0.014286
8.559445E-02	11	21	1	49	0.9167	0.0833	0.3000	0.7000	0.671429
.170969	10	8	2	62	0.8333	0.1667	0.1143	0.8857	0.833929
.2563436	**10**	**5**	**2**	**65**	**0.8333**	**0.1667**	**0.0714**	**0.9286**	**0.869643**
.3417182	7	4	5	66	0.5833	0.4167	0.0571	0.9429	0.879762
.4270928	7	4	5	66	0.5833	0.4167	0.0571	0.9429	0.879762
.5124674	4	3	8	67	0.3333	0.6667	0.0429	0.9571	0.886310
.597842	2	3	10	67	0.1667	0.8333	0.0429	0.9571	0.886310
.6832166	2	3	10	67	0.1667	0.8333	0.0429	0.9571	0.886310

P65 A novel explanation for profound shock in meningococcal sepsis

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Background: A principle feature of Gram negative sepsis is the rapid onset of profound shock. The failure of anti-endotoxin antibodies to produce significant improvement in outcome [1] and the profound hypocalcaemia we have observed in meningococcal sepsis led us to re-evaluate the possible aetiologies of shock in Gram negative infection.

Objective: To test the hypothesis that Gram negative organisms directly or indirectly may be capable of proteolytic breakdown of albumin thus explaining in part the aetiology of shock and hypocalcaemia seen in severe Gram negative sepsis.

Methods: Urine was collected from patients with severe meningococcal sepsis (11) and from controls including patients admitted to intensive care (2) and patients with known proteinuria (4). The urine was dialysed and subjected to polyacrylamide gel electrophoresis (SDS-PAGE) and Western blotting with a sheep anti-human albumin antibody.

Albumin was incubated with lipopolysaccharide (LPS) derived from various Gram negative organisms and the incubates were subjected to SDS-PAGE to ascertain the presence of albumin degradation products. Albumin was also incubated with homogenates of cultured *Neisseria meningitidis* and again the incubates were subjected to SDS-PAGE.

Results: Multiple albumin fragments were detected in urine collected from patients with meningococcal sepsis. *In vitro* incubation of human albumin with crude LPS derived from gram negative organisms and subsequent SDS-PAGE also showed cleavage of albumin into multiple fragments. Similar *in vitro* studies with homogenates of *N. meningitidis* failed to show evidence of breakdown. No albumin cleavage products were detected in the urine of control patients.

Conclusion: This study suggests that in meningococcal sepsis there is release into the circulation of protease(s) which cleave albumin. We were not able to distinguish whether the protease action was of exogenous or endogenous origin. This may have profound significance for the treatment of meningococcal sepsis.

Reference

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P66 Continuous infusion versus intermittent administration of meropenem in critically ill patients: a pilot study

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This prospective crossover study compares the pharmacokinetics of meropenem administered by continuous infusion with intermittent administration in critically ill patients. Fifteen patients were randomized to receive meropenem either as a 2 g iv loading dose followed by a 3 g continuous infusion (CI) over 24 h or as intermittent administration (IA) of 2 g iv every 8 h (q8h). Each regimen was performed over a period of 2 days followed by a cross over to the alternative regimen for the same time. Pharmacokinetic parameters (mean ± SD) of CI included following: concentration at steady state (C_{SS}) was 11.9 ± 5.0 mg/l, area under the curve (AUC) was 117.5 ± 12.9 mg/l/h. Maximum and minimum serum concentration of meropenem (C_{max}, C_{min}) and total meropenem clearance

(Cl_{tot}) for IA were 110.1 ± 6.9 mg/l, 8.5 ± 1.0 mg/l and 9.4 ± 1.2 l/h, respectively. The AUC during IA regimen was larger than the AUC during CI ($P < 0.001$). In both treatment groups meropenem serum concentrations remained above the minimal inhibitory concentration for the most important bacterial strains all the time. We conclude that CI of meropenem is equivalent to the IA regimen and is therefore suitable for treating critically ill patients. Additionally, a CI regimen can save costs of antibiotic therapy as bactericidal serum levels can be achieved with only 50% of the amount of drug used for IA.

P67 Clearance of meropenem during continuous renal replacement therapy in critically ill patients

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Meropenem is a new carbapenem antibiotic with a broad spectrum of activity against Gram-positive and Gram-negative strains including β-lactamase producers. Thus, it is particularly useful in intensive care patients (pts) with septic complications due to unknown pathogens. The present study was conducted to evaluate the pharmacokinetic properties of meropenem in nine critically ill patients treated by continuous venovenous hemofiltration (CVVH).

All pts received one single dose of 1 g meropenem intravenously. High-flux polysulfone membranes (Diafilter-30, Amicon, Ireland) were used as dialyzer. Meropenem serum concentrations as well as filtrate aliquots were determined by high-performance liquid chromatography.

Peak serum concentrations were 28.1 ± 2.7 µg/ml, trough levels 6.6 ± 1.5 µg/ml after 6 h CVVH. The post-to-pre hemodialysis ratio was 0.24 ± 0.06, total removal was 35.8 ± 10.1% and the mean difference of meropenem concentration between arterial and venous line was 23.4 ± 4.9%. The calculated pharmacokinetic parameters were: half-life 2.3 ± 0.4 h, elimination constant 0.31 ± 0.05 h^{-1}, AUC 118.0 ± 15.8 mg/l/h and the clearance during CVVH was 49.7 ± 8.3 ml/h. No side effects were seen.

The calculated total daily meropenem requirements in these patients with acute renal failure and CVVH was 2482 ± 321 mg. Based upon these data we conclude that patients with severe infections on CVVH can be treated effectively with 1 g meropenem every 8 h.

P68 Meropenem clearance by continuous haemofiltration: a comparison of *in vivo* and *in vitro* data

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Often a new drug is licensed for use in the critically ill before its pharmacokinetic profile has been fully described. In particular information relating to the amount removed by continuous renal replacement therapies, such as haemofiltration, is sparse. This relates to the difficulties associated with patient recruitment and standardisation for *in vivo* studies. This study describes the removal of meropenem, a broad spectrum antibiotic, by an *in vitro* model of haemofiltration and compares the data with that obtained in a previous *in vivo* investigation [1]. The *in vitro* model incorporated a polyacrylonitrile membrane (Hospal, Multiflow 60) employing a blood pump (Hospal BSM22SC) to circulate carrier fluid (3.5% human albumin solution in Tyrode Ringer) around an extracorporeal circuit. Ultrafiltration rates were manipulated using a peristaltic pump attached to the ultrafiltration line. Pre-membrane, post-membrane and ultrafiltration samples were collected from the model at timed intervals, employing three different UFR rates. Meropenem concentrations were measured by HPLC and used to calculate the drugs' sieving coefficient (S) and filter clearance (FCL), using standard equations [2]. The results were then compared to values obtained from a previous *in vivo* study [1] employing a similar membrane (Hospal, Multiflow 100). A mean (± SD) S value of 0.99 ± 0.07 ($n = 13$) was calculated for the *in vitro* model for al UFR rates used which compared favourably with a mean (± SD) S of 0.95 ± 0.03 reported during the *in vivo* study, involving four patients. A significant linear correlation was seen between UFR and FCL for both *in vitro* and *in vivo* data ($r = 0.98$, $P < 0.05$ and $r = 0.90$, $P < 0.05$, respectively). The results of this study suggest that the *in vitro* model is capable of providing accurate meropenem filter clearance data. Although further validation of this model using a range of drugs is required, this preliminary work suggests that, in the absence of *in vivo* pharmacokinetic information, extracorporeal drug clearance determined using an *in vitro* model could be used to aid prescribing in patients receiving haemofiltration.

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P69 Is a single daily dose the correct way to administer ceftriaxone in intensive care patients?

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Introduction: The bactericidal activity of β-lactam antibiotics on gram-negative bacilli is related to the time that concentrations of antibiotic in tissues and plasma exceed a certain threshold. The effect is maximal and constant at relatively low concentrations (four times the MIC of the organism). The dosing regime should maintain these serum levels for the entire dosing interval, as there is no significant post-antibiotic effect. Pharmacokinetic data from healthy patients may not be adequate in the critically ill.

Objectives: To determine if the current recommended regimen for ceftriaxone maintains adequate serum concentrations for antibacterial efficacy in critically ill patients.

Methods: We administered ceftriaxone in the maximum recommended dose (2 g daily IV) to 10 intensive care patients without renal or hepatic failure. Plasma samples were taken at timed intervals over 24 h with a further trough sample taken on day 4. Ceftriaxone concentrations were measured by high performance liquid chromatography and analysis performed with Kinetica™ (Simed SA, Creteil, France).

Results: The pharmacokinetics were different to reported data in healthy subjects. Vd (20.5 l vs 11.1 l) and Cl were increased (2.4 l/h vs 1.24 l/h), resulting in a similar, but slightly prolonged $T_{1/2}$ (7.2 h vs 6.1 h). However, there was large inter-patient variability in drug concentrations (Fig. 1), and four patients had plasma ceftriaxone concentrations less than the desired four times MIC (8 μg/ml) of common gram-negative organisms found in ICUs. On day 4, trough ceftriaxone concentrations were <8 μg/ml in four patients. There was no clinical predictor of which patients would have low plasma concentrations.

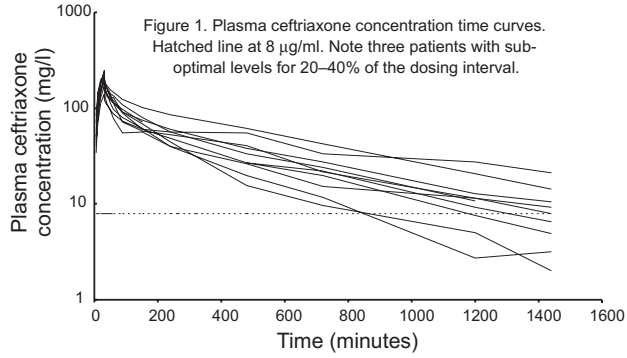

Figure 1. Plasma ceftriaxone concentration time curves. Hatched line at 8 μg/ml. Note three patients with sub-optimal levels for 20–40% of the dosing interval.

Conclusion: Because of large inter-patient variability in critically ill patients, the recommended dosing regimen for ceftriaxone may result in sub-optimal tissue concentrations and loss of bactericidal efficacy in some patients. This may be overcome by more frequent boluses or possibly by continuous infusion.

P70 Pruritus: a clinical sign we can use to detect the vasodilating effect of vancomycin

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We observed that the administration of vancomycin (V) is sometimes accompanied by pruritus, a clinical sign which appears a few minutes after the beginning of V infusion and lasts soon after V administration has been stopped. Generally it is not associated with a cutaneous rash. The aim of this study was to evaluate the hemodynamic behaviour which follows the appearance of pruritus.

Method: We studied 45 patients undergoing elective coronary surgery. The inclusion criteria consisted of stable hemodynamics without i.v. cardiovascular drugs, normovolemia and no history of anaphylactic reactions. After ECG, radial artery cannula and pulmonary artery catheter were put in place, vancomycin (15 mg/kg) was administered by a syringe pump, at a constant rate, over 30 min. The hemodynamic data were collected before the administration of V (time 1), 15 min (time 2) and 30 min (time 3) after the beginning of V infusion, and 15 min after the administration of V has been stopped (time 4). The patients were divided into two groups: group A who had pruritus during V infusion, and group B who did not. Statistical analysis was performed by ANOVA test, significant for $P < 0.05$.

Results: Group A included 17 patients, group B 28 patients. In patients of group A SVRI decreased significantly, CI increased

Times		1	2	3	4
MSP	A	85 ± 17	81 ± 21	81 ± 18	84 ± 17
(mmHg)	B	88 ± 18	88 ± 20	88 ± 21	92 ± 20
SVRI	A	2808 ± 577	2533 ± 507	2351 ± 602*	2559 ± 539
(dynes.s.cm^{-5}.m^2)	B	2654 ± 968	2780 ± 1091	2568 ± 889	2813 ± 786
CI	A	2.34 ± 0.5	2.42 ± 0.5	2.64 ± 0.5*	2.5 ± 0.4
(l/min/m^2)	B	2.67 ± 0.6	2.56 ± 0.5	2.74 ± 0.6	2.58 ± 0.5
HR	A	60 ± 11	59 ± 11	60 ± 9	58 ± 8
(beats/min)	B	65 ± 11	63 ± 12	64 ± 12	62 ± 11

MSP, mean systemic pressure; SVRI, systemic vascular resistance index; CI, cardiac index; HR, heart rate. *$P < 0.05$ versus time 1.

significantly and no change was observed in MAP and HR at time 3 if compared with time 1. In patients of group B the hemodynamic data did not change significantly at the four times of the study (Table). No patient showed a cutaneous rash throughout the study.

Discussion: The analysis of our data points out that in patients who showed pruritus during the administration of vancomycin, SVRI went down. This vasodilating effect was offset by the increase in CI. As a result MSP was well maintained. Certainly this compensation was possible because the patients studied were normovolemic. But we would like to know what would happen if pruritus appears in patients with hypovolemia? Probably the compensatory mechanism would not be so effective and hypotension could occur. We conclude that pruritus which follows the administration of vancomycin can be considered an alarm-bell indicating a condition of peripheral vasodilatation, and must lead us to evaluate the patient in order to detect the hypovolemic state and to compensate for it before continuing the infusion of vancomycin.

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P71 Acute peritonitis leads to early remote microvascular dysfunction

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Introduction: Remote organ injury, as evidenced by loss of functional capillaries and impaired microvascular function, has been demonstrated in a resuscitated normotensive 24-h chronic model of intra-abdominal sepsis [1,2]. Our objective has been to develop an acute intra-abdominal model of sepsis which can be used to observe the temporal evolution of this remote microvascular dysfunction.

Methods: Twenty-eight male Sprague Dawley rats were randomised to either sham (SH) laparotomy or modified caecal ligation and perforation (CLP) and divided into three experimental groups. Haemodynamic variables were monitored for 4-h post laparotomy in all animals. Group A ($n = 8$) provided microbiological and haematological data prior to and 4-h post laparotomy. Group B ($n = 10$) provided blood lactate data at 4-h post laparotomy. Group C ($n = 10$) proceeded to intravital microscopy of the hind limb to asses the effect of acute normotensive sepsis at 1 and 4-h on capillary blood flow in a remote organ.

Results: Data are reported as mean ± SEM. Blood and haemodyanmic data were compared between groups and by time using ANOVA (SPSS v8.0). Capillary density measurements were analyzed using Repeated Measures ANOVA (SPSS v8.0). Blood cultures from all CLP animals were positive for a combination of *E. coli*, *Proteus* and *Bacteroides*. There were no differences in haemodynamics or arterial blood gases between CLP or SH animals at different time points. However, there were significant differences in white blood cell count (WBC's), blood lactate and stopped capillary flow (CD_{stop}) density measurements between the groups (Table).

Conclusion: In this acute model of sepsis remote organ damage occurs early and is equivalent to that seen at 24 h. Therapies aimed at MODS prevention need to be commenced at the first possible opportunity.

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	SH 1 h	CLP 1 h	*P* value by group	SH 4 h	CLP 4 h	*P* value by group
WBC's $\times 10^9$/l	9 ± 1.72 $n=4$	8.1 ± 1.15 $n=4$	0.5	6.2 ± 1.83 $n=4$	2.8 ± 0.18 $n=4$	0.008
Lactate mmol/l	–	–	–	1.4 ± 0.4 $n=5$	2.5 ± 0.7 $n=5$	0.027
CD_{stop} caps/mm	2.5 ± 0.6 $n=5$	3.4 ± 1.02 $n=5$	0.3	2.78 ± 0.6 $n=5$	6.6 ± 1.03 $n=5$	0.028

P72 Does transforming growth factor-β inhibit nitric oxide synthesis and prevent septic shock?

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Objective: We measured nitrite/nitrate (NOx) levels and transforming growth factor beta (TGF-β) levels in septic shock, and assessed these factors during the onset of shock.

Patients: Twenty-two patients with sepsis not complicated by shock and 23 patients with septic shock.

Measurements and main results: NOx levels were significantly higher in the septic shock group than in the sepsis-alone group.

NOx levels were significantly higher in the group that died than in the group that survived. TGF-β levels were significantly higher in the sepsis-alone group than in the septic shock group. TGF-β levels were significantly higher in the group that survived than in the group that died. Twenty-one (80.8 %) of the 26 patients with NOx levels of 92.9 µmol/l or more (mean + standard deviation in the sepsis group without shock) had sepsis complicated by shock, as opposed to only 2 (10.5%) of the 19 patients with NOx levels below 92.9 µmol/l, and the rate of occurrence of shock as a complication of sepsis was significantly higher when the NOx level was 92.9 µmol/l or more. Two (12.5%) of the 16 patients with TGF-β levels of 19.3 ng/ml or more (mean + standard deviation in the septic shock group) had sepsis complicated by shock, versus 21 (72.4%) of the 29 patients with TGF-β levels below 19.3 ng/ml, and the rate of occurrence of shock as a complication was significantly higher among the patients with TGF-β levels below 19.3 ng/ml. There was a significant negative correlation between NOx levels and TGF-β levels.

Conclusion: NO is involved in the pathogenesis of septic shock. TGF-β appears to inhibit NO production, and may act to prevent septic shock.

P73 Albumin clearance in the endotoxemic rat after administration of *N*ω-nitro-L-arginine methyl ester (L-NAME)

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Introduction: Endotoxin (LPS) is a powerful activator of the inducible nitric oxide (NO) synthase. Whereas NO seems to be one factor behind the decreased responsiveness of the circulation to adrenergic stimulation in septic shock, the role of NO in increased vascular permeability is less clear. In a former study [1] we have shown that although NO production increased after LPS there was no increased extravasation of albumin in a wide variety of rat tissues examined; on the contrary clearance was decreased in the entire gastrointestinal tract. In this study tissue extravasation was examined after administration of the nitric oxide synthase inhibitor L-NAME.

Methods: Anaesthetised Wistar rats were given *E. coli* lipopolysaccharide (LPS) 3 mg/kg i.v. and were studied for 5 h. Mean arterial pressure (MAP) and heart rate (HR) were recorded. As an indicator of NO production methemoglobin (metHb) was measured in the beginning and end of experiments. 2 h after LPS a bolus of L-NAME 100 mg/kg, or saline, was given i.v. The tissue clearance of albumin was studied over the last 2 h of the experiment by means of a double isotope method [2].

Results: In response to LPS all rats had a drop in MAP. After administration of L-NAME ($n = 7$) MAP increased significantly as compared to controls ($n = 8$). MetHb increased during experiments in controls but not in NAME-treated rats. Tissue plasma clearance for albumin increased in the NAME-group in skin, skeletal muscle and heart and decreased in testes as compared to controls.

Discussion: We have shown an increased production of NO after LPS and the dose of L-NAME administered abolished this. No differences in gastrointestinal albumin clearance were detected between groups, however in heart, skeletal muscle and skin albumin extravasation was increased. We conclude that this is most likely due to changes in regional hemodynamics with locally increased capillary pressures leading to increased albumin filtration in certain tissues only. In the majority of tissues no differences were found.

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P74 Loss of erythrocyte deformability during systemic sepsis is prevented by nitric oxide synthase inhibition

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Introduction: 'Rigid' red cells in sepsis are thought to play a role in multiorgan failure by plugging the microvasculature and compromising oxygen delivery. During sepsis endogenous nitric oxide (NO) production is increased. What effect this has on erythrocyte deformability (RBCd) is unclear. We report the effects on RBCd and capillary blood flow when NO overproduction was prevented in septic rats.

Methods: Acute sepsis was induced in Sprague-Dawley rats via cecal ligation and perforation (CLP). At 2 h post CLP, aminoguanidine (AG), a selective inducible nitric oxide synthase inhibitor was infused (i.v. 60 mg/kg/h) to maintain baseline NOx levels. Capillary blood flow in the EDL skeletal muscle was filmed using intravital video microscopy. Plasma NOx (NO_2^-/NO_3^-) levels were measured by chemiluminescence and deformability was assessed by membrane displacement, using the micropipette aspiration technique.

Results: At 6 h, an increase in plasma NOx of 260% ± 46 SEM in CLP animals was associated with a 12% ± 1.6 SEM loss in red cell deformability and a twofold increase in stopped flow capillaries ($P < 0.05$, relative to Sham). Infusion of AG prevented the increase in NOx, the loss of deformability and the increase in stopped capillary flow, ($P < 0.05$). In sham rats, AG augmented RBCd ($P < 0.05$), but had no effect on stopped flow.

Conclusion: Eliminating nitric oxide overproduction in septic rats was associated with preventing 1) the loss of red cell deformability and 2) the increase in stopped capillary blood flow, resulting in the maintenance of the microvascular circulation.

P75 Nitric oxide synthase activities in white blood cells of septic patients

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Introduction: The bulk of data that links inducible nitric oxide synthase (iNOS) activity to the pathophysiology of sepsis originates in animal studies. However, the role of iNOS in human sepsis is controversial. Therefore, we measured in this pilot study iNOS activity in inflammatory cells from septic ICU patients compared to normal controls.

Methods: Blood samples from 5 ICU patients with clinically and bacteriologically documented sepsis, and from four healthy volunteers were centrifuged to separate the plasma/buffy coat. The buffy coat was layered onto Histopaque 1077 and centrifuged at 400 g to finally isolate white blood cells (WBCs). Constitutive (cNOS) and iNOS activities were analyzed in WBCs by the [^{3}H] L-arginine-L-citrulline assay and measured in Units (pmol L-citrulline evolved/min/mg protein). The metabolic end-products of nitric oxide (nitrite/nitrate; NO_x^-) were also determined in plasma from these subjects by chemiluminescence.

Results: Plasma NO_x^- levels were elevated in septic compared to control subjects (208 ± 107 vs 26 ± 7 μmol/l, respectively).WBCs from septic patients exhibited low cNOS activities (0.1 ± 0.1 vs 1.0 ± 0.6 Units for controls). iNOS activity from the septic WBCs was elevated, compared to controls (3.1 ± 1.8 vs 0.5 ± 0.3 Units, respectively).

Conclusion: This pilot data suggests, that consistent with the plasma accumulation of nitric oxide metabolites, inflammatory cells of septic humans produce high levels of iNOS compared to healthy controls while cNOS production is suppressed. These findings support the theory that iNOS has an important role in the pathogenesis of human sepsis.

P76 PLA_2 antagonists suppress inducible nitric oxide synthase and inducible cyclooxygenase in lipopolysaccharide-induced Raw264.7 cells

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Phospholipase A_2 (PLA_2) regulates eicosanoids and platelet activating factor production and plays an important role in regulating critical mediators in inflammatory diseases. PLA_2 activity is significantly enhanced during sepsis and multiple organ failure and therefore offers an intriguing target in developing anti-inflammatory drugs. We have identified several kinds of biflavonoids with inhibition of PLA_2 activity, which are isolated from plant sources, as potential putative anti-inflammatory and anti-septic agents. Two of them (bilobetin and ginkgetin) potently inhibit several kinds of type II 14 kDa PLA_2 but exhibits a weaker inhibition of type I 14 kDa PLA_2 using 2-linol-[1-^{14}C]PE as substrate. These inhibitors have been tested for their ability to inhibit the production of TNF-α and the formation of two enzymes, inducible NO synthase (iNOS) and inducible cyclooxygenase (COX-2) using LPS-stimulated Raw264.7 macrophages as assay systems. In the Raw264.7 cells, bacterial LPS induced the protein of COX-2 and iNOS as well as TNF-α release. The inhibitors consistently inhibited the production of TNF-α in a dose-dependent manner. The inhibitory effect of TNF-α was observed at concentrations similar to those related by PLA_2. Moreover, treatment of cells with bilobetin and ginkgetin inhibited nitrite production, one of the stable end products of NO production measured in culture supernatants. The inhibition of NO products is caused by decreased iNOS protein levels as assessed by immunoblotting using a specific anti-iNOS antibody. The inhibitors treatment also reduce the expression of COX-2 protein level to about 80% in LPS-stimulated cells, which coincided with reduction of the iNOS protein. These results suggest that inhibition of PLA_2 and subsequent metabolism of arachidonic acid by COX-2 contribute to LPS-induced NOS pathway including TNF-α in Raw264.7 cells and these two inhibitors may develop as useful agents for anti-inflammation.

P77 Fusidin down-regulates the production of IL-6 in septic patients: a pilot study

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Septic shock is characterized by pathophysiological derangements in the function of multiple organs. Many of the manifestations of shock have been related to high levels of circulating cytokines. Fusidic acid is an antiotic with a tetracyclic structure. Its chief clinical use is in the treatment of staphylococcal infections. It has been proposed, that the acid form as well as the sodium salt of the drug (Fusidin) possess antiinflammatory properties.

Aim: The present pilot study was carried out to test the hypothesis that fusidin downregulates the production of pro- and anti-inflammatory cytokines in septic patients. The study was approved by the Regional Ethical Committee and informed consent was obtained from each patient or a close relative.

Material and methods: Five consecutive septic patients received fusidin 500 mg × 3 i.v. for 1 day. Blood samples were drawn two times before fusidin administration, six times during the 24 h where fusidin was given and 24 h after the last dose. The pro-

inflammatory cytokines IL-1a, IL-1b, TNFα and IL-6 and the antiinflammatory cytokines IL-10 were analysed using ELISA.

Results: Three females and two males were included. age 21–72 years (range). APACHE II score 13–24 (range). Two patients died in the ICU. No clinical or biochemical side effects were seen in relation to fusidin administration.

The proinflammatory cytokines IL-1b, TNFα and IL-6 and the antiinflammatory cytokine IL-10 were detectable in peripheral blood in al patients while IL-1a was undetectable. Treatment with fusidin was associated with a decline in plasma concentrations of IL-6 from 183 (78–293) to 116 (67–406) pg/ml 12 h later (median values with range) ($P < 0.05$). No changes occurred in the other cytokine levels. The measured cytokines were characterized by large interindividual variations.

Discussion: The results from this pilot study provide further *in vivo* evidence for the antiinflammatory properties of fusidin. Fusidin may be useful in the management of the systemic inflammatory response in septic patients.

P78 Human vascular endothelial cells produce TNF-α after stimulation with proinflammatory cytokines

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Vascular endothelial cells are one of the main targets of tumor necrosis factor α (TNF-α) action. We studied whether these cells are capable of producing TNF-α after stimulation with proinflammatory cytokines and bacterial lipopolysaccharide (LPS).

Human umbilical vein endothelial cells (HUVECs) were incubated with interferon-γ (IFNγ) interleukin β (IL-β), and LPS, or their different combinations for 2–48 h. TNF-α was measured by time-resolved immunofluorometric assay. Unstimulated HUVECs did not produce detectable amounts of TNF-α but IFNγ IL-β and LPS in combination induced TNF-α production in a time-dependent manner. Immunofluorescent staining confirmed that the TNF-α was synthesized by endothelial cells. IFNγ IL-β or LPS alone did not induce TNF-α production, whereas IFNγ and IL-β in combination induced TNF-α production, which was further increased with LPS. TNF-α messenger-RNA expression was detected with RT-PCR in stimulated, but not in unstimulated HUVECs.

Human vascular endothelial cells are capable of producing TNF-α after proinflammatory cytokine stimulation, and may therefore contribute to the increased amount of TNF-α found in states like cachexia and septic shock.

P79 Cytokine plasma levels during weaning in critically ill patients with sepsis

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Introduction: Poor muscle functions play a pivotal role in developing ventilator dependency after long term ventilatory support and studies have shown that sepsis may be associated with decreased muscle contractility. The aim of the study was to evaluate plasma levels of TNF alpha, IL-8 and sIL-2R during ventilatory support and weaning.

Methods: After institutional approval 40 critically ill patients were prospectively studied during ventilatory support and weaning, three patients due to death were excluded. All patients were weaned according to standard weaning protocol. Blood samples were drawn daily and collected until analysis. Apache II score, organ failure score (Goris), sepis organ failure assessment score (SOFA), ventilatory days and 'weaning' days were recorded. After successful weaning patients were divided in two groups according to the length of weaning (W): group S (W ≤3 days, $n = 15$), group L (W >3 days, $n = 22$). TNFα, IL-8 and sIL-2R serum levels were selected and measured at the time of admission (T1), on the last day of full ventilatory support (T2), on the day when weaning was started (T3) and on the first day of spontaneous ventilation (T4). Values are expressed as a mean ± SD (or median and 25th and 75th percentiles), *t*-test or Mann Whitney Rank Sum test were used for statistical analysis (SigmaStat, Jandel Co., USA), $P < 0.05$ was considered statistically significant.

Results: Total ventilatory and weaning days were 9.6 ± 4.8 resp. 1.7 ± 0.7 in group S and 24.6 ± 11.3 resp. 9.0 ± 3.7 in group L. Selected results (TNFα and IL-8 in pg/ml) are presented in the Table:

	T1	T2	T3	T4
Group S – TNFα	11.6(5.6)	7.72 (7.7)	4.39 (6.1)	0
Group L – TNFα	10.1 (8)	10.8 (5.8)	6.7 (6.0)	6.8 (6.0)*
Group S – IL-8	63.7 (38–81)	35.9 (0–66)	0 (0–30)	0 (0–0)
Group L – IL-8	45.7 (34–67)	62.7 (42–102)**	42.7 (26–56)***	30.5 (0–43)§

TNF – mean (SD), IL-8 – median (25%–75%), *P=0.002, **P=0.021, ***P=0.011, §P=0.001

Discussion: Serum TNFα and IL-8 levels were significantly higher and persisting in patients with prolonged ventilatory support. This suggests that these mediators may also be involved in ventilatory failure leading to difficult weaning after long term mechanical ventilation.

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P80 Cytokines and sepsis

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Introduction: Being sepsis a clinical syndrome with a very high mortality rate, this led us to the effort of monitoring some cytokines as potential diagnostic and prognostic serum markers.

Methods: In 1998 a prospective study was initiated, consisting at the moment in 24 patients, with diagnostic criteria for SIRS (Systemic Inflammatory Response Syndrome), sepsis and/or MODS (Multiple Organ Dysfunction Syndrome). The soluble serum cytokines – TNFα, IL-1β, IL-6, IL-8 and TGF-1β – were measured by a solid phase immunoassay method (RD Systems – CITOMED PORTUGAL) based on a previously established protocol. The blood samples were immediately separated in aliquots (3/cytokine) and frozen in sterile tubes at minus 70°C. Every sample of all the patients were simultaneously analysed for each cytokine, duplicated and performed by the same technician, having as references the maximum values of a healthy population.

Results: Amongst the 24 patients studied, 16 presented IL-6 >300 pg/ml. High concentrations of IL-8 and TNFα were also observed, but these were not uniformly coincident with the former. Two of these patients survived, being those in whom we were able to interfere with the cytokine profile. The 7 patients with SIRS, presented relatively low concentrations of cytokines, having one of them died. TNFα and IL-8, sometimes in very high concentrations, do not correlate with any particular organic dysfunction. IL-1β and TGF-1β always presented low values, close to the detection limits, in all of the patients.

Discussion: The high concentrations of IL-6 (the 'black smoke'?), revealed a homogenous correlation with the clinical severity, thus making it a useful diagnostic and prognostic serum marker. The rapid knowledge of the cytokine profile is important for intervention in the mechanisms, which lead to multiple organ failure. The relation of some cytokines with particular organ dysfunction, such as ARDS and cardiac failure, as well as the influence of presently known and future anti-cytokine strategies, remains to be evaluated.

P81 The perioperative course of C1-esterase-inhibitor: evidence for an early deficiency

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Objective: Since the extent of complement- and contact-activation and a low functional index of their main inactivator C1-esterase-inhibitor (C1-INH) are related to outcome in sepsis, a relative deficiency of C1-INH might contribute to the development of fatal complications. At present few data on the periperative course of C1-INH plasma levels have been published. In our study the early perioperative course of C1-INH in relation to the acute phase protein interleukin-6 (IL-6) was investigated in order to assess one possible important aspect of the balance between anti- and proinflammatory mediators.

Methods: In 19 consecutive patients undergoing elective oropharynx tumorresection functional C1-INH was measured by chromogenic substrate assay Berichrom® C1-Inactivator, the total quantity by single radial imunodiffusion assay NOR-Partigen® and cytokine IL-6 levels by MEDGENIX IL-6-45MIN-EASIA. Samples were taken before operation (t1), on ICU admission (t2) and on the first postoperative day (t3).

Results: The mean operation time was 9 h (range: 4:05 to 14:40 h) and all patients showed an uncomplicated ICU course up to 86 h.

Mean ± sd	t1	t2	t3
C1-Inh, functional (%)	105 ± 20	92 ± 20	102 ± 24.7
C1-Inh, antigenic (mg/l)	105 ± 29	87 ± 18	98 ± 28
IL-6 (pg/ml)	52 ± 84	326 ± 380	192 ± 133

IL-6 levels increased from t1 to t2 ($P < 0.01$), whereas C1-INH functional levels declined tendencially and antigenic levels dropped ($P = 0.024$). Levels of C1-INH at t3 returned to preoperative values and IL-6 declined.

Conclusion: As expected (postoperative agression syndrome) IL-6 increased significantly. Surprisingly, plasma levels of the anti-inflammatory acute phase protein C1-INH remained normal or even declined. On the first postoperative day C1-INH and IL-6 levels tended to return to preoperative values. This was associated with uncomplicated clinical course. We suggest, that this short period of disproportion between pro- and anti-inflammatory mediators may increase the 'second hit' risk, if it is longer lasting.

P82 Changes in serum cytokine levels during induced whole body hyperthermia

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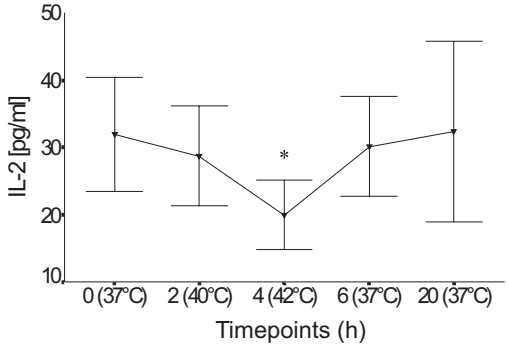
Background: Recent data from our laboratory demonstrated a significant decrease in the number of circulating T helper cells and monocytes as well as in the expression of IL-2 receptors on T cells during induced whole body hyperthermia [1,2]. The aim of further investigations was to analyze the influence of these effects on the function of TH1 cells, TH2 cells and monocytes. Therefore, we measured the levels of IL-2, IL-4, IL-6 and IFN-γ in the blood of cancer-patients, undergoing whole body hyperthermia of 42°C. This is used as part of so called 'systemische Krebs-Mehrschritt-Therapie' (sKMT) in our clinic.

Methods: Cytokine levels of 9 patients were measured by an ELISA technique. Blood samples were obtained before beginning of therapy at 37°C, at 40°C, at the end of the plateau of 42°C, at 37°C again, as well as after 20 h (on the next morning). Time between the first four investigations was about 2 h. Cytokine levels were compared by using a Wilcoxon rank sum test.

Results: We found a reversible, significant decrease ($P = 0.017$) of IL-2 at 42°C (Fig. 1), whereas the levels of IL-4 and IFN-γ decreased slightly (data not shown). In contrast, IL-6 showed a sustained increase ($P = 0.008$) during and after therapy which returned to baseline after 20 h (Fig. 2).



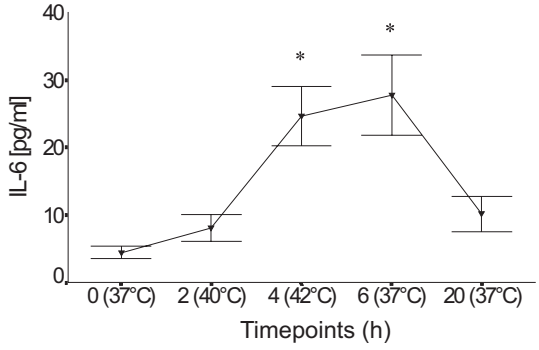


Figure 1–2. IL-2 (Fig. 1) and IL-6 levels (Fig. 2) during induced whole body hyperthermia. Data are presented as mean-values with SEM.

Conclusion: Despite a similar decrease in the number of both circulating T helper cells and monocytes, there seems to be a different change in the function of these cells during whole body hyperthermia up to 42°C. IL-2, which is postulated to be mainly produced in TH1 cells, decreased significantly; IL-4 and IFN-γ, mainly produced in TH2 cells, decreased slightly and IL-6, one of the main products of monocytes, showed a significant increase. Further investigations are necessary to verify these results.

Acknowledgement: Supported by: Deutsche Krebshilfe, Deutsche Forschungsgemeinschaft (SFB 331, GraKo 273)

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P83 Influence of mild hypothermia on cytokine gene expression in the culture of human mononuclear cells

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Crit Care 1999, **3 (suppl 1)**:P83

Introduction: Clinical studies demonstrated that moderate hypothermia may improve neurological outcome after severe head injury. On the other hand hypothermia is associated with increased incidence of infection complications. Recent studies suggest that mild hypothermia directly impaires natural host defenses – leukocyte mobility, phagocytosis and reactive oxygen species production and antibody production.

Methods: In order to investigate influence of mild hypothermia on cytokine gene expression human peripheral blood mononuclear cells (PBMC) were cultivated at normothermic (37°C) and hypothermic (33°C) conditions ($n = 3$). Additionaly parallel cultures were stimulated with phytohaemagglutinin (PHA). Multiple cytokine mRNA expression in the cultures of PBMC was estimated using reverse transcriptase-polymerase chain reaction (RT-PCR).

Results: Our findings demonstrated that moderate hypothermia (33°C) did not alter the basic levels of IFN-γ, TNF-α, IL-1α, IL-2 and IL-10 mRNA expression in PBMC, but significantly inhibited increase in IL-2 mRNA expression caused by PHA stimulation.

Conclusion: These data strongly suggest that cytokine expression in stimulated human leukocytes can be affected by hypothermia. IL-2 is one of the key cytokines of immune response. It is known to stimulate growth and differentiation of T cells, B cells, NK cells, LAK cells, monocytes and macrophages. Hence, inhibition of IL-2 mRNA expression in PHA-stimulated PBMC by hypothermia can partially explain increased risk of infections in hypothermic patients.

P84 Influence of temperature during cardiac operations on myocardial apoptosis

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Crit Care 1999, **3 (suppl 1)**:P84

Objectives: To investigate the influence of temperature (T°) during cardiopulmonary bypass (CPB) on induction of myocardial apoptosis.

Methods: Eighteen pigs were assigned to a T° group during CPB: 37°, 28° and 20°C, respectively ($n = 6$ each). Duration of CPB was 120 min and aortic clamping 60. Cardioplegia was achieved with a single dose of Bretschneider solution (4°C; 30 ml/kg). TNF-α was determined by a pig specific ELISA. Six hours post-CPB, tissue probes of the heart were taken for standard- and immunohistochemistry examinations. Apoptotic cells were detected by an *in situ* apoptosis detection kit (TUNEL).

Results: TNF-α production during and after CPB was significantly higher in group 37°C than in group 20°C. There was no TNFα production in group 28°C. Histological examination showed that the most important myocardial tissue damage in terms of intertitial edema, leukostasis and necrosis was seen in group 37°C followed by group 20°C while the least important damage was present in group 28°C. There was significantly lesser degree of apoptosis of myocardial cells in group 37°C than in both hypothermic groups.

Conclusion: Hypothermia during CPB induces a reduction of the systemic release of TNFα production and also of myocardial tissue damage. This could be due to increased apoptosis seen in the animals operated on in hypothermia. Apoptosis during cardiac operations could be in part responsible for the protective role of hypothermia.

P85 Intestinal ischemia and reperfusion: beneficial effects of a platelet activating factor antagonist

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Crit Care 1999, **3 (suppl 1)**:P85

Gut barrier dysfunction in conditions associated with intestinal ischemia and reperfusion (I/R) might contribute to the further development of multiple organ dysfunction. The present study evaluates the effects of platelet activating factor (PAF) antagonist in intestinal I/R injury.

Methods: Intestinal ischemia was induced by clamping of the superior mesenteric artery for 40 min followed by 12 h reperfusion. 15 min after the end of ischemia, the rats received intraperitoneal injections of saline or the PAF antagonist lexipafant (5 mg/kg), repeated after 6 h in the groups subjected to 12 h reperfusion. Myeloperoxidase (MPO) content in the small intestine, serum levels of interleukines-1 and 6, plasma protease inhibitors and intestinal endothelial and epithelial permeability were assesed.

Results: Intestinal I/R resulted in intestinal barrier dysfunction with pronounced plasma leakage to the intestinal lumen. A protely plasma activity was evident. MPO content significantly increased as did levels of interleukines. Treatment with the PAF inhibitor partly, though not fully, restored the changes caused by I/R.

Conclusion: PAF seems involved in the release of cytokines and consumption of protease inhibitors following intestinal I/R and the associated impairment of intestinal barrier integrity. Treatment with a PAF antagonist was effective in restoring changes caused by I/R, though not reaching normal levels.

P86 Platelets and platelet-activating factor acetylhydrolase in septic patients

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Crit Care 1999, **3 (suppl 1)**:P86

Introduction: Platelet-activating factor (PAF) and its inactivating enzyme PAF-acetyl-hydrolase (PAF-AH) are implicated in the development of sepsis and its sequela septic shock. It has been shown that the administration of *r*PAF-AH has a beneficial effect on the outcome of sepsis in animals as well as in humans.

Methods: We measured PAF-AH activity daily in 2586 plasma samples that were obtained from 240 patients admitted to our intensive care unit. Patients were screened daily for sepsis according to ACCP/SCCM criteria, and PAF-AH activities were analysed in relation to severity of sepsis and to whole blood platelet count as an indicator of platelet activation and consumption.

Results: PAF-AH activity was positively correlated to the severity of disease, but was proved to be a poor sepsis marker, when compared to others, such as neopterin, TNFα, procalcitonin etc. In patients with septic shock a low PAF-AH activity (<2.00 µmol/ml/h) could indicate a high mortality risk. Only 4 patients met these criteria, but all died. Platelet count was highest in patients with uncomplicateted sepsis, but dropped dramatically in septic shock. The overall correlation between PAF-AH and platelet count was relatively poor ($r = 0.266$), but remarkable differences were observed between patients with PAF-AH activities <2.00 or >5.00 µmol/ml/h, resp.: 125 (70/112) × 10^8/ml versus 280 (206/388) × 10^8/ml; $P < 0.0001$.

	No infection	SIRS	Sepsis	Septic shock
PAF-AH* (μmol/ml/h)	2.41 (1.76/3.24)	2.81 (2.06/3.67)	2.90 (2.32/4.26)	3.31 (2.12/4.49)
platelet count* (10^8/ml)	1.69 (1.01/2.78)	2.20 (1.31/3.53)	2.46 (1.37/3.51)	1.05 (0.54/127)

*Data are given as median with 25th and 75th percentiles.

Conclusion: Our data provide further evidence that PAF-AH has a beneficial effect in sepsis and that it can prevent platelet activation and sequestration which is known to contribute to multiple organ failure.

P87 Hypertonicity induces shedding of L-selectin: a role for p38 activation

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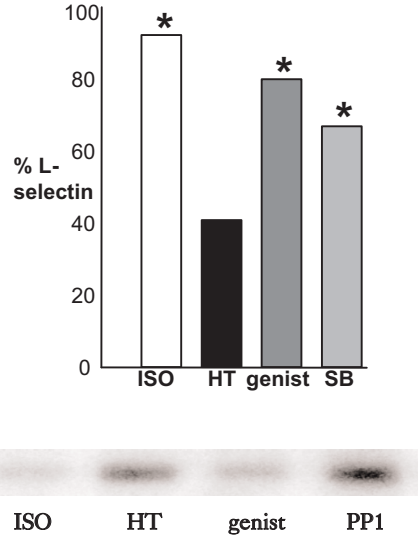
Crit Care 1999, **3 (suppl 1)**:P87

Hemorrhagic shock predisposes to adult respiratory distress syndrome, which frequently results in prolonged ICU stay and carries a 50% mortality. We have previously shown that resuscitation with hypertonic saline (NaCl 7.5%) attenuates the post-hemorrhage lung injury by preventing neutrophil (PMN) sequestration. This beneficial effect was due to multiple effects on PMN function and included shedding of the PMN adhesion molecule L-selectin. The aim of the present study was to investigate the signalling pathway underlying this immunological effect. Isolated human PMN were treated with either iso (290 mOsm) or hypertonic (500 mOsm) medium, for up to 2 h. Hypertonicity induced extensive tyrosine phosphorylation in multiple bands. The broad-spectrum inhibitor genistein, abrogated this effect and concomitantly prevented the hypertonic (HT) shedding of L-selectin (graph). In order to characterize the tyrosine kinases involved in this process, we investigated which kinases were phosphorylated upon shrinkage, and then whether pharmacological inhibition prevented shedding. We found that the non-receptor tyrosine kinases Syk, Pyk-2 and the Src-family kinase Hck were strongly phosphorylated upon shrinkage. However, PP1, a Src-family inhibitor, prevented their phosphorylation but not the HT shedding of L-selectin, suggesting that this effect is independent of Src activation. Next, we found that the p38 was activated upon hypertonic shrinkage in a genistein sensitive but PP1 insensitive way.

Moreover, the inhibition of p38 activation by SB203580 significantly reduced the HT shedding suggesting that p38 is involved in this process (graph). The LPS- and FMLP-induced shedding of L-selectin was also abrogated by SB203580. THUS: Hypertonicity



induces a unique pattern of tyrosine phosphorylation in human neutrophils, involving a variety of kinases, most Src-dependent. However, the hypertonic shedding of L-selectin seems to be selectively coupled to p38 activation. In fact, p38 appears to be a central mediator of L-selectin shedding induced by various stimuli. Hypertonicity-induced, p38-mediated L-selectin shedding appears to have an important role in the beneficial immune modulatory effect of hypertonicity, preventing neutrophil lung sequestration and cell-mediated tissue damage.

P88 No correlation between serum levels of intercellular adhesion molecules (s-ICAM) and acute renal dysfunction following coronary-artery bypass grafting (CABG)

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Crit Care 1999, **3 (suppl 1)**:P88

Introduction: Acute renal dysfunction is a common postoperative complication of CABG. Extracorporeal circulation induces an inflammatory response, causing the release of adhesion molecules by endothelial cells and leukocytes. These adhesion molecules are incriminated in the pathophysiology of renal dysfunction, but their relative importance is unknown. We investigated the relationship between levels of s-ICAM and renal dysfunction following CABG.

Methods and materials: Eighteen consecutive patients undergoing elective, uncomplicated CABG were included. Exclusion criteria were: preoperative creatinine clearance <50 ml/min, age >80 years, hypotension >1 h (MAP <60 mmHg), and congestive heart failure (NYHA III-IV). s-ICAMs were measured by RIA (in ng/ml); (a) 10 min prior to anaesthesia, (b) 2 min after aortic clamp release, (c) at admission to ICU, (d) 4, (e) 8, (f) 12, and (g) 16 h postoperatively, and corrected for haemodilution. Serum creatinine levels (sCr) were measured (a) 10 min prior to anaesthesia, (b) the first, and (c) third postoperative day, and corrected for haemodilution;

renal dysfunction was defined as a rise in sCr of >25% over baseline value. Mean levels of s-ICAM of the group of patients with (group I) and without (group III) postoperative renal dysfunction are compared at each time interval. Statistical analysis is performed by Student's *t*-test.

	n	A	B	C	D	E	F	G
Group I	8	67.4	53.8	43.9	60.1	81.2	70.8	91.5
Group II	10	68.3	45.8	43.6	54.1	73.4	67.0	84.9
P value		0.71	0.44	0.82	0.77	0.47	0.72	0.94

Results: Postoperative renal dysfunction is observed in eight patients. A comparison of mean s-ICAM (in ng/ml) of both groups is in the Table, differences are not statistically significant.

Conclusion: These results do not support a (major) role for s-ICAM in the pathophysiology of acute renal dysfunction following CABG.

P89 Procalcitonin is released by human monocytes

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Crit Care 1999, **3 (suppl 1)**:P89

Introduction: Procalcitonin (PCT), the precursor of calcitonin, was recently forwarded as a diagnostic marker of systemic bacterial infection and sepsis. Previously we have demonstrated that PCT is expressed in human peripheral blood mononuclear cells (PBMC). Aim of this study was to estimate wether PCT could be released by monocytes in culture medium.

Methods: PBMC were prepared from heparinized venous blood samples from healthy volunteers and septic patients (according to ACCP/SCCM consensus conference criteria) by density gradient centrifugation. Monocytes were obtained by differential adhesion to plastic surface and cultivated for 12 h with or without 10 µg/ml lipopolysaccharide *E. coli B4*. Supernatants were analyzed for PCT content by commercially available Lumitest® kit (B.R.A.H.M.S, Berlin).

Results: In contrast to monocytes from septic patients, monocytes from healthy volunteers did not release PCT at detectable levels (<0.1 ng/ml) under control conditions. LPS-stimulation lead to readily detectable levels of PCT both in the supernatants of healthy and septic patient monocyte cultures. In comparison to monocytes from healty volunteers monocytes from septic patients released significantly more PCT after LPS stimulation

Conclusion: Our data demonstrate for the first time that PCT can be released by human monocytes. Furthermore LPS, a key mediator of septic sequelae, can significantly increase the PCT release.

P90 Intracellular distribution pattern of procalcitonin in human monocytes and HepG2 cells

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Crit Care 1999, **3 (suppl 1)**:P90

Introduction: Procalcitonin (PCT), the precursor of calcitonin, was recently forwarded as a diagnostic marker of systemic bacterial infection and sepsis. Previously we have demonstrated that PCT is expressed in human peripheral blood mononuclear cells (PBMC). Preliminary experiments indicated a PCT expression in HepG2 cells, too. Because of several homologies with cytoskeletal elements of PCT amino acids sequence we investigated the basal expression and distribution pattern of PCT in human monocytes and HepG2 hepatoma cells.

Methods: PBMC were prepared from heparinized venous blood samples from healthy volunteers by density gradient centrifugation. Monocytes were obtained by differential adhesion to plastic surface and cultivated up to 24 h. HepG2 human hepatoma cells were incubated under standard conditions. For the experiments cell lysates were used or cellular proteins were divided in cytoplasmatic, microtubular, nuclear-microfilamentous, and resulting pellet fraction. These protein fractions were analyzed by Western blot using monoclonal anti-calcitonin or anti-katakalcin (Lumitest®, B.R.A.H.M.S, Berlin) or polyclonal anti-human calcitonin (Natutec, Frankfurt/M.) antibodies. For secondary immunofluorescence cells were fixed and incubated with the same antibodies used in western blotting.

Results: As verified by Western blotting and secondary immunofluorescence human monocytes and HepG2 hepatoma cells express PCT in association with cytoskeleton. The content of PCT seems to be higher in monocytes than in HepG2 cells. No PCT was found in cytoplasmic fraction.

Conclusion: We demonstrated for the first time an association of PCT with cytoskeletal components. Because of the high content of PCT in human monocytes it could be speculated that PCT has some intracellular physiological function outside systemic inflammation that have not been yet determined.

P91 Downregulation of procalcitonin in mechanicaly ventilated patients

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Crit Care 1999, **3 (suppl 1)**:P91

Introduction: Procalcitonin (PCT) has recently attracted attention as a possible marker of the systemic inflammatory response to

infection. Downregulation of PCT in healthy human subjects after repetitive injection of endotoxin has been published. This effect was not investigated in critical ill patients so far.

Methods: We obtained serum levels of Procalcitonin (PCT) in 14 consecutive patients with long term mechanical ventilation (30–150 days (65.0 ± 2.6 [Mean ± SEM])). All patients experienced at least two severe systemic infections. Conventional markers of infection (C-reactive proteine, fibrinogen, white blood cell count and body temperature) as well as microbiological screening was performed simultaneously.

Results: A marked rise of PCT over 2.0 ng/ml could be observed in 7 patients (group 1) in response to severe infection. On admission on ICU these patients presented PCT serum levels between 0.24 and 25.4 ng/ml (6.8 ± 1.3 [Mean ± SEM]). The remaining 7 patients (group 2) had PCT levels between 1.1 and 147.6 ng/ml (17.5 ± 7.4 [Mean ± SEM]) on admission. Recurrent microbiologically and clinically proved severe infections were not accompanied by increased levels of PCT. The mortality in group 1 was significantly lower than in the second group (43% vs. 100%) [$P < 0.05$, Chi-Square-Test].

Conclusions: Our data suggest a downregulation of PCT levels in critically ill patients. Lacking rise of PCT serum levels with recurrent severe infections seems to be associated with high mortality. The predictive value of PCT for severe infections might be impaired by this mechanism. Further studies are required to verify these findings and to explain the potential reasons for failure of PCT in detection of recurrent infections of some patients in ICU.

P92 Procalcitonin is a good marker for the diagnosis of infection and the severity of illness in patients with SIRS

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Crit Care 1999, **3 (suppl 1)**:P92

To understand the presence or absence of bacterial infection in patients with systemic inflammatory response syndrome (SIRS), the level of procalcitonin (PCT), a precursor of calcitonin, was determined. Subjects consisted of 14 SIRS patients without complication by bacterial infection, 14 SIRS patients complicated by sepsis, and 14 SIRS patients complicated by severe sepsis and septic shock. PCT levels in SIRS patients with sepsis (2.9 ± 2.3 ng/ml) were significantly higher than those in SIRS patients without complication by infection (0.7 ± 1.1 ng/ml). However, there were no significant differences in the levels of C-reactive protein (CRP), interleukin 6 (IL-6) or tumor necrosis factor-α (TNF-α) between the two groups. PCT levels in SIRS patients with severe sepsis and septic shock (172.2 ± 276.3 ng/ml) were significantly higher than those in SIRS patients with sepsis. Levels of CRP, IL-6 and TNF-α were also significantly higher in the patients with sepsis compared to those in patients with local infection. Significant correlations were observed between the levels of PCT and those of CRP, IL-6 and TNF-α in SIRS patients. It was suggested that to measure the levels of procalcitonin in patients with SIRS is useful to diagnose the infection and severity of illness.

P93 Increased procalcitonin serum levels as predictive parameter of multiple organ failure and outcome in acute pancreatitis patients

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Crit Care 1999, **3 (suppl 1)**:P93

Introduction: A high serum level of procalcitonin (PCT), an inflammatory mediator precursor of human calcitonin, has been detected in patients with inflammatory conditions from bacterial infection. The formation and release of PCT seems to be a selective induced response to bacterial inflammation or sepsis and it is sustained during a prolonged period of time compared with other inflammatory mediators. In relation to this, PCT could be an important parameter to evaluate patients with AP as systemic involvement and infectious complications that influence the antibiotic use, CT scan indication, invasive hemodynamic monitoring, and surgical intervention are frequently.

Patients and methods: A prospective study was undertaken in patients with diagnosis of AP. The clinical classification was made according to the Symposium of Atlanta and radiological findings by Balthazar's criteria. The presence of infection and multiple organ failure (MOF) were evaluated in a daily basis until hospital discharge or death. These findings were correlated with PCT serum levels that were determined by monoclonal antibodies (Lumitest; B.R.A.H.M.S. Diagnóstica; Germany). Kruskal-Wallis and Mann-Whitney tests were used for statistical analysis.

Results: Ten patients presented with mild AP and three with severe AP that had their PCT level measured in the first 48 h from admission were enrolled. Only the severe AP patients developed infection conditions and MOF. The PCT serum levels in mild and severe AP patients in admission were 0.65 ± 0.29 ng/ml (0.34 ng/ml to 1.45 ng/ml) and 13.68 ± 12.23 ng/ml (2.5 ng/ml to 26.58 ng/ml), respectively. The PCT serum levels were higher in severe AP patients ($P = 0.09$), when infectious conditions ($P = 0.08$) and MOD ($P = 0.003$) were present. All patients that died had high PCT serum levels ($P = 0.008$).

Conclusion: Increased serum PCT levels may be a predictive parameter of infection and MOF development during AP and correlated with high mortality rate.

P94 Serum procalcitonin levels in bacterial and viral meningitis

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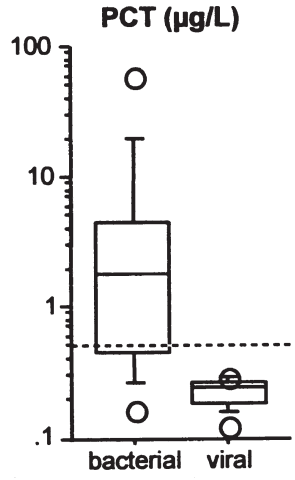
Crit Care 1999, **3 (suppl 1)**:P94

Background and objectives: Serum procalcitonin (PCT) levels increase in invasive bacterial, but not in viral infections. In patients with meningitis, the initial differential diagnosis of bacterial or viral infection is frequently difficult. The aim of this study was to test the hypothesis that serum procalcitonin levels are elevated in patients with bacterial meningitis and remain within normal limits in viral meningitis.

Patients and methods: We prospectively evaluated 30 patients (13 men and 17 women, mean age 52 years), with acute bacterial ($n = 16$) or viral ($n = 14$) meningitis. Upon admission, cerebrospinal fluid (CSF), serum PCT, C-reactive protein (CRP), white blood cell (WBC) count, and lactate were analysed. Blood and CSF cultures, CFS Gram stains and serological studies were performed. Sepsis was categorised according to the Society of Critical Care Medicine consensus criteria. Outcome was assessed upon discharge using the Glasgow Outcome Scale.

Results: Patients with viral meningitis were younger and had a shorter hospital stay. Fourteen of 16 patients with bacterial, but only five of 14 patients with viral meningitis were in a septic condition upon admission. Upon discharge, 12 patients were without any symptoms, nine patients were moderately, and nine severely disabled. No patient died. Upon admission, PCT, CRP, white blood cell and CSF leukocyte counts, CSF protein and lactate were higher, and the serum/CSF ratio was lower in patients with bacterial meningitis as compared with viral meningitis ($P < 0.001$). PCT was the parameter with the highest specificity (100%) for bacterial infections but was false-negative in five patients with bacterial meningitis (a sensitivity of 69%).



Conclusion: Our results indicate that PCT is a useful additional parameter to differentiate bacterial from viral meningitis. In patients with viral meningitis and even if viral sepsis is present, PCT levels do not increase. Elevated PCT levels indicate a bacterial origin with high specificity.

P95 Procalcitonin for early diagnosis and differentiation of SIRS, sepsis, severe sepsis and septic shock

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Crit Care 1999, **3 (suppl 1)**:P95

Objective: To determine the value of procalcitonin (PCT) in the early diagnosis (and differentiation) of patients with SIRS, sepsis, severe sepsis and septic shock in comparison to C-reactive protein (CRP), white blood cell and thrombocyte count, and APACHE-II score (AP-II).

Design: Prospective cohort study including all consecutive patients admitted to the ICU with the suspected diagnosis of infection over a 7-month period.

Patients and methods: One-hundred and eight-five patients were included, 17 patients with SIRS, 61 with sepsis, 68 with severe sepsis, and 39 patients with septic shock. CRP, cell counts, AP-II and PCT were evaluated on the first day after onset of inflammatory symptoms.

Results: PCT values were highest in patients with septic shock (12.89 ± 4.39 ng/ml; $P < 0.05$ versus patients with severe sepsis). Patients with severe sepsis had significantly higher PCT levels compared to patients with sepsis or SIRS (6.91 ± 3.87 ng/ml versus 0.53 ± 2.9 ng/ml; $P < 0.001$ and 0.41 ± 3.04 ng/ml; $P < 0.001$, respectively). AP-II scores did not differ significantly between sepsis, severe sepsis and SIRS (19.26 ± 1.62, 16.09 ± 2.06 and 17.42 ± 1.72 points, respectively), but was significantly higher in patients with septic shock (29.27 ± 1.35, $P < 0.001$ versus patients with severe sepsis). Neither CRP, cell counts nor the degree of fever showed significant differences between sepsis and severe sepsis. White blood cell count and platelet count differed significantly between severe sepsis and septic shock.

Conclusion: In contrast to AP-II, PCT appears to be a useful early marker to discriminate between sepsis and severe sepsis.

P96 Influence of extracorporeal circulation on the kinetics of procalcitonin

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Crit Care 1999, **3 (suppl 1)**:P96

Subject of the study: There are a number of clinical and laboratory parameters available for diagnosis of infections. The informative value postoperatively on the start and course of an infection is, however, considerably reduced. Extracorporeal circulation provokes a systemic immunological reaction, which shows changes of all parameters measurable at present. Procalcitonin is a new

marker for bacterial and viral infections. The aim of this study was to evaluate the kinetics of procalcitonin after cardiac surgery using extracorporeal circulation. In a second phase patients were examined who had a demonstrated postoperative infection. Procalcitonin values should be correlated with the occurrence, course and intensity of the infection.

Materials and Methods: 39 patients (mean age 66.4 years, 32 men) with uncomplicated course after ACVB operation were enrolled in a phase I study. Samples were collected preoperative, in the 1st, 6th and 12th postoperative hours and then every 24 h up to and including the 5th day. In phase 2, 20 patients (mean age 68.2 years, 10 men) were examined in whom a demonstrable infection was found postoperatively after cardiac surgery.

Results: Procalcitonin rises significantly within the first 24 h after extracorporeal circulation. The serum levels measured, however, are still within the normal range for healthy patients. Standard infection parameters which are used routinely in clinical situations show, in contrast, clearly significantly false positive values from the start of the 6th postoperative hour onwards. The serum values obtained in phase 2 showed that in some patients (8/20) there was a significant procalcitonin rise before the occurrence of a clinically manifest infection. In 3 patients there was no increase in the serum level, even in the course of the infection.

Conclusion: Procalcitonin is a new parameter that is not influenced by extracorporeal circulation which can be used for the diagnosis of an early postoperative infection.

A closed system with reduced blood/air activation was used in all patients. It must be determined in further studies what influence different perfusion techniques have on the kinetics of procalcitonin.

P97 Delayed neutrophil apoptosis in sepsis is associated with reduced Caspase-3 activity

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Crit Care 1999, **3 (suppl 1)**:P97

Apoptosis or programmed cell death is effected through a family of proteases called caspases. Mature neutrophils undergo spontaneous apoptosis mediated in part by the proapoptotic enzyme caspase-3. Since circulating neutrophils from patients with sepsis show delayed apoptosis, we evaluated caspase-3 activity in experimental and clinical sepsis.

Methods: Neutrophils from septic patients and normal controls were treated with pyrrolidine dithiocarbamate (PDTC), an inhibitor of NFκB with or without preincubation with LPS. Apoptosis was assessed as propidium iodide uptake by flow cytometry at 24 h. Caspase-3 expression was determined by western blots and activity was determined spectrophotometrically using a specific substrate (DEVD-AMC).

Results: Caspase-3 activity was reduced by exposure to LPS and in sepsis patients (results follow, mean ± SEM). Apoptosis was stimulated by PDTC in all groups.

Incubation of neutrophils with PDTC in a separate group of 4 of 6 patients with similar organ dysfunction scores demonstrated no increase in CPP32 expression at 4 h of *in vitro* culture.

Conclusion: Caspase-3 activity is reduced in clinical and experimental sepsis. Modulation of effector caspase activity may represent a novel approach to hasten the resolution of an inflammatory response.

	Control		LPS		Sepsis	
	Unstim.	PDTC	Resting	PDTC	Unstim.	PDTC
Apoptosis(%)	35 ± 4.1	61.9 ± 6.7**	15 ± 4.9	59.6 ± 6.2**	4.2 ± 1.7	24.5 ± 4.4**
Caspase-3 activity	17.2 ± 6	13.5 ± 2.5	8.8 ± 1.9*	16.5 ± 3.5	6.6 ± 0.8*	9 ± 0.9

*$P < 0.05$(vs. control);** $P < 0.05$ (vs. no PDTC)

P98 Pan-peritonitis due to intestinal perforation, and efficacy of direct hemoperfusion with polymyxin B immobilized fiber (PMX-20R)

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We used PMX-20R in the treatment of 20 septic shock patients who developed complicated multiple organ failure caused by intestinal perforation. Extracorporeal circulation was performed for 120 min with blood flow of 80–120 ml/min. In this treatment, we assessed the changes of the patient's hemodynamics and the levels of cytokine levels (TNF-α, IL-6, IL-1ra and IL-10), soluble ICAM-1, thrombomodurin, NOx and PAI-1 during and after hemoperfusion using PMX-20R. Before the treatment, the mean APACHE-2 score of the 20 patients was 24.3, mean septic severity score was 46.9, and Goris score was 4.7. Mean arterial BP and LVSWI after the treatment increased significantly compared to the values in similar patients who did not receive this treatment, while our patients showed slight decrease in platelet counts. The values of the endospecy test (the new PCA method) apparently declined at the end of PMX treatment. The two inflammatory cytokines, TNF-α and IL-6, and the anti-inflammatory cytokines,

IL-1ra and IL-10, decreased immediately after PMX and at 24 h after completing PMX. On the other hand, the levels of ICAM-1, thrombomodurin, NOx did not decline. PAI-1 decreased remarkably at the end of PMX treatment and 24 h after PMX. As a result, 15 of the 20 patients had good prognosis and 5 had a poor prognosis. Therefore, hemoperfusion with PMX-20R could be a useful therapeutic measure for patients with septic shock caused by intestinal perforation, and it is recommended that this treatment shold be begun as quickly as possible after emergency surgical treatment.

P99 Antithrombin III (AT III) prevents increased permeability and leukocyte adhesion in response to endotoxin (LPS) in the microcirculation of rat mesentery

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Background: Clinical trials with substitution of AT III in patients with sepsis showed a trend towards reduction of mortality and a positive effect on development and course of multiple organ failure. The mode of action is under discussion. Recent experimental studies suggest a possible effect on microvascular permeability and endothelial leukocyte adhesion.

Methods: By means of intravital microscopy we investigated the effect of substitution of AT III on LPS-induced microvascular leakage and leukocyte adhesion in the rat mesentery. Male CD rats (300–400 g bw) were used. The animals were infused with 0.5 mg/kg LPS (*E. coli* O55:B5) over 80 min. Vascular leakage was detected with FITC-marked rat serum albumin by fluorescence microscopy and evaluated by grey value analysis with a computer assisted image processing system. Light microscopy was used to evaluate the adherence of leukocytes to the vessel wall of postcapillary venules. Two treated groups received 500 U/kg AT III either 20 min prior (pretreatment) or 20 min after (posttreament) the beginning of LPS-infusion. Groups of animals not infused with LPS (sham), and infused with LPS ± placebo (albumin), served as controls. The observation period was 3 h after the beginning of LPS infusion.

Results: Infusion of LPS led to a significant increase in microvascluar permeability and leukocyte adherence compared to unstimulated controls. Both effects were reduced to the level of unstimulated controls by substitution of AT III. No significant differences were found between the pretreated or the posttreated group. Treatment with placebo and LPS showed no difference compared to the untreated LPS group.

Conclusion: Substitution of AT III, even when it is given after the inflammatory stimulus, ameliorates vascular leakage and leukocyte adhesion to the vessel wall as a consequence of LPS infusion. Thus, AT III could improve the microcirculation in the course of a generalised inflammatory reaction.

P100 Immunomodulation of AT III in septic disease

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Introduction: Antithrombin III is a physiological inhibitor of thrombin, a central procoagulatory factor with pleiotropic activities. Decompensated disseminated intravascular coagulation in septic patients is associated with a rapid consumption of AT III. Therefore the anti-inflammatory effects of AT III is a main point of interest in the pathway of sepsis. To determine whether AT III concentration has beneficial effects on the severity of immunological function in sepsis, the present study investigated the association between AT III and the DR-expression on monocytes.

Methods: AT III concentration, IL-6 and TNF-a were measured by standard methods in 18 patients with sepsis. Levels of DR expression on monocytes are analysed flow cytometrically. The severity of the disease was assessed at the APACHE II-score. The substitution of antithrombin III (100 IE/h) was performed in patients with AT III-level <80%.

Results: There was a significant correlation between AT III and DR-expression on monocytes ($P < 0.002$). The substitution of AT III in a standard dose was associated with higher level of DR-expression on monocytes. Also the AT III level shows a linear correlation to IL-6 and TNF-α ($P < 0.05$; $P < 0.03$).

Conclusion: The results indicate that the AT III level is not only a marker of the disseminated intravascular coagulation in septic patients. Also there is a relationship to the process of inflammation. Higher levels of AT III were associated with a higher amount of DR-expression. Thus, the study confirmed the effect of AT III on the immunomodulation.

P101 Effect of antithrombin III (AT) on lipopolysaccharide (LPS)-induced production of tissue factor and interleukin-6 (IL-6) by human umbilical vein endothelial cells (HUVECs), mononuclear cells (MNCs) and whole blood

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During disseminated intravascular coagulation (DIC), the extrinsic tissue factor (TF)-dependent pathway has been implicated as the dominant route to thrombin generation and the production of IL-6 has been shown to correlate positively with the severity of sepsis-induced DIC. Pharmacological doses of AT have been shown to reduce mortality and morbidity in patients with DIC and

there is increasing evidence to suggest that AT possesses anti-inflammatory properties in addition to its anticoagulant properties. In the present study, we have investigated the effect of AT on LPS-induced TF and IL-6 production in three different *in vitro* systems. Citrated whole blood, HUVECs and MNCs were stimulated with LPS for 4–6 h in the presence or absence of AT. TF activity was estimated by a TF-dependent clotting or chromogenic assay and IL-6 was measured by ELISA. Our results show a dose-dependent inhibition of TF and IL-6 production by AT, EC50 – ~36 and 20–35 iu/ml respectively in MNCs and HUVECs, but ~14 and <10 iu/ml in whole blood. Immunopurification experiments confirmed that the inhibitory activity was attributable to the AT and not to components that may have co-purified with the clinical product. In addition, up to 40 μM of hirudin, a specific thrombin inhibitor, did not inhibit the production of TF and IL-6 in either of the three cell systems, suggesting that the observed inhibition by AT was not due solely to the inhibition of thrombin. Our investigation has shown that, apart from the inhibition of thrombin and other activated clotting factors, AT may also down-regulate the cellular expression of proinflammatory cytokines. Consequently, AT concentrates may have value in the treatment of sepsis-induced DIC.

P102 tPA–PAI (tissue plasminogen activator–plasminogen activator inhibitor-1 complex) can be a predictive marker of multiple organ dysfunction syndrome in seriously ill acute patients with glucose intolerance — analysis under strict blood glucose control by artificial pancreas

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Background and purpose: Recently close relationships between multiple organ dysfunction syndrome (MODS) and coagulopathy, particularly hypercoagulability, have been reported in seriously ill acute patients. However, there are few studies suggesting which parameters related to coagulopathy are most intensively correlated with MODS, and whether the coagulopathy has a role of the cause of MODS or is only the result of it.

The purpose of this report is to (1) study whether PAI-1 related markers including tPA–PAI are parameters related to coagulopathy closely related to MODS, and (2) analyse whether the coagulopathy indicated by the elevation of the PAI-1 related markers is the cause of MODS in seriously ill acute septic patients with glucose intolerance. Patients under strict blood glucose control by artificial pancreas (AP) were selected in order to sample reliable PAI-1 values because fluctuation of blood glucose and serum fat levels are believed to influence the blood levels of PAI-1 related parameters. AP used was STG-22, manufactured by NIKKISOH corporation in Japan.

Materials: Nine severe septic patients with glucose intolerance without NIDDM, aged 27–83 years were investigated. Primary diseases were, four patients with hepatobiliary diseases, two with gangrene of lower extremities, two with ARDS, and one with burn.

Analyzed items were (1) regarding to the MODS: MOF score (calculated from the MOF criteria of Japanese Association for Critical Care Medicine), (2) regarding to glucose intolerance: M value (mg/kg per min, measured by the euglycemic hyperinsulinemic glucose clamp method with AP. The clamped blood glucose level was 80 mg/dl with the insulin infusion rate of 3.36 mU/kg per min), as reported in the literature, (3) regarding coagulopathy: (i) DIC (disseminated intravascular coagulation) score calculated from the DIC criteria of the Ministry of Health and Welfare of Japan, (ii) PAI-1 related markers (PAI-1 activity, PAI-1 antigen, and tPA–PAI), (iii) platelet count (PLT), (iv) fibrinogen (Fb), (v) FDP, (vi) prothrombin time ratio (PT), (vii) TAT, (viii) D-dimer, (ix) PIC, (x) antithrombin-III (AT-III), (xi) protein-C activity (PC), (xii) protein-S activity (PS), (4) thrombomodulin (TM) as a parameter of endothelial cell injury, and (5) serum fat (free fatty acid, triglyceride, cholesterol).

Results: (1) Mean value of the daily mean blood glucose levels (BSm), and M values measured within a few days after admission were 165 ± 42 mg/dl ($n = 35$) and 7.4 ± 3.6 mg/kg per min ($n = 8$), respectively. (2) MOF score was correlated with DIC score (correlation coefficient: 0.86, $n = 111$), PLT (–0.60, $n = 115$), tPA–PAI (0.57, $n = 37$), TAT (0.49, $n = 25$), and D-dimer (0.46, $n = 25$), (3) DIC score was correlated with PLT (–0.75, $n = 111$) and TPA–PAI (0.49, $n = 35$). (4) tPA–PAI was correlated with PLT (–0.54, $n = 38$), PC (–0.54, $n = 24$), TAT (0.53, $n = 24$) and Fg (–0.52, $n = 35$). (5) TM was correlated with tPA–PAI (0.62, $n = 33$). (6) There were no definite relationships between tPA–PAI and BSm, blood insulin concentration, and serum fat levels. (7) The marked change of tPA–PAI levels apparently preceded those of MOF score in three out of eight patients and were parallel to them in four out of eight.

Interpretation and conclusions: Several important relationships between tPA–PAI and DIC, hypercoagulability, endothelial cell injury, and MODS became evident. These analyses were thought to be possible because strict blood glucose control was performed by using AP. The degree of MODS correlated with that of DIC and/or hypercoagulability. Among parameters related to coagulopathy, tPA–PAI was not only a sensitive marker of DIC and hypercoabulability, but also correlated well with the severity of MODS and the endothelial cell injury. Moreover, hypercoagulable state indicated by the elevation of tPA-PAI was thought to be one of the causes of MODS, and treatment for the hypercoabulability may be justified as an important method.

P103 Inhibition of endotoxin-induced leukocyte/endothelial cell interaction by antithrombin III

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Antithrombin III (AT III) is an important inhibitor of thrombin activity, as well as of many other proteases of the coagulation system. AT III administration showed beneficial effects on

septic multiple organ dysfunction in clinical and experimental studies. This study investigates the AT III effect on leukocyte/endothelial cell interaction and microvascular perfusion. In the skin fold preparation of the hamster severe endotoxinemia was induced by repeated administration of endotoxin (LPS, 2 mg/kg), at $t_0 = 0$ h and $t_3 = 48$ h. AT III (250 U/kg) was substituted intravenously at t_0, $t_2 = 24$ h, and t_3 ($n = 6$ animals, AT III group). In control animals ($n = 5$, controls) LPS was given without AT III substitution. By intravital fluorescence microscopy (FITC dextrane, rhodamine 6G) venular leukocyte adherence was determined at t_0, $t_1 = 8$ h, t_2, t_3, $t_4 = 56$ h, and $t_5 = 72$ h. Functional capillary density (FCD) served as a measure of capillary perfusion. AT III resulted in a significant modulation of LPS-induced leukocyte adherence and in a modulation of the LPS-induced depression in FCD ($P < 0.01$, MANOVA). Thus, the number of sticking leukocytes after induction of endotoxinemia was significantly lower in the AT III group compared with control animals (AT III: $t_1 = 182 \pm 35$ cells/mm^2, $t_2 = 176 \pm 21$, $t_3 = 210 \pm 51$, $t_4 = 243 \pm 48$, $t_5 = 144 \pm 29$; control: $t_1 = 630 \pm 105$, $t_2 = 465 \pm 113$, $t_3 = 404 \pm 50$, $t_4 = 542 \pm 93$, $t_5 = 356 \pm 102$; $P < 0.05$). AT III downregulated LPS-induced leukocyte/endothelial cell interaction and prevented the depression in FCD which served as a measure of capillary perfusion. Both mechanisms may explain beneficial AT III effects in patients with severe sepsis.

P104 Effects of hydrocortisone stress-dose therapy in septic shock (part I): influence on hemodynamic stability and plasma nitrite/nitrate levels

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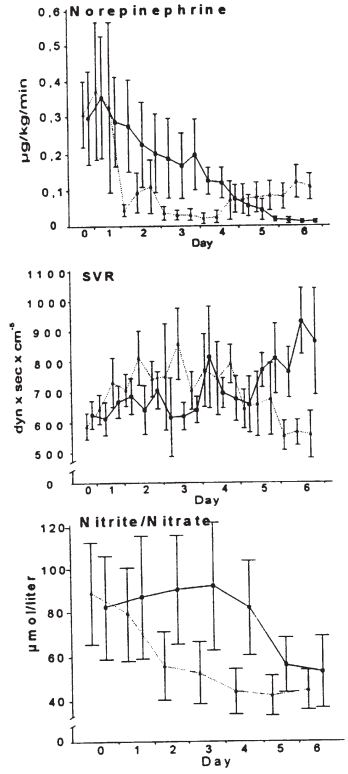
A renaissance of the 'glucocorticoid discussion' emerged during the last years with reports of 'stress dose' or 'low-dose' hydrocortisone (HC) replacement therapy in patients with septic shock, assuming relative adrenal insufficiency, improving hemodynamic stability, modulating the inflammatory response, and probably improving outcome [1,2]. Here we present results from an interim analysis for the first 20 patients enrolled in a double blinded, randomized, placebo controlled, cross-over study to investigate the effects of HC infusion on 40 patients in septic shock [3] who needed norepinephrine (NE) for hemodynamic support. Patients were randomized to receive either HC 10 mg/h after an initial bolus of 100 mg, or placebo (PL). After 3 days, the medication was switched, i.e. patients who had HC for the first 3 days received PL for another 3 days, and vice versa. Plasma nitrite/nitrate (Griess reaction) was measured before the study and daily for 6 days, hemodynamic monitoring was performed before and every 8 h throughout the study period. No differences between the two group were found for age, sex, cause of sepsis, and severity of illness at time of study entry established by SAPS II and SOFA. HC treatment allowed marked reduction of NE infusion within 48 h after study began (Fig. 1). Systemic vascular resistance (SVR) increased with HC infusion but remained unchanged in the PL-group during the first study period (Fig. 2). When HC was switched to the other group, SVR decreased despite increased NE requirement in patients who received HC before, whereas in the other group SVR increased and NE could be reduced. Mean arterial blood pressure, but not cardiac index, paralleled changes of SVR. Plasma nitrite/nitrate decreased with HC infusion, indicating suppression of endogenous nitric oxide (NO) production (Fig. 3). Interestingly, rebound phenomenon after cessation of HC was not accompanied by increased nitrite/nitrate concentrations.

Conclusions: In patients with septic shock, stress-dose HC infusion improves hemodynamic stability, reduces NE requirement and increases SVR. Improvement of SVR may be due to HC-induced suppression of inducible NO synthases (iNOS) and/or suppression of the synthesis of iNOS stimulating cytokines. Cessation of HC infusion induces rebound effects which seem to be NO-independent.



Figures 1–3. Norepinephrine administration (1), systemic vascular resistance (SVR) (2), and plasma nitrite/nitrate concentrations (3) in patients with septic shock who received stress-dose hydrocortisone (HC) therapy (see text). Day 0: values before study. Triangles, HC during day 1–3; squares, HC during day 4–6. Note that the medication was switched on day 3. Data are presented as mean ± SEM, $n = 10$ for each data point.

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P105 Effects of stress-dose hydrocortisone therapy in septic shock (part II): soluble E-selectin and interleukin-6. Preliminary results of a double blinded, randomized, placebo-controlled cross-over study

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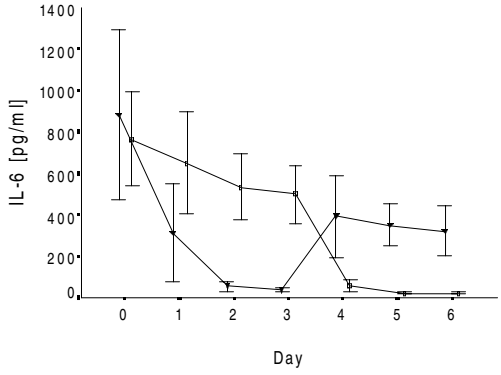
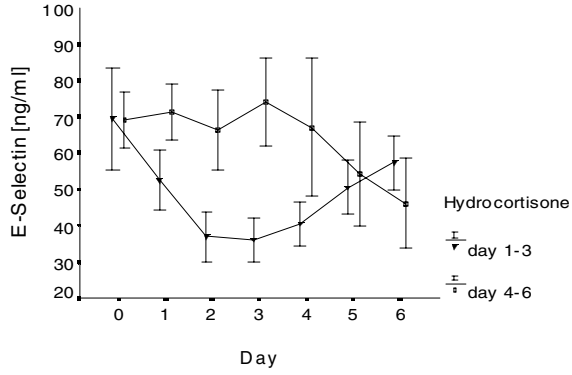
Background: E-selectin is a member of the selectin family, i.e. a transmembrane molecule which is essential for the adherence and extravasation of leukocytes. E-selectin is expressed by activated endothelial cells and interacts with circulating neutrophiles. IL-6 is a proinflammatory cytokine, produced by various cell types. Both markers are elevated in the blood of patients with septic shock; E-selectin possibly plays a role in permeability alterations and organ damage, IL-6 is a predictor of outcome and severity. Stress-dose hydrocortisone improves the clinical situation of patients in septic shock. *In vivo* studies could show that corticosteroids inhibit the endothelial expression of adhesion molecules including E-selectin.

Methods: As a part of a double blind controlled cross-over study with stress dose hydrocortisone (10 mg/h) E-selectin and IL-6 levels were monitored for six days in 20 patients with septic shock. For the first 3 days patients received either hydrocortisone or placebo as a continuous intravenous infusion, for the next 3 days medication was switched. Blood was taken before starting and then once every day. Both IL-6 and E-selectin were measured by an ELISA technique.

Results: We found a decrease in IL-6 and E-selectin levels under application of hydrocortisone compared to the placebo group as well as to the primary values. After switching to placebo, values increased again.

Conclusion: We could show that stress-dose hydrocortisone given to patients in septic shock markedly decreases soluble E-selectin and IL-6 levels. In addition to the hemodynamic effects of this therapy, there also seems to be an immunmodulating and anti-inflammatory effect, which might be organ protective.





Figures 1–2. IL6 (Fig.1) and E-selectin levels (Fig.2) in septic shock patients, who received hydrocortisone therapy (see text). Day 0: before study. Data are presented as mean-values with SEM; $n = 10$ for each data point.

P106 Effects of stress-dose hydrocortisone therapy in septic shock (part III): monocyte HLA-DR expression and blood interferon-γ concentration. Preliminary results of a double blinded, randomized, placebo-controlled cross-over study

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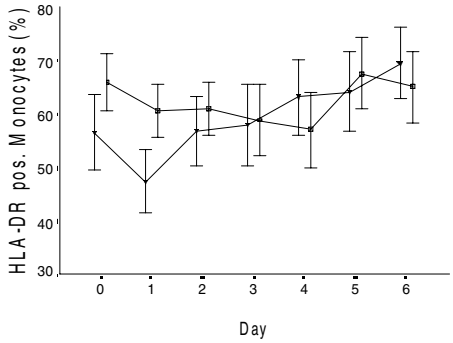
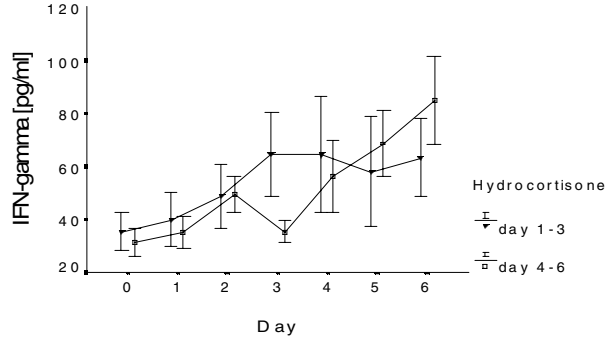
Background: Immunoparalysis, defined as a decreased level of human leukocyte antigen (HLA)-DR receptor expression on monocytes, correlates with the severity of septic shock and outcome [1].

Hydrocortisone (HC) alters the immune response at almost all levels and is considered to suppress HLA-DR expression on monocytes. IFN-γ as a potent activator of mononuclear phagocytes increases the ability of monocytes to express HLA-DR *in vitro* and *in vivo*. One of the aims of our study was to analyze immunosuppressive effects of HC stress-dose therapy in septic shock patients. Here we present results of an interim analysis of the first 20 patients enrolled in the study.

Methods: The study was designed as a double blinded, randomized, cross-over , placebo-controlled trial in 40 patients. Patients who fulfilled the criteria for septic shock according to the Consensus Conference on Sepsis and Organ Failure [2] received a dose of 10 mg/h hydrocortisone after an initial loading dose of 100 mg, or placebo for 3 days. After 3 days, patients from the HC-group switched to the placebo-group and vice versa. Blood samples were obtained before the study and daily for a period of 6 days. A whole





Figures 1–2. Monocyte HLA-DR expression (Fig. 1) and IFN-gamma concentration (Fig. 2) in septic shock patients who received hydrocortisone therapy (see text). Day 0: before study. Data are presented as mean-values with SEM; $n = 10$ for each data point.

blood flow-cytometry analysis was performed to analyze monocyte HLA-DR antigen expression. Plasma IFN-γ levels were measured by an enzyme-linked immunoassay.

Results: There were no striking differences in monocyte HLA-DR expression between patients who received HC or placebo (Fig. 1). However, compared to baseline values, a transient decrease of HLA-DR expression was observed in the group which received HC early. INF-γ increased in both groups after start of the study, but returned to baseline in the placebo-group on day 3 (Fig. 2). In the follow-up, INF-γ did not further increase in the placebo-group but noticeably in the HC-group.

Conclusion: Stress-dose HC treatment did not induce immunoparalysis in patients with septic shock during the study period. HLA-DR expression remained almost constant over the period of the trial which we postulate to be due to HC-induced increase of INF-γ synthesis.

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P107 Sex dimorphism and sepsis: a novel approach

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Experimentally it was recently well established that gender differences lead to an increased susceptibility to sepsis in males.

In a prospective clinical study gender differences were evaluated in patients of a surgical ICU in terms of survival, sex hormones and cytokine response. Fifty-two critically ill patients (19 females and 33 males) were included in this study – there was no difference in the characteristics of patients concerning the age, cause of sepsis and severity of their disease.

Mean age was 55.4 years for females and 53.1 for males. APACHE II score was 17.3 for females and 18.5 for males at entry of the study, MOD-score 9.9 versus 10.8 respectively. Biactivity of TNF and Il-6 were measured for 14 days, as well as Il-10 (ELISA), total testosteron and 17β-estradiol (RIA).

Though clinical assessment did not reveal any difference, prognosis and outcome of sepsis was significantly different in males and females: MOD-score was always similar in both groups, however, hospital mortality was significantly different with 70% (23/33) in male and 26% (5/19) in female patients ($P < 0.01$, log-rank test). Evaluation of cytokine response revealed significantly elevated TNF levels on day 10 in males ($P < 0.05$ Mann-Whitney U-test) while no difference was found for Il-6 levels. Females, however, displayed enhanced Il-10 levels compared to males from day 1 to day 10 which reached significant levels of $P < 0.05$ on day 3 and day 5. Total testosterone levels were below the normal range for males and estradiol levels were initially increased both in men and postmenopausal women with higher levels for women.

Sex dismorphism, as shown, with a significant better prognosis and outcome of sepsis in women should be considered as a novel therapeutic approach (testosterone receptor blockade) in sepsis.

P108 The impact of eligibility criteria on enrollment in ICU sepsis clinical trials

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Introduction: Although clinical trials of novel mediator-targeted compounds in sepsis employ similar entry criteria, exclusion criteria are variable. We evaluated the impact of variability in such criteria on recruitment of patients into one of three multi-center studies.

Method: We have previously developed a screen log for monitoring eligibility and enrollment of patients into multiple clinical trials. All patients admitted to the Medical-Surgical Intensive Care Unit of a large Canadian University affiliated teaching hospital were screened for study eligibility into one of three multi-center sepsis trials. The screen log defines patients who meet inclusion criteria as eligible. Reasons for non-enrollment are divided as follows: 1, study specific exclusion criteria; 2, hopeless prognosis; and 3, enrolled in another trial. Truly eligible patients were those who did not meet above criteria 1–3 and were not enrolled because informed consent could not be obtained or because the window of eligibility was missed by study personnel. Recruitment efficiency was calculated as the proportion of patients enrolled of those who were truly eligible.

	Study A (phase III)	Study B (phase III)	Study C (phase II)
Eligible (% sepsis)	117 (20.9)	40 (7.1)	116 (20.7)
Excluded (% of eligible)	85 (72.6)	30 (75.0)	108 (93.1)
met study specific excl.	[48]	[19]	[88]
hopeless prognosis	[32]	[8]	[17]
other study		[5]	[3] [3]
Truly eligible (% eligible)	32 (27.3)	10 (25)	8 (6.8)
Enrolled	27	6	4
Recruitment efficiency	84%	60%	50%

Results: During the 23-month period of screening, 559 patients were admitted with sepsis or presumed sepsis. The inclusion criteria were met for 273/559 (48.8%) patients in least one of these three sepsis studies. Only 37/559 (6.6%) were enrolled into a sepsis trial. The Table contains the number of eligible, excluded (with reasons for exclusion) and enrolled patients screened for entry into the three trials.

Conclusion: Within an institution that actively participates in sepsis clinical trials, only a minority of patients with sepsis are treated in the context of a trial. The impact of study-specific exclusion criteria is to create very different study populations. Such differences may account in part for the discordant results seen in Phase II and Phase III trials and raise important questions regarding the external validity of conclusions from trials with low inclusion or recruitment efficiencies.

P109 Antiarrhythmic effect of interleukin-1 (IL-1) in conjunction with contractile depression

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While IL-1 is known to be cardiodepressant via the induction of an inducible nitric oxide synthase (iNOS) and enhanced production of nitric oxide (NO), conflicting results have been reported regarding its potential to induce or suppress arrhythmias. Here we report a potent antiarrhythmic effect of IL-1β in conjunction with an enhanced release of NO.

Methods: Neonatal rat cardiomyocytes (CM) were incubated for 24 h in the absence or presence of IL-1β (100 U/ml) in serum-free medium. Thereafter, the production of NO was assessed by a NO-sensitive microelectrode and the Griess reaction. For testing contractile performance, cells were electrically triggered at constant pace and monitored continously.

Results: Il-1β (24 h) resulted in a significant increase in the contents of NO, nitrite and lactate (indicative of altered energy metabolism) in the culture supernatants, which was suppressed by simultaneous administration of dexamethasone (Dex.) (0.1 μM). The cardiodepressant IL-1β effect was documented by a lacking response in pulsation amplitude to the isoproterenol-challenge (control: $n = 20$, $148\% \pm 20$ versus IL-1β: $n = 27$, $103\% \pm 3$*, $P < 0.05$), which was preserved by co-incubation with Dex. (control: $n = 21$, $131\% \pm 10$ versus IL-1β: $n = 27$, $130\% \pm 8$). Arrhythmias were regularly elicited in controls upon α-adrenoceptor-stimulation (16/17), even if the duration of the electrical pulse was increased to keep the cells in pace. In contrast, recordings of IL-1β-treated CM ($n = 11$) did not display beating irregularity. If, however, Dex. was added to the incubation medium, arrhythmias occurred both in the groups without IL-1β (9/11) and with IL-1β (9/10).

Conclusion: A potentially beneficial antiarrhythmic effect of IL-1β may go along with its cardiodepressant action *in vivo*.

P110 Decreased beating rate variability of cultured cardiomyocytes by endotoxin

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A decreased heart rate variability is a marker of autonomic dysfunction and indicates poor prognosis in critically ill patients. In healthy volunteers, such a decreased heart rate variability can be reversibly induced by i.v. administration of endotoxin (*Crit Care Med* **24**:1117-1124). It is unknown if this effect is due to a direct impact of endotoxin on the heart, or if secondary release products are responsible herefore. Using isolated, spontaneously contracting neonatal rat cardiomyocytes (CM) we investigated if endotoxin narrows beating rate variability directly.

Methods: CM from three independent preparations were cultured in serum-free medium with endotoxin (1 μg/ml, 24 h, inducing inducible nitric oxide synthase and stimulating interleukin-6 production) or without additive. 100 consecutive contractions per cell

were analysed (photo-optical system), per preparation 18 control cells and 18 cells in endotoxin-containing medium.

Results: There was a significant (*$P < 0.05$) decrease in beating rate variability in endotoxin-treated CM (Table: data from one preparation, parameters equivalent to the measures of heart rate variability in patients).

Conclusion: Endotoxinemia (e.g. by intestinal translocation) could *in vivo* directly contribute to autonomic dysfunction

Parameter	*n*	Control	Endotoxin
Mean of intervals (ms)	1800	987	852
Standard error of means (ms)	1800	50	39
Median of means (ms)	1800	1025	961
Mean of pNN50	1800	38.9%	21.7%*
Median of pNN50	1800	40.0%	15.8%

P111 Proinflammatory impact of norepinephrine in cardiomyocytes: increased interleukin-6 production, which is suppressed by carvedilol

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In severe heart failure elevated plasma/serum levels of both norepinephrine and proinflammatory cytokines have been reported. Several hypotheses have been proposed to explain, why and how cytokine release is triggered in heart failure, one possible player being the neurohumoral dysbalance, while other studies suggest an overspill of cytokines from the failing heart itself. Here we report that norepinephrine *in vitro* stimulates the release of interleukin-6 (IL-6) from cardiomyocytes (CM), in keeping with a previously unrecognized direct proinflammatory effect of norepinephrine on CM.

Methods: Spontaneously beating neonatal rat CM were incubated for 8–24 h in serum-free medium supplemented with norepinephrine (0.1–1 μM) or without additive, in the absence or presence of carvedilol (10 μM). In some experiments, an inhibitor of phosphodiesterase was simultaneously added. The adrenergic response was documented by monitoring beating rate. Inflammation was assessed by measuring the IL-6 (bioassay) content of culture supernatants.

Results: In numerous experiments, norepinephrine weakly, but reproducible enhanced IL-6 release from cultured CM, resulting in about a doubling of the IL-6 content of culture supernatants after 24 h. The IL-6 release was more pronounced by simultaneous administration of an inhibitor of phosphodiesterase, but suppressed in the presence of carvedilol.

Conclusion: The release of proinflammatory cytokines in heart failure may be directly linked to the enhanced sympathetic tone.

P112 Impact of cardiopulmonary-bypass assisted surgery on markers of monocyte function

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An APACHE-II-score ≥24 on the 1 po day is a prospectively validated parameter to identify cardiac surgery patients with an escalating 'post pump' systemic inflammatory response syndrome at high risk of multiple organ dysfunction syndrome. We investigated the impact of cardiopulmonary bypass-assisted cardiac surgery on monocyte markers in a prospectively conducted study for up to 5 days (group 1: APACHE II ≥24, group 2: APACHE II <24), compared to septic non-surgical patients (Elebute sepsis score ≥12, APACHE II score ≥24).

Results: HLA-DR: significant fall from day 0 to day 1 ($P < 0.05$; generalised linear model), but no significant difference between groups 1 and 2; CD 86: no significant differences.

Mean channel fluorescence (FACS®) ± SD, corrected by isotype control:

HLA-DR	Day 0	Day 1	Day 5
Group 1	1060 ± 505 (*n* = 24)	403 ± 186 (*n* = 24)	500 ± 298 (*n* = 23)
Group 2	1099 ± 525 (*n* = 5)	380 ± 158 (*n* = 5)	472 ± 182 (*n* = 2)
Group 3		483 ± 360 (*n* = 8)	332 ± 130 (*n* = 7)
CD 86 (costimulatory)	Day 0	Day 1	Day 5
Group 1	380 ± 325 (*n* = 24)	353 ± 520 (*n* = 24)	392 ± 439 (*n* = 23)
Group 2	630 ± 773 (*n* = 5)	287 ± 205 (*n* = 5)	405 ± 98 (*n* = 2)
Group 3		618 ± 746 (*n* = 8)	243 ± 175 (*n* = 7)

Conclusion: The expression of HLA-DR and CD86 on monocytes does not allow for an early risk stratification after cardiac surgery.

P113 Cardiac surgery induces increased production of interleukin-10 and lactoferrin

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Objective of the study: The interaction of blood with nonphysiologic surfaces during cardiac operations with extracorporeal circulation activates leukocytes and endothelial cells with the release of various systemic inflammatory mediators. The balance of pro- and anti-inflammatory factors is important in the limitation of SIRS development. In this study we turned out our attention to interleukin-10 and lactoferrin (LF) which role in the regulation of immune response has already been established.

Study design: Prospective, clinical study approved by the local Ethical Committee.

Patients: We assessed 24 patients subjected to coronary artery bypass graft (CABG) operations. ECC time was 90–115 min and AC time was 70–80 min.

Methods: IL-10 and LF level was measured before the operation after induction of anaesthesia (1), during surgery (2) and then 24 (3) and 48 (4) h after the end of ECC. All measurements were done in duplicate using ELISA techniques.

Results: We observed low plasma level of both IL-10 and LF before the operation and significantly increased during the operations. Postoperatively the concentration of both mediators decreased to the baseline level.

Time of sampling	IL-10 (pg/ml)	Lactoferrin (ng/ml)
Before the operation	54.2 ± 58.6	297.3 ± 296.7
During ECC	97.3 ± 84.7	1228.8 ± 842.5
24 h after operation	60.0 ± 31.0	315.5 ± 338.8
48 h after operation	39.8 ± 23.6	259.2 ± 213.8

Conclusion: Extracorporeal circulation is associated with the excessive release of IL-10 and lactoferrin and the kinetic of production of these both factors is very similar. This may suggest that they participate in the limitation of the inflammatory process during ECC.

P114 Cardiopulmonary bypass contributes to less than half of interleukin-6 release post cardiac surgery

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Introduction: IL-6 is an important marker for impairment of left ventricular function. Former studies have shown a significant release of IL-6 during coronary artery bypass grafting (CABG). The contribution of cardiopulmonary bypass (CPB) for IL-6-release and potential effects on decrease of the left ventricular function after CABG is still unknown. Therefore we examined three different types of revascularisation procedures which allowed us to estimate the CPB induced IL-6 release in CABG.

Methods: 121 patients with coronary artery disease undergoing coronary revascularisation were examined in following groups: 1) Elective PTCA without CPB ($n = 70$), 2) CPB-supported PTCA ($n = 8$), 3) CPB-supported coronary artery bypass grafting (CPB-CABG; $n = 41$).

Results: 1) The IL-6 plasma levels increased in all three groups to a significantly different degree with maximal IL-6 levels between 3 and 24 h after intervention. 2) The levels of the three collectives were significantly different at 3, 6, and 24 h (Table). 3) The correlation of IL-6 peak levels and duration of CPB was stronger in CPB-supported PTCA than in CPB-CABG.

IL-6 levels in three different groups of revascularisation procedure

	PTCA	CPB-PTCA	CPB-CABG
3 h	9.5 ± 17.3*†	218.1 ± 158.7*	501.1 ± 305.0
6 h	10.8 ± 14.0*‡	192.5 ± 112.0*	508.5 ± 264.5
24 h	14.3 ± 18.2*§	128.6 ± 137.7*	428.6 ± 269.2

*$P < 0.001$, versus CPB-CABG; †$P = 0.01$ versus CPB-PTCA; ‡$P = 0.008$ versus CPB-PTCA; §$P = 0.163$ versus CPB-PTCA

Conclusion: The prolonged duration of the CPB may contribute to the development of a systemic inflammatory response syndrome (SIRS). Reduction of bypass duration or elimination of CPB, like it is performed in minimally invasive coronary bypass grafting, may be beneficial for patients and may further reduce the risk of SIRS.

P115 sCD14, IL-6 and TNF-receptors, but not IL-1, IL-8 or TNF-α are elevated in plasma of patients undergoing high risk coronary angioplasty with cardiopulmonary support

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Introduction: The cardiopulmonary bypass (CPB) is discussed as a potential trigger of cytokine release. Here we determined a not

investigated spectrum of pro- and antiinflammatory cytokines in high risk patients undergoing CPB-PTCA.

Methods: Patients with coronary artery disease ($n = 3$) with a high risk of coronary intervention according to the 'National registry for supported angioplasty, 1994' undergoing CPB-supported PTCA were examined. Interleukin 1α (IL-1α), IL-1β, IL-1 receptor antagonist (IL-1ra), Tumor-necrosis-factor-α (TNF-α), soluble TNF-Receptors (TNF-R-p55; TNF-R-p75), IL-6, IL-8, IL-10 and soluble CD14 (sCD14) levels were measured in specific commercially available ELISA-Tests.

Results: We detected no significant levels of IL-1α, IL-1β, IL-8 and TNF-α during CPB support. IL-1ra levels were increased. IL-6 levels increased measurable starting 30 min after begin of CPB with peak values of 20–60 pg/ml between 3 and 12 h. One patient showed significant levels of IL-10, this patient expressed the lowest level and shortest kinetic of IL-6 production and more pronounced TNFα-receptor levels, although TNF-receptor levels increased in all patients. sCD14 raised continously in all 3 patients to a maximum of 7 ng/ml followed by a plateau for more than 5 days.

Conclusion: In this study we compared the cytokine levels of patients undergoing high risk coronary angioplasty with CPB-support. There were no findings to show a significant relation of IL-1α, IL-1β, IL-8 and TNF-α to the inflammatory response after CPB-PTCA – this might be a sign for other mechanisms than systemic activation of monocytes by endotoxin may be involved. IL-6 as a marker of the degree of systemic inflammatory reaction increased significantly. We suggest, the mayor source of this increase of IL-6 levels is the CPB-support. IL-6 release might be inhibited by IL-10 production.

P116 tPA-lysis leads to reduced levels of sL-selectin in patients with acute myocardial infarction

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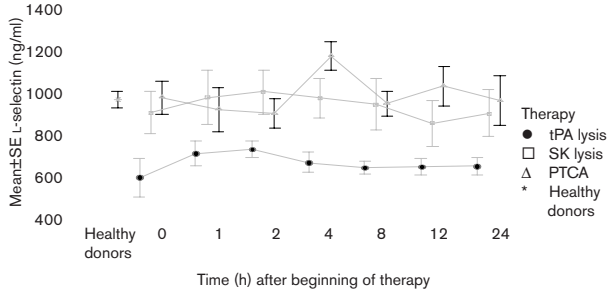
Background: Thrombolysis is still the standard therapy for patients with acute myo-cardial infarction (AMI). Studies have demonstrated, that an inflammatory process is induced by the reopening of the occluded coronary artery. Adhesion of leukocytes to endothelial cells is the initial event in an inflammatory response and is mediated by expression of several adhesion molecules (e.g. selectins), leading to a reperfusion injury.

Methods: 30 patients with AMI underwent treatment with tPA ($n = 10$), streptokinase ($n = 10$) or PTCA ($n = 10$) within 6 h, respectively. Blood samples were taken immediately prior and 1, 2, 4, 8, 12 and 24 h after treatment, as well as from 10 healthy donors. The serum levels of soluble L-selectin were measured with a commercially available EIA (R&D Europe). Statistic was performed by the Mann-Whitney-U-Test.

Results: Patients treated with tPA had significantly reduced levels of sL-selectin ($P = 0.003$) compared to healthy donors and to patients treated with streptokinase or PTCA ($P = 0.03$), respectively. Clinically, tPA-treated patients tended to have more complications and a higher reocclusion-rate, and more additional interventions were necessary.



Conclusion: The reduced circulating sL-selectin levels probably reflect an inflammatory process and could be a sign of a panendothelial activation in the occluded and then reperfused myocardial area.

P117 Catheterization of cardiac lymph trunk for evaluation of myocardial TNFα production and myocardial cell damage during cardiac operations

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Objectives: To test the hypothesis that the myocardium is a site of TNFα production and that cardiac lymph is more sensitive than venous blood from the coronary sinus (CS) to investigate myocardial cell damage related to cardiac operations in an experimental model.

Methods: In 14 young pigs the efferent cardiac lymph trunk and CS were cannulated before conventional cardiopulmonary bypass (CPB); lymph and blood were collected for perioperative TNFα and troponin I (TnI) measurement.

Results: TNFα was in similar range in cardiac lymph and in CS before, during and after CPB. There was no significant myocardial TNFα production related to CPB. TnI concentrations were significantly higher in cardiac lymph than in CS during and after CPB. A significant elevation of TnI related to CPB occurred in both cardiac lymph and CS, lymphatic concentrations reaching 100 times venous ones.

Conclusion: Our results exclude the myocardium as a major source of TNFα and indicate myocardial cell damage with loss of important contractile cell proteins during CPB.

The significantly higher TnI concentrations in cardiac lymph (draining the myocardial interstitium) than in CS imply that determinations of plasmatic concentrations of TnI in the CS leads to strong underestimation of myocardial cell damage related to cardiac operations.

P118 Predictors of outcome after primary PTCA for acute myocardial infarction complicated by cardiogenic shock

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Direct coronary angioplasty of the infarct related artery is well accepted as one of most important therapeutic options for cardiogenic shock (CS) complicating acute myocardial infarction (AMI). However, in-hospital still remains high. The aim of the following study was to analyse which clinical and procedural factors were associated with high or low in-hospital mortality when primary PTCA is applied systematically to all patients with CS within 12 h of symptom-onset. Patient chararcteristics: $n = 78$, age 60 ± 14 years, male 67%, primary venticular fibrillation, mechanical ventillation 59%, total branch block 24%.

Procedural data: Single-vessel-disease 41%, ejection fraction (acute biplane) 0.51 ± 0.16, infarct-related artery: LAD 38%, LCX 8%, RCA 54%; intra-aortic-balloon-pumping 17%, coronary stents 28%, successful angioplasty 87% (TIMI 3, residual stenosis <50%), in-hospital mortality (0–30 days) 49%. The most important predictors for a high in-hospital mortality rate were: acute ejection fraction <40% ($P = 0.0035$), unsuccessful PTCA ($P < 0.05$) and patient age >75 years ($P < 0.05$). A high in-hospital mortality rate was also seen in patients requiring mechanical ventillation. Mortality did not depend on the infarct location (inferior versus anterior), patient sex, ventricullar fibrillation or total branch block prior to intervention, single- or multi-vessel-disease. Furthermore mortality was independent of the time between onset of symptoms and PTCA and was also not affected by the employment of coronary stents or intra-aortic balloon conterpulsation.

Conclusion: Systematic primary-PTCA results in a lower in-hospital mortality rate when compared to conservative therapy of AMI with CS. However, mortality remains extremely high if angioplasty is unsuccesful. But even if myocardial perfusion is able to be re-established, patients initially requiring mechanical ventillation or with a low acute ejection-fraction as well as the very elderly >75 years of age maintain a poor prognosis.

P119 The storage-lesion in murine red blood cells: comparison to stored human red blood cells and applications for an animal model of transfusion efficacy

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Crit Care 1999, **3 (suppl 1)**:P119

Introduction: Under storage conditions, red blood cells (RBCs) undergo significant biochemical and biomechanical changes that compromise their ability to unload oxygen to the tissues. The clinical benefit of RBC transfusions are, therefore, less than anticipated and may lead to tissue injury rather than improvement. The development of an animal model is an important step in characterizing the loss of effective oxygen availability and assessing the efficacy of transfusion therapy. The aim of this study was to determine when stored rat RBCs develop a storage-lesion similar to human RBCs near the end of their shelf life.

Methods: Human and rat RBCs were collected in CPDA-1, packed and stored at 4°C for 29 days according to Red Cross standards. ATP and 2,3 DPG concentrations were assessed in rat and human RBCs during the storage. Biomechanical changes were assessed by assaying RBC membrane deformability (RBCd) using the micropipet aspiration technique. Stored RBCs were treated with a rejuvenation solution to determine the effect on biochemical and biomechanical function.

Results: The storage-induced decline in ATP and 2,3 DPG in human RBCs were consistent with the literature. These changes, however, occurred more rapidly in rat RBCs; ATP levels after 7 days of storage declined to the same extent as human RBCs after 4 weeks (40% decrease). DPG levels in rat and human RBCs fell by 60% and 90% after 7 days of storage. By day 7 of storage the mean membrane deformability had dropped 45% ($P < 0.001$). RBCs exposed to the rejuvenation protocol at day 7 had ATP levels returned to baseline while the mean RBCd showed almost complete recovery to baseline levels. Significantly, 12% of the population of rejuvenated cells still showed compromised membrane deformability (i.e. membrane displacement less than 80% of baseline).

Conclusion: The biochemical data from this study suggest that rat RBCs stored for 7 days develop a storage-lesion similar to that of human RBCs stored for 29 days. Rejuvenation of RBCs improves RBCd and may be related to improved ATP levels. Using rat RBCs stored for 7 days gives researchers a valuable tool to assess blood storage and the consequences on transfusion efficacy and tissue oxygen availability.

P120 Systemic inflammation promotes erythrocyte sequestration

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Crit Care 1999, **3 (suppl 1)**:P120

Introduction: Changes in red blood cell (RBC) flexibility and membrane surface properties affect their circulatory clearance. Glutaraldehyde (GLUT) stiffened RBC are cleared by about 70% within 30 min after transfusion [1]. Recently, we have shown that endotoxin (ETX) increases RBC adhesion to human vascular endothelial cells [2]. In this study we investigated the effects of endotoxin and cecal ligation and perforation induced sepsis (CLP) on RBC survival and sequestration in healthy and septic rats.

Methods: *Groups:* Rats were randomized to six groups. Groups H/N, H/E and H/S were healthy rats (H) receiving naive (N), endotoxin treated (E) or septic (S) RBC. Groups S/N, S/E and S/S were septic rats (24 h CLP)(S) receiving naive (N), endotoxin treated (E) or septic (S) RBC. *RBC solutions:* Blood was harvested from healthy or septic (24 h after CLP) donor rats. ETX treated RBC were prepared by incubating whole rat blood with ETX (75 μg/ml). RBC and plasma were separated by centrifugation (15 min, 1000 **g**). After washing with phosphate buffered saline, RBCs were labeled with ^{51}Chromium (^{51}Cr) and resuspended in plasma to the experimental animal's hematocrit. Infusion of labeled RBC solution was performed by an isovolemic and simultaneous exchange transfusion. Blood samples were taken after the exchange transfusion every 5 min for 30 min and in 60 min intervals over 4 h for ^{51}Cr measurements. Organs were harvested for tissue ^{51}Cr measurements. Cardiac output, body temperature (TEMP), mean arterial (MAP) and central venous pressure (CVP) were measured before and 4 h after exchange transfusion.

Results: Infusion of naive, ETX-treated or septic RBC did not affect cardiac index, TEMP, CVP or MAP in healthy (H/N, H/E, H/S) or septic rats (S/N, S/E, S/S). The amount of radiolabeled RBC in the circulation remained unchanged for the first 30 min in all groups. After 60 min, however, intravascular survival of septic and ETX treated RBC started to fall in healthy rats and was significantly lower than survival of naive RBC at 240 min. In septic rats, not only the E and S-RBC but also the naive RBC were cleared by 15% at 240 min. In healthy animals, sequestration of transfused S- and E-RBC in liver and spleen was higher than sequestration of N-RBC. In septic animals, no difference in sequestration was found between N-, E-, and S-RBC. In skeletal muscle, lungs, intestine, femur, diaphragm and skin, sequestration was not different between healthy or septic recipients nor between the different groups of transfused RBC.

Conclusion: Both ETX and sepsis induced alterations of the RBC membrane increase RBC clearance. However, the kinetics of ETX treated or septic RBCs clearance are completely different from the kinetics of RBC stiffened by GLUT. The majority of the injured and cleared RBC are entrapped in liver and spleen while other organ systems play only a minor role. Furthermore, RBC sequestration also appears to depend on the host's inflammatory state indicating RBC-host interactions in the microcirculation going beyond changes in RBC deformability.

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P121 Oxygen-ozone treatment improves p50 std value in patients with peripheral vascular disease

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In our previous study [1] we demonstrated that the ozonized autohemotransfusion increases erythrocyte filterability and reduces plasma and total blood viscosity, thus supporting the theory that the ozone-induced improvement of peripheral vascular disorders (PVD) might be related to its influence on the hemorheologic properties of blood.

Given that oxygen delivery to tissues is dependent on its affinity for hemoglobin, in the present study we evaluated the effect of oxygen-ozone treatment on hemoglobin oxygen affinity in 15 patients suffering from PVD (clinical stage IV according to Fontaine).

Before and 30 min after slow reinfusion of 150 ml of autologous venous blood exposed in a glass box to an O_2–O_3 mixture (3.6 mg of total ozone erogation with a Multiossigen Medical 93 Multi Tech Milano, Italy) we evaluated hemoglobin oxygen affinity using p50 STD value. This value is defined as oxygen tension in mmHg at 50% oxygen saturation, at pH 7.4, at 37°C and at pCO_2 40 ± 2 mmHg and is calculated according to the formula: p50 std = antilog [log p02 (log s02/2.7) – 0.4 (7.4-pH)].

		p50 std (mmHg)	2,3 DPG (mmol/l)
Treatment (ozonized autohemotransfusion)	Before	28 ± 0.9	2.5 ± 0.2
	After	32 ± 1.1	2.5 ± 0.3
Control test (non-ozonized autohemotransfusion)	Before	27.5 ± 1.0	2.5 ± 0.3
	After	28.1 ± 1.1	2.4 ± 0.5

15 Patients paired Student *t*-test $P < 0.005$.

The value of 2,3 diphsophoglycerate (2,3 DPG), an important regulator of oxygen unloading were also evaluated before and after ozone treatment. Control studies in the same patients were done in other occasions and random order to test the influence of blood manipulation (non-ozonized autotransfusion). The results (Table) show that after ozone treatment, p50 value increased ($P < 0.005$),

whereas plasma value of 2,3 DPG did not significantly change. No significant changes were induced by control tests (non-ozonized autohemotransfusions).

These results strengthen the conclusions of our previous '*in vitro*' study [2] proving that the ozone treatment shifts to right the oxygen hemoglobin dissociation, ultimately resulting in improved tissue oxygenation.

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P122 Sudden cardiac failure following treatment of metabolic alkalosis with hydrochloric acid

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Crit Care 1999, **3 (suppl 1)**:P122

Introduction: Severe metabolic alkalosis is a common problem in ICU due to high gastric reflux, diuretic drugs or parenteral nutrition. The mortality is considerable. Therapy of severe metabolic alkalosis with hydrochloric acid is widely accepted and described as save and effective.

Patients: We report five unexplained cases of acute cardiac arrest on our ICU in 1998 following infusion of hydrochloric acid in mechanically ventilated patients with severe metabolic alkalosis. Treatment with HCl (0.2 N, 10–15 ml/h) was commenced at pH 7.55 and BE +10 mmol/l. All patients suddenly showed a marked fall of oxygen saturation followed by bradycardia, hypotension and cardiac arrest 30 to 140 min after onset of HCl-infusion. CPR and high dose adrenalin (up to 5 mg in bolus) showed no effect. Oxygenation could not be improved by FiO_2 1.0. No patient survived the incident. The clinical aspect suggested a fulminant pulmonary embolism as the most likely cause of death. Autopsy was performed in three patients. The cause of death remains unclear. A fulminant pulmonary embolism could be excluded in these patients.

	Age	Underlying disease	Postop. day	HCl infusion period	Infusion-rate
Pat. 1	71	Peritonitis	3	140 min	15 ml/h
Pat. 2	63	Chest wall abscess	15	50 min	15 ml/h
Pat. 3	58	Perforated gastric ulcer	11	70 min	20 ml/h
Pat. 4	50	Empyema of pleural cavity	4	40 min	20 ml/h
Pat. 5	73	Peritonitis	2	30 min	10 ml/h

Conclusions: The therapy of severe metabolic alkalosis with HCl is suggested to be linked with potentially lethal complications. The observed and reported cases of death should be considered before application of HCl in treatment of severe metabolic alkalosis. Further studies are requested to analyze the reasons for sudden cardiac failure during HCl-infusion.

P123 Effects of epidural and halothane anaesthesia on vasoconstrictive properties of cell-free haemoglobin

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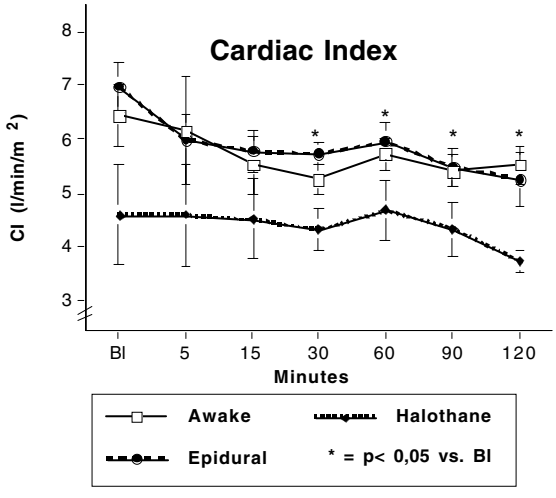
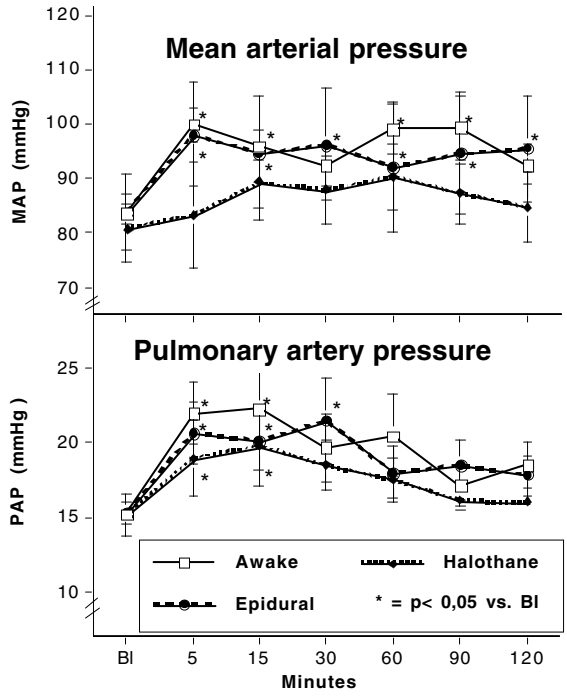
Introduction: In the moment haemoglobin based oxygen carries (HBOC) are under clinical investigation. Only few studies looked for the interactions between anaesthetic drugs and HBOC. The effects of HBOC during regional anaesthesia have never been analysed. Therefore, we investigated the hemodynamic changes after HBOC infusion during different kinds of anaesthesia.

Methods: Sheep were assigned to three different groups: a) 6 not anaesthetised sheep, b) 6 sheep with a halothane anaesthesia (2.0 Vol. % in oxygen), c) 6 sheep had an thoracic epidural anaesthesia with bupivacaine. After a stabilisation period all 18 animals received an i.v. bolus of 100 mg Pyridoxalated Haemoglobin Polyoxyethylene Conjugate/kg.

Results: The vasoconstrictive effects of a HBOC were similar in awake sheep and in sheep with epidural anaesthesia. Anaesthesia





with halothane reduced the effects on mean arterial pressure and cardiac index but did not abolish the pulmonary vasoconstriction.

Conclusion: The selection of the anaesthesia method may alter hemodynamic side effects of HBOC.

P124 'Wet' and 'dry' lungs: a useful sonographic distinction

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Pulmonary edema develops when the movement of liquid from the blood to the interstitium exceed the return of the liquid to the blood. The diagnosis of this interstitial expansion is based on chest X-ray and the basic clinical signs appear when the pulmonary compliance is reduced (aspecific dyspnea), a large mismatch exists between ventilation and perfusion or with the onset of alveolar flooding (moist and fine crepitant rales, wheezes or extreme breathlessness). The detection of an interstitial edema is a crucial step in the diagnostic procedure in a dyspneic patient and the intensivist or the emergency physician must make daily therapeutic decisions on the basis of a bedside clinical examination, often difficult, and chest X-ray, wich is known to be often technically deficient.

Methods and patients: During a 4-month period, 83 patients (49 males and 34 females, mean age 74 years) admitted to our Emegency Room (ER) were included in a prospective study.They showed dyspnea (>25 breaths/min) and/or discomfort and signs of augmented work of breath (inspiratory retraction of the intercostal spaces and supraclavicular fossa) or orthopnea. Immediately after the clinical examination, all patients underwent chest sonography. Longitudinal scans of the anterior, lateral and posterolateral (or posterior in the sitting patient) chest wall were taken using a Toshiba SSA250A portable unit equipped with a 3.75 MHz convex transducer. We particularly studied the respiratory motion of the pleuropulmonary surface (gliding sign) and the comet tail artifacts arising from the lung surface. These artifacts are roughly vertical narrow based projections spreading up to the edge of the screen and appear when there is a marked difference in acoustic impedance between subpleural septa thickened by edema and the alveolar air (alveolar-interstitial syndrome). Chest radiographs of all patients performed during the same period of ER evaluation were interpreted by radiologists unaware the sonography findings and classified on the basis of widely accepted criteria. Once the diagnosis of wet lungs was sonographically confirmed, the patients were considered for hearth failure treatment (diuretics and vasodilators) in absence of other diagnostic possibilities or particulary controindications, while the patients with dry lungs underwent advanced diagnostic work up. Finally we evaluated the effect of the diuretic therapy (in 3 h), the correlations between radiologic and sonographic patterns and the usefulness of ultrasonography in the diagnostic approach to the critically ill patients.

Results: All patients were successfully and quickly (<5 min) analysed using ultrasound (feasibility 100%). Twenty-nine subjects (34%) showed 'wet lungs' with diffuse bilateral comet tail artifacts. Of these, 21 (72%) had associated pleural effusions (bilateral in 13 cases), with water levels (WL) between 1 and 8 cm. Chest X ray discovered congestion or edema in 30 pts. (flow inversion, enlarged/iperdense ila: 5 pts. blurred ila, perivascular/peribronchial cuffs, Kerley B lines: 13 pts.; patchy alveolar edema: 7 pts. and confluent alveolar edema: 5 pts.), 29 of them exibiting diffuse artifacts. Pleural effusions were shown radiologically in 13 subjects with eight missed diagnoses (effusions with WL <2 cm). One discordant case was noted (sonographic false negative) but none of 51 patients with normal X rays had significant comet tail artifacts. Sonographic imaging led to a change in the initial diagnosis (hearth failure) in 11 pts. (13% of the whole group studied), six with COPD, three with pulmonary embolism and one with important anemia, these subjects showed normal chest X rays and sonographic 'dry lungs'; one patient had the diagnosis changed from COPD to hearth failure.

Conclusion: We think that echography offers a new method for the diagnosis of alveolar-interstitial syndrome at bedside and may provide vital informations when a radiograph is not readily available or undesiderable. Moreover it may be valuable for differentating cardiogenic pulmonary edema from decompensated COPD or pulmonary embolism showing, in our experience, a sensibility of 96% and a specificity near to 100% for diagnosing 'wet lungs'.

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P125 A comparison between impedance plethysmography and thermodilution for the measurement of cardiac output in pre-operative haemodynamic optimization

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Introduction: New developments in Impedance Plethysmography (IP) (IQ, Renaissance Technology, PA, USA) have been reported to allow accurate measurement of cardiac output in patients on the intensive care unit.

Methods: Ten patients on the ICU admitted pre-operatively for haemodynamic optimization were prospectively studied. Each patient had measurement of cardiac output by a thermodilution right heart catheter technique and also by IP. Data sets were obtained during the procedure of haemodynamic optimization. Data was analyzed using regression analysis for the differences between cardiac output measurements between the two techniques, depending on both the patient and the absolute level of cardiac output.

Results: Ten patients were analyzed with a total of 51 pairs of cardiac output measurements. Thermodilution cardiac outputs were obtained between 4.1 l/min and 10.5 l/min. Regression analysis revealed a significant difference between cardiac output measurements for the two techniques ($P < 0.0001$). Differences existed when the data was analyzed between patients and also when looking at different measurements for individual patients.

Discussion: IP would be ideal non-invasive tool for the measurement of cardiac output in ICU patients. This study suggests, however, that there are major differences between the cardiac outputs obtained from thermodilution and IP for pre-operative patients on the ICU.

P126 Hemodynamic monitoring by double indicator dilution technique in patients after orthotopic heart transplantation

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Background: Cardiac index (CI) and preload monitoring by pulmonary artery catheter (PAC) is increasingly confronted with criticism. We evaluated the less invasive arterial double indicator dilution method (TDD) as an alternative. Preload with this technique is determinated by measuring intrathoracic blood volume index (ITBVI) and global enddiastolic volume index (GEDVI) instead of filling pressures CVP and PCWP. As there is no clinical experience in patients with denervated hearts, we investigated this monitoring method in patients after heart transplantation.

Methods: Forty patients (34 male, 54.4 ± 8.5 years) were studied with the TDD and PAC methods. Measurements were performed at the ICU at 3, 6, 12, 24, 36, 48 and 72 h postoperatively. Based on Frank-Starling law, ITBVI, GEDVI, CVP, and PCWP have been investigated on their usefulness as preload indicators and for this purpose correlated with stroke volume index (SVI).

Results: No difference between femoral and pulmonary artery CI were found ($r = 0.98$, bias 0.35 l/min/m^2). Changes of CVP ($r = -0.23$) and PCWP ($r = -0.06$) did not correlate significantly to changes in SVI. ITBVI ($r = 0.55$) and GEDVI ($r = 0.63$) showed significant correlations. Equally directed changes of SVI with GEDVI and ITBVI occurred in 70.3% and 66.9% respectively, of SVI with CVP and PCWP in 41.1% and 41.9%.

Conclusion: CVP and PCWP are not as reliable preload parameters as ITBVI and GEDVI. The latter even in denervated hearts show good correlations to SVI. They can be obtained less invasively and therefore should be the method of choice.

P127 The cardiac chemoreflex sensitivity (cCRS) and the influence of respiration

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Introduction: Assessment of cCRS may be a predictor of serious arrhythmic events after survived sudden cardiac death. However, chemoreceptor (CR) stimulation produces not only cardiovascular but also respiratory responses. The aim of this study was to correct the respiratory influence on apparent values of cCRS.

Methods: The cCRS was assessed in 47 healthy volunteers during free breathing (FB). Twenty subjects underwent further monitoring during controlled breathing (CB, fixed minute ventilation). Peripheral arterial CTs were stimulated by 5 min of hypoxia (10% O_2 in N_2). Cardiac CRS was calculated as Δheart rate interval/ΔpO_2. We developed a mathematical model to reduce the respiratory influence on cCRS, and calculated a respiration independent second cCTS value using this correction. The corrected cCRS was compared with cCRS values experimentally obtained during CB.

Results: Cardiac chemoreflex sensitivity under free and controlled breathing

	CB	FB	FB (corrected values)
pCCS (ms/mmHg)	1.53 ± 0.32	3.64 ± 0.81*	0.89 ± 0.91 NS

*$P < 0.05$ versus controlled breathing (CB), NS, not significant versus CB.

Conclusions: Our results suggest that ventilation causes a major disturbance in the measurement of cardiac chemoreflex sensitivity. We argue that this disturbance should be minimised to obtain correct values of cardiac chemoreflex sensitivity for predicting serious arrhythmic events.

P128 Do we need a basis bolus concept for sedoanalgesia of mechanically ventilated patients in ICU?

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Introduction: Tolerance for mechanical ventilation is generally achieved by continuous application of analgesics and sedatives. Their effect is usually controlled by physical examination. The dosage in daily routine occasionally is not adapted to the patients needs in the circardian course. Evidence exists that classical neurological and hemodynamic parameters do not always reflect the level of sedoanalgesia. Neuromonitoring with heart-rate-variability (HRV) is a new opportunity to evaluate the patients neurological status. HRV is a window for usually invisible central autonomic regulation. This phenomenon is caused by oscillation in the interval between consecutive heart beats. It represents a quantitative marker of autonomic activity. Currently monitoring of autonomic nervous system is no routine tool for mechanically ventilated patients. Our study presents first results of continous neuromonitoring of autonomic nervous system with heart-rate-variability in the setting of an intensive care unit.

Methods: We studied 10 mechanically ventilated patients (5 male, 5 female) without any cardiovascular diseases in case history who received analgesics (Fentanyl®) and sedatives (Dormicum®) continuously. Heart-rate-variability was recorded with a flash-memory recorder, the analysis of HRV was performed by a special software (both elamedical, Munich). We investigated over a period of 24h in each case.

Results: The investigations show considerable variations regarding to the level of HRV parameters in the circadian course. During night time frequency domain parameters of HRV go down (total power: 85.88 ± 19.10 ms^2), while they increase during daytime (170.66 ± 57.29 ms^2) with a considerable variation. Nursing and medical manipulations as well as the doctor's round at bedside in the morning time lead to a conspicuous increase of total power [mean ± SEM]:

Frequency domain	1 h before doctor's round	During doctor's round	1 h after doctor's round
Total power (ms^2)	46.10 ± 11.55	193.20 ± 54.50	62.50 ± 20.82
Low freq. (ms^2)	5.40 ± 1.54	14.30 ± 4.23	7.30 ± 3.13
High freq. (ms^2)	8.30 ± 3.15	31.50 ± 15.76	10.50 ± 3.70

Conclusion: Continuous monitoring of the autonomic nervous system with heart-rate-variability is a new approach to demonstrate the status of the patients sedoanalgesics. It shows considerable variations of autonomic activity in the circadian course. Especially during manipulations at the patients bedside a dysbalance of central autonomic activity seems to appear. A basis-bolus-administration of sedoanalgesia seems to be a useful concept to compensate the undesirable and obvious dysbalance of central autonomic activity under stress situations like doctor's round at the bedside of mechanically ventilated patients with sedoanalgesics.

P129 Multigated radionuclide blood pool scans (MUGA) for preoperative assessment of patients undergoing orthotopic liver transplantation (OLT)

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Introduction: OLT is a major cardiovascular stress both intra- and postoperatively. The ideal preoperative cardiac screening test for patients with end-stage liver disease (ESLD) has not been determined [1]. We evaluated the value of MUGA in predicting perioperative morbidity and mortality in patients undergoing OLT.

Methods: After IRB approval we retrospectively examined the medical records of 170 ESLD patients who had MUGA scans prior to OLT from January 1994–April 1998. Morbidity was defined as reperfusion syndrome (fall in MAP >33%), requirement for intra- or postoperative inotropes, myocardial infarction (AMI), need for haemodiafiltration or ICU stay >5 days. Mortality was restricted to 30 days. MUGA scans were defined as normal if ejection fraction (EF) was >55% [2]. Analysis of results was by Chi-squared test.

Results: There were 127 patients in group A (EF >55%) and 37 patients in group B (EF <55%). Six patients were excluded because of incomplete data. No patients had AMI. Two patients in group A died and there were no deaths in group B.

Conclusion: For patients undergoing OLT, MUGA is not a useful screening test for predicting perioperative morbidity and mortality. Based upon these findings we have revised our method of preoperative cardiac assessment of patients presenting for OLT.

Event	Group A (No. (%))	Group B (No. (%))	*P* value
Reperfusion	67 (53)	23 (65)	0.28
Inotropes (intra)	42 (33)	16 (43)	0.27
Inotropes (post)	20 (16)	9 (24)	0.24
CVVHD	11 (9)	3 (8)	0.6
ICU stay >5 days	49 (38)	16 (43)	0.21

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P130 Lithium dilution cardiac output (LiDCO) measurement using peripheral venous injection of lithium chloride

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Background: We have previously described a simple indicator dilution method of measuring cardiac output in which lithium chloride is injected via a central venous catheter and its plasma concentration-time curve measured in arterial blood using a lithium selective electrode [1]. This technique has the advantage of requiring only central venous and arterial cannulation and therefore avoids pulmonary artery catheterisation.

There are many patients who have arterial cannulae and peripheral, rather than central, venous access in whom cardiac output measurements would greatly assist management.

We have therefore explored the feasibility of measuring cardiac output using a peripheral rather than central venous injection of lithium chloride.

Methods: Ten stable patients with peripheral (antecubital vein), central venous and arterial cannulae on a General Intensive Care Unit were studied. For each patient, 10 consecutive LiDCO measurements of cardiac output were made at 5-min intervals. The injections of lithium chloride were given alternately via the peripheral and central venous cannulae and the cardiac outputs calculated from the arterial plasma concentration-time curves. For each patient the average of the five LiDCO measurements obtained using peripheral venous injection was compared with the average of the five LiDCO measurements obtained using the central venous route.

Results: There was good agreement between the two methods ($r^2 = 0.98$) and the results are summarised in the Table.

Patient No.	Peripheral venous injection		Central venous injection	
	Mean LiDCO (l/min)	SEM	Mean LiDCO (l/min)	SEM
1	7.55	0.40	7.24	0.33
2	12.22	0.15	12.47	0.41
3	5.23	0.12	5.12	0.21
4	7.23	0.08	7.16	0.18
5	4.98	0.18	5.24	0.14
6	7.37	0.14	7.74	0.14
7	4.90	0.10	4.54	0.12
8	5.06	0.05	5.02	0.03
9	5.63	0.20	6.04	0.21
10	9.32	0.22	10.08	0.29

Conclusion: This study shows that LiDCO can be measured using peripheral or central venous injections of lithium chloride. Safe, quick and reliable cardiac output measurements can therefore be obtained in patients with arterial and antecubital venous access.

Reference

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P131 PiCCO monitoring during anesthesia

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Introduction: The Pulse Contour Cardiac Output (PiCCO) is an innovative technology that monitors the cardiac preload volume through the global end diastolic volume (GEDV) and gives an extimation of the intrathoracic blood volume, an indicator of circulating volume and of the extravascular lung water (EVLWI), which is considered to be a good extimator of interstitial lung edema.

Moreover PiCCO, through a 'beat to beat' analysis of the arterial pressure wave, measures continuous cardiac output. The aim of this study is to evaluate the new volumetric hemodynamic monitoring during major surgery and during liver and lung transplantation (Tx).

Methods: After approval from ethical committee 41 patients undergoing lung transplantation (11), liver transplantation (10), thoracic surgery (10) and major abdominal surgery (10) were included in the study. In all pts were placed a Swan-Ganz catheter (IntelliCath-Baxter, Irvine CA-USA, connected to Vigilance Monitor-Baxter) and a 4 F fiberoptic-thermistor catheter was inserted into the femoral or brachial artery (Pulsion PiCCO-Medizintechnik, Munchen). Hemodynamic volumetric data were collected in different phases: during lung Tx (MV = after induction of anesthesia; CL1 = after the first pulmonary artery clamping; REP1 =after the reperfusion of the first lung; CL2 = after the second pulmonary artery clamping; REP2 = after the reperfusion of the second lung; Fin = end of surgery); during liver Tx (A = after induction of anesthesia; B = anephatic phase; C = end of surgery); during thoracic (A = after induction of anesthesia; B = during surgery in one lung ventilation; C = end of surgery) and abdominal surgery (A = after induction of anesthesia; B =during surgery; C = end of surgery).

Results: See Table.

Discussion: Other authors reported GEDV modifications correlated to cardiac index rather than standard cardiac filling pressures such as CVP and PAWP, so that GEDV is considered a 'pure' volume indicator. EVLWI can be considered a potential indicator of lung damage and pulmonary function, and it is hypothesized to be a better endpoint than PAWP during fluid management.

In conclusion monitoring EVLWI, as pulmonary edema indicator and GEDV, as cardiac preload value, lead our diagnostic and terapeutic management during major surgical procedures.

	Phases	A (MV)	(CL1)	B (REP1)	(CL2)	(REP2)	C (FIN)
CI	Thoracic	2.4 ± 0.3		3.7 ± 0.6			4.7 ± 1.8
(l/min/m^2)	Abdominal	2.7 ± 0.7		3.3 ± 0.5			3.5 ± 1.2
	Liver Tx	3 ± 1		3 ± 1			4 ± 1
	(Lung Tx)	(3.2 ± 0.7)	(4 ± 1)	(5.1 ± 1)	(3.6 ± 1)	(4 ± 1)	(3.4 ± 1)
mAP	Thoracic	68 ± 7		74 ± 14			89 ± 23
(mmHg)	Abdominal	67 ± 6		92 ± 6			88 ± 21
	Liver Tx	82 ± 12		81 ± 16			84 ± 13
	(Lung Tx)	(74 ± 9)	(77 ± 11)	(83 ± 17)	(88 ± 11)	(100 ± 15)	(82 ± 6*)
mPA	Thoracic	23 ± 5		21 ± 4			25 ± 4
(mmHg)	Abdominal	20 ± 4		20 ± 5			23 ± 3
	Liver Tx	17 ± 3		19 ± 4			22 ± 4
	(Lung Tx)	(31 ± 10)	(43 ± 10)	(34 ± 8)	(42 ± 14)	(27 ± 7*)	(23 ± 5)
CVP	Thoracic	11 ± 6		8 ± 2			10 ± 4
(mmHg)	Abdominal	6 ± 1		15 ± 3			10 ± 2
	Liver Tx	9 ± 2		12 ± 4*			11 ± 3
	(Lung Tx)	(9 ± 2)	(15 ± 5)	(18 ± 5)	(18 ± 6)	(15 ± 4)	(13 ± 6)
PAWP	Thoracic	14 ± 3		14 ± 2			15 ± 7
(mmHg)	Abdominal	12 ± 2		12 ± 3			14 ± 2
	Liver Tx	12 ± 3		14 ± 4			15 ± 4
	(Lung Tx)	(17 ± 9)	(25 ± 8*)	(22 ± 9)	(26 ± 6)	(17 ± 4)	(15 ± 4)
GEDVI	Thoracic	904 ± 214		1045 ± 142			1350 ± 427
(ml/m^2)	Abdominal	1165 ± 236		1124 ± 145			1208 ± 322
	Liver Tx	773 ± 180		763 ± 173			945 ± 137
	(Lung Tx)	(711 ± 201)	(657 ± 228)	(650 ± 95)	(647 ± 118)	(818 ± 112)	(789 ± 104)
EVLWI	Thoracic	7 ± 3		7 ± 3			11 ± 2
(ml/kg)	Abdominal	6 ± 2		4 ± 1			4 ± 1
	Liver Tx	8 ± 3		12 ± 9			12 ± 10
	(Lung Tx)	(9 ± 4)	(11 ± 6)	(18 ± 8*)	(23 ± 21)	(21 ± 12)	17 ± 8

*$P < 0.05$.

P132 Measurement of aortal blood flow in supranormal cardiac output

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Introduction: In order to minimize complications of invasive techniques for measurement of cardiac output, non-invasive methods will be of growing importance in anesthesiology and intensive care. The validity of non-invasive measurements has frequently been questioned. In our study the validity of non-invasive measurements was assessed in supranormal cardiac output.

Methods: In 12 patients, who underwent whole body hyperthermia (WBH) in general anesthesia, aortal blood flow was measured using an esophageal Doppler probe (DYNEMO 3000, Sometec, France). Measurements were performed at 37°C, 40°C, 42°C and 39°C body core temperature. At the same time cardiac output was determined by the invasive thermodilution method using a pulmonary artery catheter (Swan-Ganz-Catheter) as well an arterial catheter (PULSION COLD®). Blood flow in the descending aorta is assumed to represent approximately 70% of total cardiac output, accordingly 70% of the value measured with the invasive technique was compared to the non-invasive measurement. For cardiac output measured by Doppler ultrasound median values were evaluated over a period of 5 min. Statistics were performed using the Mann-Whitney-U-Test.

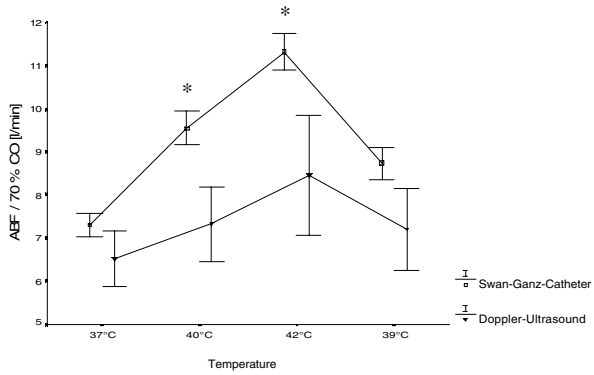

Figure. ABF and 70% CO during WBH.

Results: There were no significant differences between values obtained with the two different invasive techniques. Values measured with Doppler ultrasound were significantly lower at 40°C ($P = 0.04$) and 42°C ($P = 0.01$) compared to invasive measurements, despite a growing tendency with rising temperature (see Figure).

Conclusion: Under conditions with increasing supranormal cardiac output measurements with Doppler ultrasound do show a tendency, but absolute values are significantly underestimated with an increasing difference towards growing values.

P133 Trends of volemic indicators in a group of critically ill patients

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Introduction: The aim of this prospective non intervention study is to analyse the clinical utility of traditional preload indicators, as central venous pressure (CVP, mmHg) or pulmonary capillary wedge pressure (PCWP, mmHg), and the meaning of a pure volume indicator, as intrathoracic blood volume (ITBV, ml/m² BS).

Material and methods: Eighty-four medical or surgical patients were studied (mean age 51, SD 17; mean SAPS II (1st day) 56, SD 9). After 6 h of ICU stay, a 7.5 F pulmonary artery catheter and a 4 F femoral artery catheter, with thermistor and fiberoptics were inserted and connected to 'COLD System', an integrated monitoring system which uses the double indicator technique for studying blood volumes. All patients were in CMV (PEEP <8 cmH_2O); haemodynamic management was realized in order to optimize cardiac output (CO, l/min/m² BS) and systemic oxygen delivery. Infusion of crystalloids and colloids was guided by measurements of CVP and PCWP. All data were recorded at the beginning of the study (T0) and after 6 (T1), 12 (T2), 24 (T3) and 36 (T4) h. Statistical analysis of data was performed using Manova Test, considering the significant differences in the times of study between group A (38 pts., ITBV in T0 <1 l/m² BS) and group B (46 pts., ITBV in T0 >1 l/m² BS) and analysing the variance of repeated measures. Levels of $P < 0.05$ were accepted.

Result and conclusions: The Table shows the trends of parameters in the times of study (data are expressed as mean and (SD); A vs B, $^{\$}P < 0.0001$; $^{*}P < 0.05$; T vs T0, $^{\S}P < 0.05$).

When preload is the main determinant of CO, CVP and PCWP may be misleading in management of volemia in mechanically ventilated patients, on the contrary ITBV may be useful to optimize central filling and haemodynamic conditions.

	Time 0	Time 1	Time 2	Time 3	Time 4
CO	A 4 (1.5)* B 5.1 (1.7)	4.6 (1.8)*§ 5 (1.7)	4.8 (1.9)§ 5.1 (1.8)	4.6 (1.6)§ 5.2 (2.1)	4.8 (1.6)§ 4.9 (1.6)
CVP	A 7.9 (5.2) B 8.3 (4.6)	7.5 (4.1) 7.9 (3.6)	7.5 (4.2) 8.1 (3.3)	8 (4) 8 (4.2)	8 (4.7) 8.4 (4)
PCWP	A 11.5 (5.2)* B 14.9 (6.8)	11.1 (4.3)* 14.2 (6)	12.2 (3.6) 13.9 (5.4)	12.2 (4.3) 13.9 (6.4)	13.1 (4.5) 15.7 (7.3)
ITBV$	A 804 (129) B 1285 (237)	922 (238)§ 1234 (248)	1023 (305)§ 1314 (285)	928 (205)§ 1321 (384)	985 (323)§ 1269 (288)

P134 Usefulness of intrathoracic blood volume in the early phase of hemodynamic instability of patients with sepsis or septic shock

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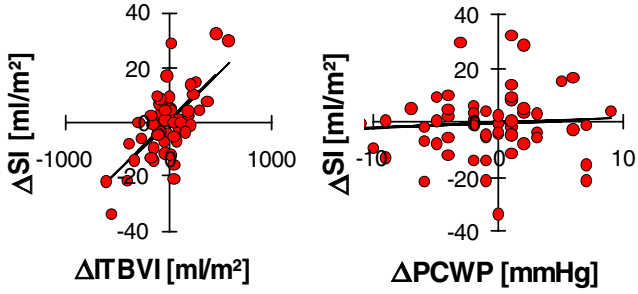
Introduction: Previous studies in cardiac surgical and ARDS patients suggested that the intrathoracic blood volume index (ITBVI) is a more reliable indicator of cardiac preload than the pulmonary capillary wedge pressure (PCWP). Since these studies were under controlled conditions, we analysed the value of both preload variables with respect to stroke index (SI) in patients with sepsis and septic shock under actual ICU conditions of frequent changes in ventilation, volume loading and catecholamine treatment.

Methods: We analysed 581 hemodynamic profiles in 57 septic patients (60 ± 15 years, SAPS II 53 ± 15, SOFA 15 ± 3) who received a 7.5 F pulmonary artery catheter and a 4 F flexible aortic catheter. Hemodynamic profiles were at least 15 min apart, the maximum time period was 24 h (8.25 ± 5.30 h).



Results: In all second profiles, changes in stroke index were accompanied by changes in ITBVI ($r = 0.67$) and not PCWP ($r = 0.07$). Increases in SI ($n = 265$) were more often associated with increases in ITBVI ($n = 189$, 71.3%) than in PCWP ($n = 122$, 46.0%). Decreases in SI ($n = 256$) were associated with decreases in ITBVI in 176 (68.8 %) and for PCWP in 119 cases (46.5%).

Conclusion: In the early phase of hemodynamic stabilisation of patients with sepsis or septic shock, ITBVI is a more reliable indicator of cardiac preload than the PCWP.

P135 Assessment of intrathoracic blood volume and extravascular lung water by single transpulmonary thermodilution

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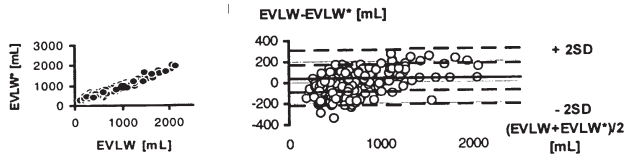
Crit Care 1999, **3 (suppl 1)**:P135

Introduction: The transpulmonary double-indicator dilution technique enables to measure the intrathoracic blood volume (ITBV) and extravascular lung water (EVLW). Since this technique is relatively time consuming and expensive, we studied whether the global end-diastolic volume (GEDV) which can be derived only from single indicator dilution (thermodilution) allows the estimation of intrathoracic blood volume.

Methods: In a heterogeneous population of 57 critically ill patients (56 ± 15 years) we found by structural regression analysis a correlation of ITBV=(1.25×GEDV)–28.4 [ml]. We then applied this equation on the first double-indicator measurements in 209 other patients (52 ± 19 years) with sepsis ($n = 98$), ARDS ($n = 31$), head injury ($n = 38$), hemorrhagic shock ($n = 19$), intracranial hemorrhage ($n = 19$), brain infarction ($n = 3$), and heart failure ($n = 1$). Each patient received a 4 F flexible aortic catheter with an integrated thermistor and fiberoptic. Bolus injections used cooled (0–4°C) indocyanine green dissolved in glucose 5% in a concentration of 2 mg/ml.

Results: By using the equation mentioned above, thermodilution ITBV (ITBV*) and correlated ITBV*=(1.06×ITBV)–124.3 [ml], $r = 0.98$, $P < 0.0001$. For thermodilution EVLW (EVLW*) linear regression analysis showed EVLW*=(0.83×EVLW)+133.9 [ml] ($r = 0.96$, $P < 0.0001$).



Conclusion: At least for patients on a surgical intensive care unit, single transpulmonary thermodilution is sufficiently accurate for the estimation of intrathoracic blood volume and extravascular lung water.

P136 Diagnostic determinants for capillary leakage syndrome (CLS) in septic shock patients

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Crit Care 1999, **3 (suppl 1)**:P136

Objectives: CLS is a frequent complication in sepsis characterized by loss of intravasal fluids leading to generalized edema and hypotension. Despite the importance there are still no standardized diagnostic criteria available for CLS. The aim of this study was to evaluate diagnostic determinants for CLS.

Design: Prospective clinical study.

Methods: The study was performed in 4 patients with septic shock (SOFA-Score = 12 ± 2), multiple organ failure and CLS compared to 4 control patients. CLS was judged clinically by generalized edema, positive fluid balance and weight gain. Plasma volume by indocyanin green (PV_{ICG}), red blood cell volume by tagged chromium-51 (RBC:^{51}Cr), extracellular fluid volume (ECF) calculated by inulin space technique and colloid osmotic pressure (COP) were measured before (T0 = 0 min) and after (T1 = 90 min) administration of 300 ml of albumin 20%. Measurement of total body water (TBV) and the phase angle (phi, degrees), a global parameter of the body composition were performed using bioelectrical impedance analysis (BIA).

Results: PV_{ICG} was measured in CLS patients with 45.9 ± 14.6 ml/kg/total body weight (BW) and in controls with 67.8 ± 15.2 ml/kg/BW. The RBC:^{51}Cr averaged 20.2 ± 1.3 ml/kg/BW in CLS patients and in the controls 24.4 ± 3.7 ml/kg/BW. ECF was expanded in CLS patients compared to controls (45.1 ± 8.5%BW vs. 29.5 ± 6.7%BW; $P < 0.05$). Increase of COP level at T2 in CLS patients was smaller than in the control patients (1.1 ± 0.4 mmHg vs. 2.4 ± 1.0 mmHg; $P < 0.05$). Phi was low in CLS patients (2.1 ± 0.8° vs. 4.8 ± 1.2°; $P < 0.05$) and TBV was elevated compared to controls (76.5 ± 12.0 kg vs. 55.7 ± 3.8 kg; $P < 0.05$).

Conclusion: These results suggest that measurements of phi and TBV using BIA combined with a difference of COP levels before and after administration of albumin are promising approaches to discriminate CLS from non-CLS patients at the bed-side.

P137 Evaluation of the use of bioelectrical impedance analysis in assessing the hydration and fluid balance of infants with bronchiolitis requiring intensive care

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Objective: To examine whether regular bioelectrical impedance (Z) measurements in babies with bronchiolitis detects daily changes in fluid status and if it may be used as a guide to hydration when compared to age matched well babies.

Methods: Bioelectrical impedance was measured using a Xitron 4000B machine, with electrodes placed 6 cm apart on the dorsal surface of the hand and foot. In babies with bronchiolitis measurements were made as soon as possible after admission and every 24 h until discharge. Data on fluid balance over the previous 24 h were recorded at each measurement period.

Results: There was a clear linear relationship between impedance (ohms) plotted against body mass index ($r = 0.95$, $P < 0.0001$) in the control babies. Using control data for BMI and Z, an equation was developed using linear regression to predict Z from BMI values. This equation was used (Z=19.04BMI + 114.6) to predict values for $Z_{expected}$ in the babies with bronchiolitis on admission. These values were compared with those at admission (Z_1), where using paired *t*-test a significant difference existed ($P < 0.0008$) and at discharge (Z_2) where there was no significant difference. There was no significant relationship between changes in body impedance and changes in fluid balance (both positive or negative) although impedance changed appropriately in association with fluid boluses or with diuretics.

Conclusion: Regular impedance measurements give a guide to the state of hydration of babies requiring intensive care and help determine whether the baby is adequately hydrated or not. There is a poor relationship between measured changes in fluid balance and changes in impedance and it may not be used to calculate absolute values of fluid required.

P138 External cardiac pressures and the left ventricular pressure–volume relationship

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Crit Care 1999, **3 (suppl 1)**:P138

Introduction: Wide variations in external cardiac pressures are known to occur in clinical situations and can have significant effects on cardiac performance [1,2]. We designed an experimental situation where external cardiac pressure conditions were controlled and adjusted to physiological extremes to mimic clinically relevant situations, while cardiac performance was assessed using left ventricular pressure–volume relationships (LVPVR) which are relatively preload and afterload independent.

Methods: Healthy adult pigs ($n = 4$) were anesthetized, received central vascular catheters, a pericardial catheter, and bilateral pleura drains. Left ventricular volume was assessed by the conductance technique [3]. External cardiac pressures were manipulated: pneumothorax (20 ml/kg air injected in the pleura), and pericardial infusion (mean pressure of +6 mmHg). End sytolic elastance (Ees), preload recruitable stroke work (PRSW), preload-adjusted maximal power (PWRmax/EDV2) [4].

Results: During pericardial infusion, where the end-systolic pressure was low and limited in beat-to-beat decrement during the preload reduction, only elastance increased while the other derived systolic parameters decreased. During pleura insufflation, all the systolic function parameters increased.

Discussion: These data suggest that relatively load-independent means are needed to assess cardiac function in the setting of extreme extracardiac pressure. LVPVR provides beat-to-beat insight into heart function at wide ranges of loading conditions. Further work is warranted to validate clinically applicable means to implement this type of assessment, as well as to further develop reference methodology for experimental and clinical heart volume assessment.

	Pleural intervention		Pericardial infusion	
	Control	Insufflation	Control	±6 mmHg
EDV (ml)	85 + 10	54 + 4	86 + 13	62 + 11
EDP (mmHg)	13 + 2	12 + 0.2	13 + 1	13 + 1
ESV (ml)	42 + 6	22 + 3	47 + 7	33 + 6
ESP (mmHg)	90 + 3	70 + 14	88 + 3	47 + 5
Pericardial pressure (mmHg)	0.8 ± 1.3	5.1 ± 1.8	-0.6 ± 1.1	6.4 ± 0.7
dP/dt max (ms)	1557 + 152	1581 + 453	1622 + 260	809 + 63
Ees (mmHg/ml)	1.24 + 0.2	1.72 + 0.3	1.25 + 0.2	2.26 + 0.9
PRSW (mmHg ml/ml)	50 + 4.1	60.1 + 11.3	51.6 + 4.4	43.6 + 6.2
PWRmax/EDV2 (dE/dt)	3.1 + 0.8	6.6 + 2.0	3.0 + 0.8	2.5 + 0.6

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P139 Computer simulation of the left ventricular pressure–volume relationship (LVPVR)

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Crit Care 1999, **3 (suppl 1)**:P139

Background: The concept of time-varying elastance developed by Suga and Sagawa in the 1970s integrates on the same graph all the components of LV function: contractility (Ees, slope of ESPVR [1]), preload (Ved), afterload (slope Ea ~ HR.SVR), matching of LV with arterial system (graphical analysis of SV) and LV efficiency [2]. A computer simulation makes it a remarkable didactic tool.

Methods: *Input data*: volume (V); compliance of capacitive vessels (Cv); venous resistance at the entry of LV(Rv); LV compliance (C_{LV}); (Ees); zero-volume intercept (Vd); systemic resistances (SVR); heart rate (HR). *Output data*: $Ved = (MSP.C_{LV}) - (MSP.C_{LV} - Ves) \times e^{(-t/Rv.C_{LV})}$ with loading time (t) = (60/HR)–0.2 and mean systemic pressure (MSP)=V/Cv; $Ped = e^{(0.33/C_{LV})(Ved-Vd)} - 1$; Ea=HR.SVR; Ves=(Ea.Ved+Ees.Vd)/(Ees+Ea); SV=Ved–Ves PES=Ea.SV; LVEF=SV/Ved; CO=HR.SV; Pressure–volume area PVA=EW+PE; external work EW (SV.(Pes–Ptd/2); Potential energy PE=1/2(Ves–Vd).Pes; $MVO_2 = 2.5 \times APV + 0.3 \times Ees + 1$; 1 mmHg ~ 1.333×10^{-4} J; mechanical efficiency ME=EW/MVO_2.

Results: The computer calculates output values according to input data and simultaneously modifies the classic graph on the screen.

Discussion: The software simulates realistically the altering of preload (Ved) and afterload (Ea, HR, SVR), contractility (Ves, Vd) and the corresponding modifications of ME. LVF and ME evolve according to theoretic and experimental expectations, i.e. ME = 0.28 to Ved = 250 ml; ME max to Ea/Ees = 0.5.

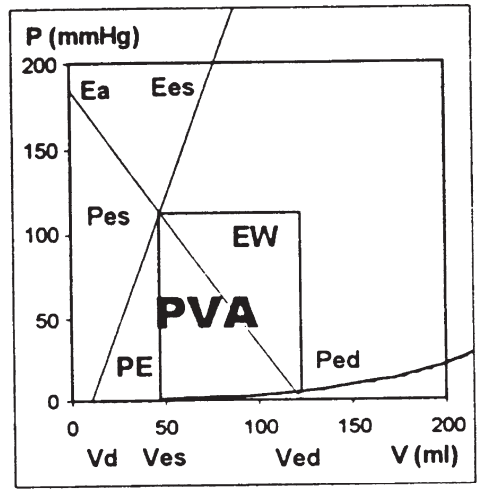

Figure 1. Results for V = 5500; Cv = 660; Rv = 0.03; C_{LV} = 20; Ees = 3; Vd = 10; SVR = 20; HR = 75; Ea = 1.5; Ea/Ees = 0.5; Ved = 123; Ves = 48; LSV = 75; Ped = 5; Pes = 113; CO = 5.6; EF = 0.61; WE = 1.1; PVA = 1.4; MVO_2 = 5.4; ME = 0.21.

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P140 Prospective, randomized trial of the effect of supranormal oxygen delivery on morbidity and mortality in high risk surgical patients

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Crit Care 1999, **3 (suppl 1)**:P140

Introduction: This prospective, controlled study was undertaken to evaluate the response to therapy aimed at achieving supranormal cardiac and oxygen transport values (cardiac index >4.5 l/min/m^2, oxygen delivery >600 l/min/m^2, and oxygen consumption >170 l/min/m^2) in patients older than 60 or with previous severe cardiorespiratory illnesses, who have undergone elective extensive ablative surgery planned for carcinoma or abdominal aortic aneurism.

Method: Thirty-seven consecutive high risk patients who underwent major surgery were randomized. The postoperative hemodynamic and oxygen transport variables and outcomes in 18 patients (control group) treated to maintain normal hemodynamic values were compared with 19 patients (protocol group) treated to maintain supranormal values. Therapy in both groups consisted of volume expansion, vasopressors, and when necessary, dobutamine (3–30 µg/kg/min), to reach their target values, during the surgery and 24-h postoperative period.

Results: We interrupted the study as a significative difference in mortality rate was seen. The mortality rate in control group (50%) was significantly higher ($P < 0.05$) when compared with protocol group (15.7%). The incidence of clinical and infectious complications was higher in control group ($P < 0.05$) and organ dysfunction evaluated by SOFA score occurred more frequently in non-achievers.

Conclusions: Patients with a previous cardiorespiratory illness or older patients submitted to extensive surgery had a reduction in morbidity and mortality with the use of supranormal values as therapeutic goals during and after the surgical trauma.

P141 Are supranormal values of DO_2 defined well?

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Crit Care 1999, **3 (suppl 1)**:P141

Introduction: The physiological assumption of oxygen debt elimination is a spontaneous or therapeutically induced increase of DO_2 in relation to the values of DO_2 recorded before the occurrence that led to the oxygen debt formation. The target of this research was to analyse the relation between post-operative achievement of DO_2I >600 ml/min/m^2 and the dynamics of changes of DO_2 during the perioperative period and in that way to give an answer to the question if the achievement of so called 'supranormal values' of DO_2 is equal to the physiological principle of oxygen debt elimination.

Methods: There were included 36 high-risk surgical patients in the prospective research (age 53 ± 15 years, 28 male and 8 female, 58% extensive ablative surgery for carcinoma). PA catheter and arterial catheter were inserted 12 h before surgery in the average. The target of therapeutical approach was to reach DO_2I >600 ml/min/m^2 within 12 h from the end of surgery in every patient and then to keep these values during following 36 h. Haemodynamic measurements and laboratory analyses of blood samples, including arterial lactate, were analysed during the first 48 h after an interval of 6 h. While the data were analysed, we were comparing the dynamics of changes of DO_2 and arterial lactate in the peri-perative period in relation to the real achievement of the therapeutical target (DO_2I >600 ml/min/m^2 within 12 h after the end of surgery) and the survival rate of the patients.

Results: The 28-day mortality was in the whole group of patients 31% (11/36). We achieved therapeutical target in 22 patients (61%). The mortality was 23% (5/22) in this group which was not statistically lower compared to the group of patients where the target was not achieved (43%, 6/14). When we compared the dynamics of changes of DO_2 and arterial lactate during the perioperative period in relation to the real achievement of the therapeutical target and surviving of patients, we found out in group of patients which achieved target the results which are demonstrated on the following figures. The results which were found out in group of patients which did not achieve target were the same.

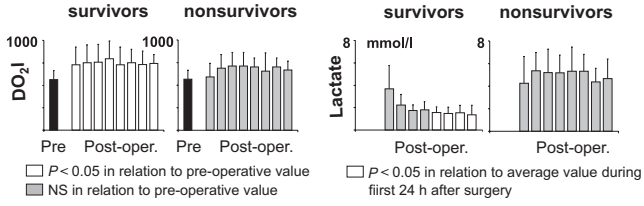

Figure 1. Perioperative oxygen delivery.

Figure 2. Postoperative arterial lactate.

Conclusion: Regardless of post-operative achievement of DO_2I >600 ml/min/m^2, in survived patients there was observed that they were achieving statistically higher values of DO_2 in comparison with pre-operative values of DO_2 and this process was accompanied by a decrease of arterial lactate level. We suppose that supranormal values of DO_2 should be define in relation to the pre-operative (i.e.normal) values of DO_2 and not in relation to the 'magic number' 600 ml/min/m^2.

P142 Correlation between three methods of calculating oxygen extraction ratio (OER)

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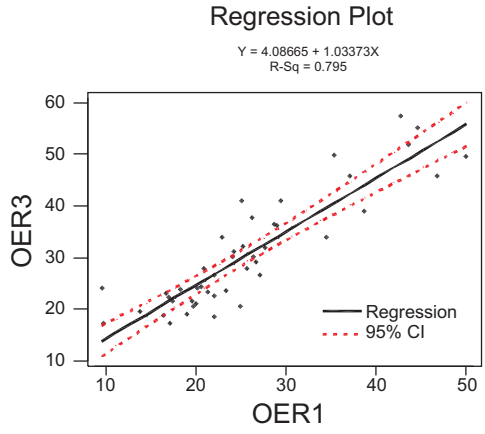
Introduction: OER can be calculated using OER = (SaO_2–SvO_2)/SaO_2. SaO_2 and SvO_2 can be measured by blood gas analysis or by continuous non-blood sampling display. The aim of this study was to compare the three methods of calculating OER.

Methods: Sixty-five sets of measurements from 16 patients were studied. Arterial and continuous cardiac output with SvO_2 (SvO_2–CCO, Baxter) catheters were inserted. Simultaneous blood samples were taken for arterial and mixed venous blood gas measurements using co-oximetry. Continuous SaO_2 from pulse oxymetry (SpO_2) was recorded. OER was calculated using three methods for each set of measurements: Conventional blood sampling method: OER1 = (SaO_2–SvO_2)/SaO_2; Partial blood sampling method: OER2 = (SaO_2–SvO_2-CCO)/SaO_2; Non-blood sampling method: OER3 = (SpO_2–SvO_2-CCO)/SpO_2. Simple linear regression with 95% confidence intervals was applied to test the correlation between the three methods.

Results: There was a significant positive correlation ($P < 0.001$) between the three methods.



Discussion: These three methods can be used to calculate OER. However, the conventional method (OER1) appears to have more variability than OER2 and OER3. OER3 (SpO_2 and SvO_2–CCO), in contrast, is the simplest and most accurate method for continuous monitoring of OER in intensive care management.

P143 Relationship between oxygen extraction (OER) and age in septic patients

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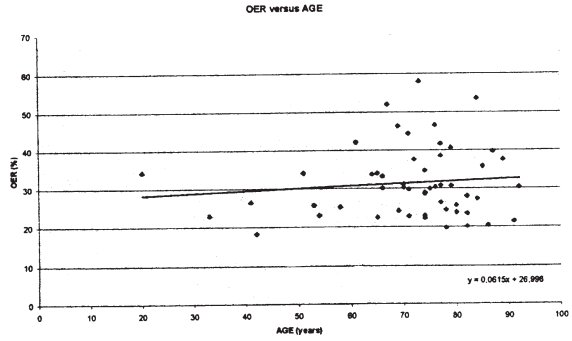
Crit Care 1999, **3 (suppl 1)**:P143

Introduction: A pathologic dependency between oxygen consumption (VO_2) and oxygen transport (DO_2) is characteristic of septic patients. Septic state appears to be associated with a defect in oxygen extraction (OER = VO_2/DO_2), causes possible cellular hypoxia, mitochondrial dysfunction and development of multiple organ failure. We studied the relationship between the mean OER and age in septic patients in a 12-bed ICU.

Methods: We investigated 53 septic patients (age range 20–93 years), invasively monitored in a descriptive study. DO_2, VO_2 and OR were obtained in each patient in triplicate during the first 24 h of sepsis diagnosis. Cardiac output (CO) was determined during thermodilution. Lactate concentrations were obtained in 46/53 patients (86%) and were elevated in 39%.

Results: We obtained a significant increase of the mean OER ($r = 0.30$; $P = 0.027$, two-tailed) in elderly septic patients. We noted also a significant decrease of DO_2 ($P < 0.0001$) and VO_2 ($P = 0.004$) in relation with age. No significant modifications were demonstrated with venous saturation of O_2 (SvO_2, $P = 0.16$), arterial saturation of O_2 (SaO_2; $P = 0.7$), hemoglobin concentration ([Hb], $P = 0.56$) and CO ($P = 0.2$)] in relation with age.



Conclusion: In this descriptive study, mean OER increases in elderly septic patients. These results are probably explained by the decrease of DO_2 and VO_2 in relation with age.

P144 Cardiac index estimation using central venous oxygen saturation (Scv O_2) in critical illness

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Background: The use of PA catheter is associated with increased costs and risks to the patients. Central venous (superior vena cava) oxygen saturation obtained by a less risky and costly manner can be used to estimate Sv O_2 with great accuracy up to 92% according to our results.

Objective: The aim of this study was to find whether estimated values of Sv O_2 can estimate with accuracy cardiac index using Fick method in comparison with thermodilution in critically ill patients.

Material and methods: Sixty-one critically ill patients were catheterized (Opticath PA Catheter P7110 Abbot) upon their admission and the values of Sv O_2, Scv O_2 and CI were simultaneously measured.

Results: The value of Sv O_2 was 68.6% ± 1.1 (X ± SEM) , the value of Scv O_2 was 69.4% ± 1.1, pearson correlation coefficient was $r = 0.95$ and $r^2 = 0.89$ with standard error 3.01. The power model of regression analysis which has the expression Sv O_2 = b0 (Scv O_2)^{b1} [in our patients Sv O_2 = 1.1612 (Scv O_2)$^{0.9617}$] was found to better describe the relation between the two variables with value of $r^2 = 0.92$. That means we can estimate the value of Sv O_2 from the value of Scv O_2 with accuracy 92%. We used estimated values of Sv O_2 with power model in Fick equation to estimate CI values and we correlated the estimated CI values with thermodilution CI values. Thermodilution CI values were 3.93 ± 0.17 (range = 1.85–9.3) and Fick method CI values were 3.88 ± 0.18 (range = 1.3–9.76). Pearson correlation coefficient between them was $r = 0.86$ and $r^2 = 0.73$ with high significance ($P < 0.001$).

Discussion–conclusion: Scv O_2 can be used as a mirror of Sv O_2 for the initial evaluation of critically ill patients with value of $r = 0.95$ and $r^2 = 0.89$. These results are in accordance with other authors [1,2]. However, some others found that there is poor correlation and questioned the usefulness of Scv O_2 measurement [3]. Power model of regression analysis which has the expression Sv O_2 = 1.1612 (Scv O_2)$^{0.9617}$ can estimate the value of Sv O_2 from the value of Scv O_2 with accuracy 92% (r^2 = 0.92). The use of estimated (with power model) value of Sv O_2 in Fick equation can estimate the value of CI with accuracy 86% in comparison with thermodilution (value of $r = 0.86$).

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P145 AKBR (arterial ketone body ratio) associates with lactate in the lactic acidosis

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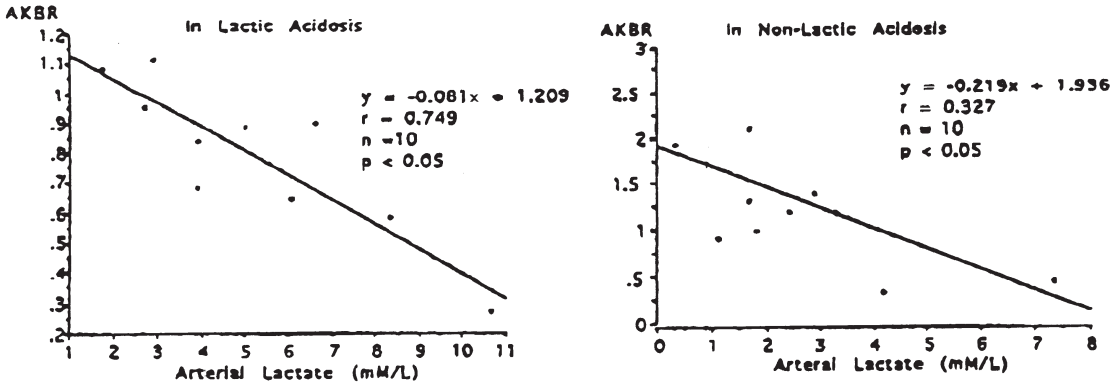
Crit Care 1999, **3 (suppl 1)**:P145

Introduction: Lactate anion is a normal product of anaerobic glycolysis of mitochondria. Lactic acidosis, the serum lactate concentration in increased and metabolic acidemia, relates to the prognosis of Multiple Organ Dysfunction Syndrome (MODS).

While the AKBR reflects the glycolysis function of liver mitochondria, we hypothesized similar relationships between the blood concentrations of lactate and the AKBR in lactic acidosis because when the function of mitochondria is low, aerobic glycolysis in the Krebs cycle is disordered and hyperlactemia is caused.

Methods: We studied 20 MODS patients in our ICU. We surveyed their blood concentrations of lactate and AKBR and analyzed arterial blood gas when they were in a state of shock. Then we studied the correlation between the lactate concentrations and AKBR in lactic acidosis and non-acidosis. The correlation coefficient was



found by regressional analysis each in lactic acidosis and non-lactic acidosis.

Results: Among 20 MODS patients, in 10 lactic acidosis patients who were all type A lactic acidosis the blood levels of lactate and the AKBR were interrelated. The correlation coefficient was 0.75 and that showed the blood levels of lactate correlated closely with the AKBR in lactic acidosis. When the AKBR was low, the blood level of lactate rose, but in the other 10 non-lactic acidosis patients, the blood levels of lactate had no relation with the AKBR.

Conclusion: We conclude that the AKBR has a strong relation to the concentration of lactate in lactic acidosis, but in non-lactic acidosis there was no relation. This study clinically proves that in lactic acidosis the blood concentration of lactate reflects the AKBR which is shown by the malfunction of liver mitochondria. Now right at the bed side, we can survey lactate concentrations easier and at a lower cost than the AKBR.

P146 Blood lactate: an excellent prognostic indicator in high-risk surgical patients

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Objectives: To evaluate the prognostic value of blood lactate levels in high-risk surgical patients.

Methods: Forty-four consecutive patients admitted to a general ICU for high-risk non-cardiac post-operative care. We recorded blood lactate levels, mean arterial pressure (MAP), heart rate (HR) and PaO_2/FIO_2 ratio at admission, 12, 24 and 48 h. We also recorded SAPS II score, surgery duration, number of complications, length of ICU and hospital stay for all patients.

Results: 39 patients survived, and 34 had no complications during their stay in the ICU. The survivors had blood lactate levels lower than the non-survivors at 12 (1.67 ± 0.8 vs 3.16 ± 1.7; $P = 0.004$) and 24 h (1.5 ± 0.7 vs 2.3 ± 0.6; $P = 0.05$) but not at the admission. The blood lactate levels decreased in the survivors ($P = 0.002$) but not in the non-survivors. Blood lactate levels was lower among non-complicated patients (none complication) at admission (2.12 ± 0.85 vs 3.21 ± 2; $P = 0.01$); 12 h (1.63 ± 0.8 vs 2.5 ± 1.6; $P = 0.02$) and 24 h (1.36 ± 0.47 vs 2.1 ± 0.9; $P = 0.004$). Blood lactate levels decreased in the non-complicated patients ($P = 0.004$) but not in the complicated patients. All others variables were not statistically different between groups. The length of ICU stay was greater in the non-survivors ($P < 0.0001$) but not the hospital stay.

Conclusion: Blood lactate level was the best prognostic indicator in our population when compared to other variables often used at bedside, including SAPS II score.

P147 Outcome of early hyperlactataemia in critically ill children

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Crit Care 1999, **3 (suppl 1)**:P147

Objective: To examine the relationships between hyperlactataemia, acidosis, organ failure, and mortality in children admitted to intensive care.

Design: Prospective observational study. Children with lactate levels >2 mmol/l within 24 h of admission were enrolled. Post-operative patients and those with inherited metabolic disease were excluded. The Paediatric Risk of Mortality (PRISM) score, Multiorgan System Failure (MOSF) score, length of ICU stay, and outcome were recorded. Data were collected for pH, base deficit (BE), and lactate (mmol/l) on admission, at 12 and 24 h. Data are reported as median (range). Fifty children aged 20.3 months (0.1–191) were enrolled. Data were analysed by the Mann-Whitney, Fisher's Exact, Kruskal-Wallis tests, and the Chi-squared test for trend.

Results: Median PRISM score was 19 (4–49), median MOSF score 2 (0–5), and observed mortality 32/50 (64%). Median duration of ICU stay was 6 days (2–32) in survivors, and median time until death 3 days (0–13) in nonsurvivors. Eleven nonsurvivors (34%) died within 24 h.

Admission lactate did not increase with increasing MOSF score ($P = 0.5$). However mortality increased with increasing MOSF score ($P = 0.005$).

Conclusion: Early hyperlactataemia is associated with a high mortality in critically ill children. Organ failure and peak lactate levels may distinguish nonsurvivors in this group.

Parameter	Survivors ($n=18$)	Nonsurvivors ($n=32$)	P
Age (months)	19 (0.1–184)	21 (0.1–191)	0.5
MOSF score	2 (0–4)	3 (1–5)	0.005
Admission pH	7.32 (6.8–7.6)	7.3 (7.0–7.7)	0.6
Admission BE	–7.5 (–14 to 5)	–8 (–30 to 3)	0.45
Admission lactate (mmol/l)	3.8 (0.9–8.5)	4.6 (1.2–22)	0.27
Peak lactate (mmol/l)	5.0 (2.0–9.3)	6.8 (2.3–22)	0.02

P148 Artificial colloids influence survival rate of human monocytes

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Introduction: Monocytes are within the first line of an organisms immune defense. However in the course of sepsis they undergo apoptotic cell death [1,2]. It is unclear whether this serves to protect the organism from a hyperreactive inflammatory response or is a sign for immune dysfunction.

The artificial colloids hydroxyethylstarch (HES), dextran (DEX) and gelatine (GEL) are essential in perioperative volume replacement as well as in the treatment of trauma, shock and sepsis. In this study we investigated whether artificial colloids influence survival or apoptosis of human monocytes *in vitro*.

Methods: Monocytes were isolated from buffy coats of healthy donors by gradient centrifugation and adherence to plastic culture dishes. They were incubated for 8 h with HES, DEX and GEL at 10 to 40 mg/ml. Staurosporine was added to induce cell death. Alive, apoptotic and necrotic cells were identified by Annexin V/Propidium Iodide staining and 10 000 cells were analysed by flow cytometry. Presence of apoptotic cell death was confirmed by electron microscopy, TUNEL, and cell death detection ELISA. Regression analysis of colloid concentration against cell status was performed. Slope values were tested with Students'*t*-test against 0. Significance was assumed for $P < 0.05$.

Results: All artificial colloids reduced the fraction of viable cells in a concentration dependent manner. This effect was significant with DEX. Apoptotic cells, which were calculated as a fraction of dead cells were reduced with DEX more than with HES, but increased significantly with GEL.

Incubation with staurosporine reduced cell viability and increased the fraction of apoptotic cells. Neither colloid nor concentration had additional influence. Only the results for HES are shown.

Conclusion: DEX, HES, and GEL promote monocyte death *in vitro*. This effect is concentration dependent, but most obvious beyond concentrations found in clinical practice. Cell viability is reduced most by DEX, whereas GEL seems to delay the course of cell death, as apoptotic cells undergo secondary necrosis in vitro. Staurosporine induced cell death is not blocked.

References

1. Baran J *et al.*: *Infect Immun* 1996, **64**:4242-4248.
2. Ayala A *et al.*: *J Trauma* 1996, **40**:568-574.

Culture medium	Colloid added	Status of monocytes	Concentration of colloids (mg/ml) 0	10	20	40
Standard	HES	Alive	58.15	53.33	50.35	45.25
		% apototic/dead	17.63	17.35	16.77	15.23
	GEL	Alive	58.15	53.8	52.58	52.48
		% apototic/dead	17.63	23.96	25.53	26.6
	DEX	Alive	58.15	53.25	51.86	43.93
		% apototic/dead	17.63	17.24	16.45	12.2
Staurosporine 400 nM added	HES	Alive	31.15	31.05	32.81	29.29
		% apototic/dead	34.39	34.27	33.75	33.64

P149 Determination of the clearance factor for TSE agents during the manufacturing process of polygeline

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Polygeline (a polymer prepared from heat-hydrolyzed gelatine) is a plasma substitute used by infusion as a 3.5% solution in the

management of hypovolaemic shock. TSEs (transmissible spongiform encephalopathies) are a group of fatal neurodegenerative (CNS) diseases affecting humans (e.g. Kuru, CJD) and animals (e.g. ovine scrapie, bovine BSE), all caused by a common class of agents, Prions. The link between TSEs and polygeline lies in its precursor, the gelatine which derives from bovine bones; bones may be at risk due to adjacent CNS (skull and vertebrae) contamination. In this experiment the main steps of the manufacturing process of polygeline were validated in order to see if the process is able to reduce the risk of iatrogenic transmission of the infectious agent, if present. It is the first time that results of a validation study on a gelatine-derived product have been published. Three steps of the process were validated separately: in step 1, gelatine was subjected to three alternative autoclaving schedules (1A: 121°C for 1.5 h; 1B: 121°C for 3 h; 1C: 133°C for 40 min). Step 2 was the crosslinking and distillation phase, and Step 3 the final sterilization at 121°C for 45 min. The hamster-adapted 263K strain of scrapie was used as the TSE model. The infective spike was added to each material before being processed and titrated in hamsters. Each assay was performed in duplicate, and animals were monitored for 1 year. The initial hamster-titrated infectivity of the spike resulted in $10^{9.0}$ LD50/2 ml. From the preliminary results of the experiment, only based on symptomatology (histological results of all brains expected till February 1999), the average step-clearance of infectivity (mean of two replicates) was (LD50/2 ml): $10^{6.0}$ (1A), $10^{6.9}$ (1B) and $\geq 10^{7.4}$ (1C), $10^{2.4}$ (2) and $10^{4.6}$ (3). It is clear that heating the gelatine (step 1) was very effective in reducing the infectivity of TSE agents. Taking also into account that the initial experimental contamination level adopted was extremely high, that raw materials used in the real production are carefully selected from a BSE-free country (USA) and exclude the skull and spinal cord, that the starting material - gelatine - is already produced by BSE-reducing procedures, and that steps 2 and 3 also contribute to lowering the infectivity, if any, it may be concluded that the polygeline manufacturing process is capable of inactivating BSE agents to a very high extent.

P150 Persistent pruritus after hydroxyethyl starch (HES) infusions in critically ill patients

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Introduction: It was noticed that severe persistent pruritus was a common complaint in patients attending our nurse-led ICU follow up clinic. Pruritus is a known adverse effect after hydroxyethyl starch (HES) infusions [1]. We therefore undertook this retrospective study to clarify any association between pruritus and HES infusions.

Method: Questionnaires were sent to all surviving patients who, over a 6 month period, had been on ICU for greater than 24 h ($n = 100$). The 19 questions covered a wide range of areas including general well-being, quality of life, mood and memories of intensive care. Two questions asked about itching. Respondents complaining of pruritus and non respondents were telephoned. Standardised questions were asked to identify incidence, severity, duration, triggering or relieving factors and the parts of body affected. For patients, the volume of HES received in the ICU was identified from ICU charts. Statistical analysis was by Mann-Whitney U test, with significance determined by $P < 0.05$.

Results: Details were obtained from 73 patients. 34% had experienced pruritus since their discharge from ICU. Of these 44% had severe persistent pruritus, which had not resolved with conventional treatments. In patients with pruritus, the total volume of HES infused ranged from 0–27350 ml, (median 2000 ml), infused over a mode of 2 days. The 'non pruritus' group, total HES volume ranged from 0–13350 ml, (median 500 ml), infused over a mode of 1 day. There was a significant relationship between the volume of HES and the occurrence of pruritus ($P = 0.003$).

Conclusion: This retrospective study shows that HES infusions may be associated with persistent pruritus. This may seem a trivial problem after a life-threatening illness, but our experience suggests that it significantly detracts from quality of life in survivors.

Reference

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P151 Volume replacement after cardiac surgery: a comparative study between hydroxyethylstarch (6%, 70/0.5), gelatin (3.5%) and Ringer's solution

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Introduction: During hypothermic cardiopulmonary bypass (CPB) patients often experience vasoconstriction and later their peripheral circulations gradually dilate over a period of several hours. The redistribution of circulation produces hypovolemia for which volume loading is necessary. Our aim was to compare 6% hydroxyethylstarch (70/0.5), 3.5% polygelin and Ringer's solution when used for volume restoration during the first 6 h after CPB. We were especially interested in hemodynamic stability, plasma viscosity, bleeding, volume uptake and oxygenation index (PaO_2/FiO_2).

Methods: Ninety adult patients undergoing cardiac surgery and CPB were randomized before surgery to one of three fluid regimens. The groups were comparable with respect to age, sex, heart function and pre-existing diseases. Hemodynamic function, plasma viscosity, mediastinal blood loss, and volume uptake were

measured after 30 min, 60 min postoperatively and then every hour during the first 6 h after surgery. The oxygenation index was measured 1, 3 and 6 h after surgery. A P value <0.05 was considered significant.

Results: There were no significant intergroup differences in any of the hemodynamic variables MAP, CVP and HR. There was no significant difference among the three groups in the plasma viscosity after surgery. Mediastinal blood flow increased significantly in the HES group 2–6 h after surgery ($P < 0.05$) compared with the geline and Ringer's group. The two colloid groups needed significantly less fluid compared with the Ringer's group ($P < 0.05$). There were no differences in diuresis. There were no significant intergroup differences in the oxygenation index. The need for postoperative ventilatory support did not vary between the three groups.

Conclusion: This randomized comparison of two colloid and a Ringer's solution fluid regimens after cardiac surgery shows that there is no difference in hemodynamic stability, plasma viscosity, oxygenation index and duration of intubation. The HES group has a significantly higher blood loss. The Ringer's group has a significant higher volume uptake. The colloid-free regimen did not affect the pulmonary function.

The colloid-free Ringer's solution regimen is clinically fully acceptable and economically more favourable than the two colloid fluid regimens studied.

P152 Extracellular fluid variations during a fluid challenge: a comparison of normal saline (NS) and hydroxyethyl starch (HES) in stressed patients

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The controversy regarding the use of crystaloids or colloids for fluid resuscitation of critically ill patients continues. Fluid remaining in the vascular compartment would have an obvious advantage. We used bioimpedance, a technique allowing assessment of body cell mass and extracellular water, to compare NS and HES, a relatively new colloid.

Methods: Twenty-two critically ill patients requiring a fluid challenge were randomized to receive either 500 ml of NS or 500 ml of HES 10% (Fresenius, Germany). Vital signs (heart rate, systolic blood pressure, central venous pressure (CVP) and urine output) were noted before and immediately after the challenge. Bioimpedance changes, using a tetra-polar system working on 800 microamperes and 50 Khz (BIA-109), Ackern) were measured before and after the fluid challenge. Body cell mass (BCM) and extracellular water (ECW) were then derived. Results are expressed as the mean ± SD.

Results: Ten patients (mean age 57 ± 18.6 years) received HES 10% and twelve (mean age 56.9 ± 13.9 years) received NS. There were no significant differences between the two groups regarding pre- and post-challenge hemodynamic parameters, in particular change in CVP. Bioimpedance measurements before and after fluid challenge were as follows:

	NS group ($n=12$)		HS 10% group ($n=10$)	
	Before	After	Before	After
BCM (kg)	43.0 ± 11.4	43.3 ± 10.7	30.7 ± 14.5	31.1 ± 16.1
ECW (%)	55 ± 10.3	56.3 ± 10.6*	63.0 ± 5.3	63.9 ± 6.4

*$P < 0.03$ versus before value

Conclusion: We showed that there is an increase in extracellular water in critically patients receiving a fluid challenge with normal saline but not with HES. This could indicate a beneficial effect of HES on extravascular extravasation of water in stressed patients.

P153 HES 130/0.4, a new HES specification: tissue storage after multiple infusions in rats

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Hydroxyethyl starches (HES) are widely used in volume replacement therapy. One point of concern is tissue storage after repetetive dosing [1]. A controlled, multi-dose study was performed in 48 female rats. Daily infusions of ^{14}C radio-labelled HES 130/0.4 or HES 200/0.5 (0.7 g/kg bw) were administered on 18 consecutive days. HES tissue storage was measured 3, 10, 24 and 52 days after the last administration in the total body, carcass, liver, spleen, kidney and lymph nodes.

Significantly reduced HES storage ($P < 0.01$) was observed in the HES 130/0.4 group in total body, carcass and liver compared to the HES 200/0.5 group, while no differences were found in spleen, kidney and lymph nodes. These results clearly demonstrate significant differences of HES tissue storage between two HES specifications after repetetive administration of clinically relevant dosages. Even if the clinical relevance of tissue storage remains under debate the reduction in the HES 130 group per se seems advantageous. (See overleaf for Table.)

Reference

1. Ginz *et al.*: **Excessive tissue storage of colloids in the reticuloendothelial system.** *Anaesthesist* 1998, **47**:330-334.

Radioactivity per organ expressed as percentage of the administered total HES dosage (mean)

	Days after the last administration							
	3		10		24		52	
Organ	HES 130	HES 200	HES 130	HES 200	HES 130	HES 200	HES 130	HES 200
n	8	8	8	8	4	4	4	4
Total	4.32*	7.72	2.04*	3.97	1.38*	2.86	0.65 *	2.45
Carcass	3.03*	6.02	1.56*	3.29	1.09 *	2.33	0.49 *	2.03
Liver	1.09*	1.44	0.37*	0.56	0.24 *	0.45	0.05	0.26
Spleen	0.07	0.12	0.05	0.06	0.03	0.04	0.03	0.06
Kidney	0.11	0.13	0.05	0.05	0.02	0.02	0.02	0.02
Lymph node	0.02	0.01	0.01	0.01	0.00	0.03	0.06	0.08

*$P < 0.01$ (student's *t*-test)

P154 HES 130/0.4, a new HES specification: pharmacokinetics after multiple infusions of 10% solutions in healthy volunteers

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An open, one-way, multiple-dose study was performed in twelve (12) healthy male volunteers. Daily infusions of 500 ml of HES (130/0.4) 10% solution were administered within 30 minutes on 10 consecutive days. The plasma and urine HES concentrations were determined repeatedly in the course of the study, up to 72 h after the final infusion.

Both the peak plasma HES concentration and the time course of the plasma concentrations were similar on Day 1 and Day 10 of treatment. There was a marginal increase in the plasma HES concentration 24 h after the infusion, from approximately 0.23 mg/ml on Day 1 to approximately 0.48 mg/ml on Day 10. HES was eliminated from the plasma rapidly, with α- and β-half-lives of some 1.2 h to 1.4 h and 21.9 h, respectively. The β-half-life on Day 1 could not be determined with sufficient reliability since the next infusion was given only 24 h later. Although the baseline-corrected $AUC_{0-\infty}$ on Day 1 is thus likely to have been underestimated, the geometric mean of 32.8 h·mg/ml was in fairly close agreement with the result of 35.7 h·mg/ml determined for the $AUC_{0-\infty}$ on Day 10. The results for the urinary recovery of 69% on Day 1 and of 70% on Day 10 agreed very well. It was demonstrated that no clinically relevant accumulation of HES occurred in plasma after multiple-dose administrations of 10 times 500 ml of 10% HES (130/0.4) solutions.

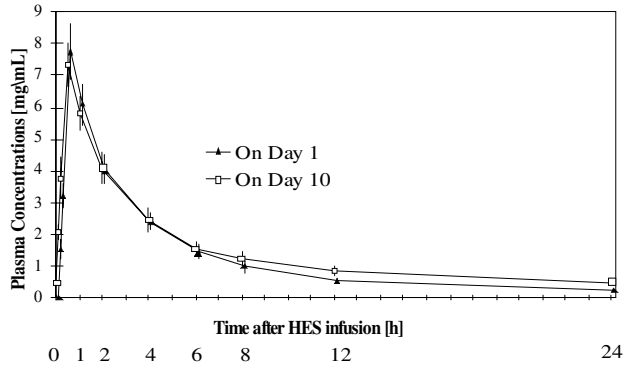

Fig.1 Plasma Levels of HES After Infusion of 500 mL HES (130/0.4) on day 1 and day 10 (mean +/- SD) n = 12

P155 Effect of hypertonic dextran on intestinal mucosal perfusion during porcine endotoxin shock

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Crit Care 1999, **3 (suppl 1)**:P155

Introduction: Mucosal hypoperfusion during sepsis might impair the epithelial barrier function leading to translocation of luminal bacterial products and further aggravation of the septic state. Supporting perfusion of the intestinal mucosa could ameliorate barrier dysfunction. The microcirculatory effects of hypertonic vs isotonic colloid volume resuscitation during sepsis have with respect to mucosal perfusion been sparsely reported.

Aim: To evaluate the effects of hypertonic vs. isotonic colloid volume resuscitation to maintain mucosal perfusion during porcine endotoxemia.

Interventions: Fasted, anesthetised, mechanically ventilated pigs (30.6 ± 2.0 kg, mean ± SEM) received infusion of LPS (EC seropype 0111: B4) during 2 h to establish septic shock and were then observed for another 90 min. After 1 h of LPS infusion, animals were randomized to resuscitation (4 ml/kg for 10 min) with isotonic dextran (Macrodex®, ISO, $n = 6$) or hypertonic dextran (RescueFlow®, HYPER, $n = 6$).

Measurements and main results: Mean arterial pressure (MAP), cardiac output (CO), portal venous blood flow (QPV), mucosal perfusion by laser-Doppler flowmetry (LDF) and tonocapnometry (giving regional $prCO_2$ and the pCO_2 gap from $paCO_2$) were assessed. Statistical analyses were made by ANOVA. $^{\S}P < 0.05$ vs. 60 min. $^{*}P < 0.05$ vs. ISO.

LPS-infusion resulted in hypodynamic shock after 60 min with no intergroup differences. Resuscitation with HYPER improved the mesenteric and specifically the mucosal circulation, whereas ISO was ineffective in this respect. HYPER also tended to improve CO while this effect failed to gain statistical significance ($P = 0.11$).

Conclusion: Volume resuscitation with hypertonic colloid proved superior to isotonic colloids to support intestinal and in particular mucosal perfusion during hypodynamic septic shock. The results indicate that hypertonic colloids might be of special value to support mucosal perfusion and thereby possibly barrier function in sepsis.

		Baseline	60 min	120 min	180 min	210 min
MAP	HYPER	96 ± 10	54 ± 7	43 ± 3§	44 ± 5	38 ± 6§
	ISO	109 ± 4	56 ± 7	45 ± 9§	35 ± 10§	35 ± 9§
CO	HYPER	4.6 ± 0.5	3.2 ± 0.4	3.5 ± 0.4	3.4 ± 0.5	2.8 ± 0.7
	ISO	44.8 ± 0.4	3.0 ± 0.3	3.2 ± 0.4	2.1 ± 0.4	1.3 ± 0.5
QPV	HYPER	958 ± 49	916 ± 147	1143 ± 326§	1152 ± 164§	972 ± 258*
	ISO	946 ± 76	882 ± 145	1082 ± 248§	698 ± 146	283 ± 152
LDF	HYPER	268 ± 48	220 ± 25	255 ± 41	234 ± 28	194 ± 12*
	ISO	248 ± 18	177 ± 14	185 ± 34	153 ± 25	103 ± 18§
TONO	HYPER	1.6 ± 0.6	2.9 ± 1.1	2.9 ± 0.9	3.9 ± 1.0	4.1 ± 0.9*
	ISO	1.4 ± 0.6	2.6 ± 0.6	3.5 ± 1.3	5.5 ± 1.0§	8.3 ± 0.5§

P156 Splanchnic microcirculation after resuscitation with hypertonic saline in a porcine model of cardiac tamponade

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Background: The beneficial effects of hypertonic saline (HS) for resuscitation in hypovolemic shock have long been known, it has also been reports on positive effects of HS on microcirculation in different organ systems. HS is known to increased cardiac output, reduce afterload and blood viscosity, it is also known to improve capillary blood flow by endothelial deswelling. However, there is very few data on the effects of HS on microcirculation in low cardiac output stakes.

Aim: The aim of this study was to investigate the effects of HS on splanchnic microcirculation in a model of cardiac tamponade with subsequent disturbances in splanchnic microcirculatory flow.

Materials and methods: The study design was randomised and crossover. Seven pigs of both sexes, weighing 27–35 kg were included in the study. After induction of anaesthesia all animals were tracheotomized. Central hemodynamics, portal venous blood flow and gastric, hepatic and renal microcirculation were measured simultaneously. Microcirculation was measured with Laser-Doppler technique. Cardiac tamponade was established with infusion of dextran in the pericardium. After stabilization of the tamponade the animals were resuscitated with either HS or Ringer's acetate (4 ml/kg) during 20 min. Changes of perfusion were evaluated with ANOVA and paired comparisons were made by Wilcoxon* $P < 0.05$ HS versus R–Ac.

Results: There was a significant increase in portal venous flow in the HS group, there was also a significant increase in microcirculatory flow in gastric mucosa, hepatic and renal surface microcirculation in the HS group. Those changes were not present in the R-Ac group. Values in Table are absolute changes by volume resuscitation during cardiac tamponade.

	CO (l/min)	Gastric (PU)*	Liver (PU)*	Kidney (PU)*	v.Porta (ml/min)*
HS	**+0.28**	**+19.4**	**+48**	**+5.9**	**+71**
R–Ac	*+0.22*	*−2.8*	*+2*	*−8.6*	*+7*

Conclusion: We conclude that HS is beneficial for microcirculation in this model of cardiac tamponade and associated disturbances microcirculatory flow in the splanchnic system. The increase of microcirculatory flow could prevent initialization of inflammatory processes and bacterial translocation and thereby prevent initiation of multi organ failure.

P157 A randomised controlled trial of low-dose dopamine in postoperatively ventilated patients in the ICU: renal effects and the influence on outcome

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Crit Care 1999, **3 (suppl 1)**:P157

Background: Despite the widespread use of low-dose dopamine in the ICU, there are only a few conflicting studies on its (protective) renal effects, some of them with contradictory results [1,2]. Consequently, we investigated renal effects as well as morbidity and mortality rates in patients being ventilated postoperatively in our ICU.

Patients and methods: Three hundred and forty-seven urology and abdominal surgery patients were randomised into two groups: A) no dopamine ($n = 174$) and B) dopamine at 2 µg/kg/min for the duration of intensive care treatment ($n = 173$). Creatinine and urea were determined at admission in our ICU (day 1) and the next day at 7 a.m. (day 2) together with hourly diuresis. Complications, length of stay and outcome from ICU treatment were recorded. The study was approved by the local Ethics Committee and informed consent was obtained from the patient prior to admission for surgery. Paired and unpaired Student's *t*-tests, Fisher's Exact Test and Chi square tests were used for statistical analysis.

Results: The individual differences for creatinine and urea (day 2–day 1) (mean ± S.D.) are shown in the table: (Complications: Group A) 38 pts. (22%), B) 38 pts. (21.8%) [n.s.]).

Conclusion: In our study, dopamine caused a significant diuresis without significant changes in creatinine or urea levels. Low-dose dopamine was not associated with a higher incidence of adverse cardio-circulatory reactions. We observed no protective effect on the incidence of ARF and our results indicate that low-dose dopamine may be associated with unfavourable outcomes, in particular higher mortality.

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	Creatinine (µmol/l)	Urea (mmol/l)	Diuresis (ml/kg/h)	Cardio-circulatory events	Acute renal failure (ARF)	Mortality
Group A	+1.9 ± 37.1	+0.03 ± 1.2	2.2 ± 1.2	13 pts. (7.5%)	None	None
Group B	−1.1 ± 40.1	−0.1 ± 1.7	3.1 ± 1.3	10 pts. (5.8%)	5 pts. (2.9%)	7 pts. (4.0%)
Significance	n.s.	n.s.	$P < 0.001$	n.s.	$P < 0.05$	$P = 0.007$

P158 Effect of a dopexamine induced increase in cardiac output on splanchnic hemodynamics in septic shock

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Objective: In patients after cardiac surgery dopexamine is known to increase both global and hepato splanchnic blood flow. Sepsis per se and the infusion of noradrenaline may alter the response to the onset of dopexamine. Therefore we determined the changes in global and regional hemodynamics in patients with septic shock.

Patients/methods: Twelve patients with septic shock were studied. All patients had a cardiac index (CI) ≥3 l/min/m² and needed noradrenaline ≥0.04 µg/kg×min⁻¹ to maintain mean arterial pressure (MAP ≥60 mmHg). In addition to routine systemic hemodynamics and gas exchange we inserted a balloon-tipped Swan Ganz catheter into a hepatic vein to determine splanchnic blood flow (Qspl), hepatic venous pressure (HVP) and the hepatic venous occlusion pressure (HVOP) as an estimate of portal venous pressure. Splanchnic blood flow was measured using the steady-state indocyanine green (ICG) infusion technique. Measurements were done before, during and after dopexamine infusion. Data were always obtained after at least 90 min of hemodynamic steady-state. Dopexamine was titrated (1–4 µg/kg×min⁻¹) to obtain a 30% increase in CI.

Results: See Table.

Conclusion: The dopexamine induced increase in Qspl paralleled that of CI. A preferential effect on splanchnic circulation could not be detected. The increase in Qspl was due to a decreased prehepatic resistance.

Median/range	Baseline	Dopexamine	Baseline
CI (l/min/m²)	3.7 (7.6–3.1)	4.9 (10.3–3.9)#	4.2 (7.6–3.1)*
Qspl (l/min/m²)	0.86 (1.42–0.24)	0.96 (2.23–0.25)#	0.94 (1.63–0.23)*
HVOP (mmHg)	15 (18–8)	16 (25–8)	16 (26–8)
HVP (mmHg)	12 (17–7)	12 (16–5)	12 (15–6)
CVP (mmHg)	11 (15–6)	10 (14–3)	11 (15–4)
SVRi (mmHg/l*min⁻¹)	17 (21–6)	14 (16–5)#	16 (21–8)*
SPLRi (mmHg/l*min⁻¹)	76 (268–36)	65 (296–29)#	70 (284–40)
Qspl/CI (%)	21 (40–7)	19 (53–5)#	20 (47–6)

Statistics Friedman-test; Wilcoxon test; #$P < 0.05$ versus baseline; *$P < 0.05$ versus dopexamine

P159 Effect of dopexamine on CO_2-gradients and splanchnic energy balance in septic shock

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Objective: Septic shock is characterized by enhanced hepatosplanchnic blood flow resulting from increased metabolic activity. This hypermetabolism may lead to mismatch of regional O_2 supply and demand reflected by increased CO_2-gradients and lactate/pyruvate ratios. In patients after cardiac surgery dopexamine is known to increase splanchnic perfusion. Therefore, we studied the effect of dopexamine on regional CO_2-gradients and energy balance in patients with septic shock.

Patients and methods: Twelve patients with septic shock were studied. Cardiac index (CI) was ≥3 l/min/m^2 and noradrenaline ≥0.04 µg/kg×min^{-1} was infused to maintain mean arterial pressure (MAP) ≥60 mmHg. In addition to routine systemic hemodynamics and gas exchange we inserted a Swan Ganz catheter into a hepatic vein to measure splanchnic blood flow (Qspl) using primed continuous infusion of indocyanine green (ICG) dye. Moreover, we assessed splanchnic lactate uptake (Fick principle), hepatic venous lactate/pyruvate ratio as well as PCO_2 (PCO_2hv), splanchnic O_2 delivery (DO_2spl) and consumption (VO_2spl). The gastric mucosal PCO_2 (PCO_2gm) was determined via a nasogastric tube. Measurements were done before, during and after dopexamine infusion. Data were obtained after 90 min of hemodynamic steady-state. Dopexamine was titrated (1–4 µg/kg×min^{-1}) to obtain a 30% increase in CI.

Results: See Table.

Conclusion: The unpredictable changes in the metabolic state and regional PCO_2 gradients after a dopexamine-induced increase in DO_2spl, underscores the independent response of hepatosplanchnic perfusion and metabolism to therapeutic interventions.

Median/range	Baseline	Dopexamine	Baseline
DO_2 index spl (l/min/m^2)	116 (211–39)	130 (323–38)#	120 (233–34)
VO_2 index spl (l/min/m^2)	66 (88–17)	62 (142–14)	61 (113–16)
Lactate utilisation (µmol/m^2/min)	239 (876–358)	425 (1448–590)	345 (2040 to –578)
Lactate/pyruvate ratio	27 (61–20)	30 (185–22)	42 (75–21)
PCO_2gm–PCO_2art (kPa)	2.8 (5.2–0.0)	2.2 (4.2 to –0.3)	2.8 (4.5–0.3)
PCO_2mv–PCO_2art (kPa)	0.9 (1.5–0.1)	0.6 (1–0.1)	0.8 (1.3–0.3)
PCO_2hv–PCO_2art (kPa)	1.2 (2.3–0.3)	0.8 (1.7 to –0.1)	1.1 (1.8–0.5)

Statistics: Friedman-test; Wilcoxon-test; #$P < 0.05$ versus baseline

P160 Dopeamine does not improve intestinal mucosal perfusion measured by scanning laser Doppler flowmetry

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Background: There is conflicting evidence that dopexamine hydrochloride exerts a selective vasodilating effect upon the gastrointestinal mucosa. Whilst some human studies conducted in the critically ill and in high risk surgical patients have suggested that dopexamine may cause an increase in tonometrically measured gastric intra-mucosal pH (pHi) and an improvement in clinical outcome, this has not been confirmed in other randomised trials. Furthermore, there is no data with regard to dopexamine's influence upon small bowel perfusion. Laser Doppler flowmetry has been used to measure gastrointestinal mucosal blood flow, and the recent advent of scanning laser Doppler flowmetry appears to overcome some of the limitations of the single point method. This study employed this new technique to assess the effect of dopexamine on ileostomy mucosal blood flow.

Method: The study was prospective and double-blind. Fourteen patients with ileostomies were randomised into treatment ($n = 7$) and placebo groups ($n = 7$). The stomas were exposed to the air for a period of 20 min whilst the laser Doppler scanner (Moore Instruments, Axminster, Devon, UK) was positioned above the patient at a distance of 32 cm. A laser scan was then made, and the stoma outlined on the photographic image. This equated to over 2500 individual perfusion measurements on the corresponding perfusion image, allowing calculation of mean perfusion units (PUs) within the stomal mucosa. Heart rate and mean arterial pressure were recorded. An intravenous infusion of either dopexamine (2 µg/kg/min) or of a placebo was then commenced and after 30 min the recordings were repeated. The infusion was then stopped and a final set of recordings made after 30 min. The results were analysed using the Mann–Whitney test for non-parametric data.

	Pre infusion		Intra infusion		Post infusion	
Mean PUs (SD)	Dopexamine	Control	Dopexamine	Control	Dopexamine	Control
Mucosal perfusion	357 (165)	432 (210)	342 (170)	448 (185)	315 (165)	315 (180)

Results: There were no significant changes in systemic arterial in either group during the study. However, in the dopexamine group there was a significant increase in mean (SD) heart rate from 80 (14) to 94 (7) beats per minute during the infusion and a subsequent fall to 83 (12) beats per minute after its cessation (in both cases $P < 0.05$). There was no significant change in mucosal perfusion measured using the scanning laser Doppler during dopexamine or placebo infusion (in all cases $P > 0.05$).

Conclusion: This study is the first to directly measure the influence of dopexamine hydrochloride on ilea mucosal perfusion. The scanning laser Doppler flowmeter produced easily interpreted images of the stomas. Dopexamine caused no demonstrable increase in ileostomy blood flow, and this finding suggests that any improvement in outcome caused by the drug in the critically ill may be caused by an alternative mode of action.

P161 Dopexamine does not improve jejunal or gastric tube mucosal perfusion following oesophageal resection

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Crit Care 1999, **3 (suppl 1)**:P161

Background: There is conflicting evidence that dopexamine hydrochloride exerts a selective vasodilating effect upon the gastrointestinal mucosa. Whilst some human studies conducted in the critically ill and in high risk surgical patients have suggested that dopexamine may cause an increase in tonometrically measured gastric intra-mucosal pH (pHi) and an improvement in clinical outcome, this has not been confirmed in our randomised trials. Furthermore, there are no previously published reports of the effect of dopexamine on human small bowel mucosal perfusion. An increase in splanchnic perfusion in general or gastric mucosal perfusion in particular following oesophageal resection may potentially reduce the incidence of anastomotic leaks and strictures as these complications are thought to be caused by hypoperfusion and consequent tissue hypoxia at the gastric end of the oesophagogastric anastomosis. This study assessed the effect of dopexamine on gastric tube and jejunal mucosa pHi measured tonometrically following oesophagectomy.

Methods: Twelve patients undergoing oesophageal resection for carcinoma and reconstitution of gastrointestinal continuity using a gastric tube were randomised into dopexamine and control groups. During surgery tonometer balloons (Tonometric Division, Instrumentarium Division, Helsinki, Finland) were placed 5 cm distal to the anastomosis within the stomach and 10 cm during the duodeno-jejunal flexure within the jejunum. These were connected to separate 'Tonocap' analysers (Datex, Helsinki, Finland). 24 h following surgery all the patients were sedated, ventilated and cardiovascularly stable. Three measurements of heart rate, mean arterial pressure, central venous pressure as well as gastric and jejunal pHi were made at 30 min intervals prior to the commencement of an intravenous infusion of either dopexamine (2 μg/kg/min) or of a placebo. Four further sets of measurements were made at 30 min intervals during the infusion, and after 2 h it was stopped and three measurements over the next 90 min were made. The results were analysed using the Mann–Whitney test for non-parametric data.

Results: There were no significant changes in systemic arterial or central venous pressure in either group during the study. However, in the dopexamine group there was a significant increase in mean (SD) heart rate from 85 (12) to 104 (10) beats per minute during the infusion and a subsequent fall to 94 (10) beats per minute after its cessation (in both cases $P < 0.005$). There were no significant changes in either gastric or jejunal pHi during dopexamine or placebo infusion (in all cases $P > 0.05$).

Conclusion: Dopexamine hydrochloride does not increase gastric tube pHi following oesophagectomy. Furthermore there is no evidence from this study that dopexamine is capable of influencing jejunal mucosal perfusion, and its potential role not only in protecting gastrointestinal anastomoses but also in reducing mortality due to MODS by directly influencing splanchnic perfusion is not supported by the findings of this study.

	Pre infusion		Intra infusion		Post infusion	
Mean pHi (SD)	Dopexamine	Control	Dopexamine	Control	Dopexamine	Control
Gastric pHi	7.21 (0.09)	7.23 (0.07)	7.18 (0.08)	7.24 (0.08)	7.21 (0.06)	7.24 (0.05)
Jejunal pHi	7.26 (0.08)	7.25 (0.06)	7.26 (0.07)	7.26 (0.06)	7.26 (0.09)	7.25 (0.05)

P162 Cytokines and endotoxin generation and the effects of dopexamine in patients undergoing abdominal aortic reconstruction (AAR)

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Hypothesis: Colonic ischaemia may increase morbidity and mortality following AAR. Animal studies suggest ischaemic colon causes endotoxin and cytokines release, initiating the systemic inflammatory response and multiorgan dysfunction syndrome.

Aim of study: (1) Study the effects of temporary ischaemia, caused by aortic cross clamping (AXC); (2) confirm ischaemic colon as

source of endotoxin and cytokine release in humans; (3) investigate any modification of the degree of ischaemia and cytokine and endotoxin generation with dopexamine hydrochloride.

Study design: Placebo-controlled prospective trial, 15 patients undergoing AAR randomised to receive dopexamine hydrochloride ($n = 8$) or normal saline ($n = 7$). Inferior mesenteric vein (IMV) sampled for IL-6, TNF-α, endotoxin, pH, P_{CO2} and P_{O2} prior to AXC and 30 min postreperfusion. Peripheral systemic cytokines and endotoxin measured 24 h preoperatively and postoperatively. Hepatic and renal functions studied perioperatively.

Results: A statistically significant rise occurred in IMV IL-6 ($P = 0.001$) between pre-clamping and postreperfusion but not in TNF-α and endotoxin. IL-6 and endotoxin levels showed negative correlation with IMV pH ($r = –0.49$ and $–0.47$ respectively). Patients with IMV pH <7.3 had higher levels of endotoxin ($P = 0.04$).

Dopexamine (1 µg/kg/min) produced an improvement in colonic pH without statistical significance between groups. Dopexamine produced statistical difference in postoperative creatinine clearance ($P = 0.02$), serum albumin ($P = 0.02$) and INR ($P = 0.05$).

Conclusion: Results confirm hypoperfused colon generates cytokines which, with endotoxin, are related to the IMV pH. Pharmacological modification of this response was not statistically significant. Dopexamine could improve renal and hepatic functions during AAR.

P163 Dopexamine reduces the incidence of colonic ischaemia following aortic surgery: a randomized placebo controlled study

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Background: Mechanisms involved in the development of colonic ischaemia following aortic surgery are not fully understood and there are conflicting reports regarding predisposing factors. Dopexamine hydrochloride, a synthetic catecholamine with both dopaminergic and β_2 agonist properties, has been demonstrated to have anti-inflammatory properties.

Aims: To evaluate the effect of dopexamine hydrochloride on the incidence of colonic ischaemia following aortic surgery

Methods: Thirty patients, mean age 65.1 years (range 46–84), undergoing elective infrarenal aortic surgery were randomized to receive a peri-operative infusion of either dopexamine at 2 µg/kg/min ($n = 12$) or 0.9% saline placebo ($n = 18$). All patients underwent colonoscopy and biopsy following induction of anaesthesia and at one week post-operatively. Sections were stained with haematoxylin and eosin, mast cell tryptase (MCT), myeloperoxidase (MPO) and both the inducible (iNOS) and endothelial (eNOS) isoforms of nitric oxide synthase. Sections were analysed blind and independently by two histopathologists. Patient and operative related data were collected and stored separately.

Results: Colonic ischaemia was noted in 9 (30%) patients based on microscopic findings. Endoscopy alone had a sensitivity of 55.5%. There was a significantly lower incidence of colonic ischaemia in patients receiving dopexamine compared to placebo ($P < 0.05$). One death resulted from colonic infarction in the placebo group 11 days post-operatively. There was increased MPO and MCT expression in patients with histological evidence of ischaemia ($P < 0.05$). iNOS staining within the vascular ($P = 0.001$) and lamina propria ($P < 0.05$) components of the mucosa was also significantly greater. No association was found with eNOS.

Conclusions: Peri-operative dopexamine infusion confers a degree of protection to colonic mucosa following aortic surgery, possibly through an anti-inflammatory effect.

P164 Endothelin-1 (ET-1) blockade improves mesenteric perfusion in a porcine low cardiac output model

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Background: Various vasomediators regulate the hemodynamic response to acute circulatory failure, including endothelin-1 (ET-1) which is one of the most potent vasoconstrictors known. Mesenteric vasoconstriction reduces the perfusion and oxygenation of the gut mucosa, compromising mucosal barrier integrity. A growing body of evidence links mucosal barrier dysfunction with the development of multiple organ failure (MOF). Improving gut perfusion could preserve mucosal barrier integrity and thus reduce the risk of MOF.

Aim: To investigate if the combined ETA-ETB blocker Ro 61-0612 improves gut microcirculation and micro-oxygenation during acute circulatory failure.

Materials and methods: Seven fasted, anesthetised (pentobarbital), mechanically ventilated pigs (30–34 kg) were instrumented to measure cardiac output (CO), portal venous blood flow (QPV; Transonic Systems Inc.), jejunal mucosal microcirculation by laser Doppler flowmetry (LDF, Perimed AB), jejunal tonocapnometry (giving arterial to regional PCO_2 gap, Tonocap, Datex Instruments) and jejuna mucosal micro-oxygenation (tPO_2, Licox, GMS). A pericardial drainage catheter was inserted to establish cardiac tamponade by infusing dextran (reducing QPV to 2/3 of baseline). Measurements were made at baseline (BL), after 90 min of cardiac tamponade (T90) and 90 min following the administration of Ro 61-0612 (at 1 mg/kg/h) during tamponade (T90RO). Statistical analyses were made by ANOVA and Fischer's PLSD. A P value < 0.05 was considered statistically significant.

Results: Cardiac tamponade significantly decreased CO, MAP, QPV, LDF, while the pCO_2 gap increased as compared to baseline (BL). The change in tPO_2 failed to gain statistical significance ($P = 0.08$). Administration of Ro 61-0612 increased QPV, LDF, tPO_2 and decreased PCO_2 gap, as compared to T90.

Conclusion: ET-1 blockade in acute circulatory failure improved mesenteric perfusion illustrating the importance of ET-1 induced mesenteric vasoconstriction. Importantly ET-1 blockade restored mucosal blood flow and oxygenation which might be particularly significant considering the implications for maintenance of mucosal barrier integrity.

	CO (l/min)	QPV (ml/min)	MAP (mmHg)	LDF (PU)	PCO_2 gap (kPa)	tPO_2 (kPa)
BL	2.97 ± 0.2	721 ± 65	84 ± 6	175 ± 14	2.0 ± 0.4	14.6 ± 2.1
T90	1.55 ± 0.1*	470 ± 40*	47 ± 5*	127 ± 15*	3.9 ± 0.3*	11.5 ± 1.8
T90RO	1.98 ± 0.2	758 ± 92**	44 ± 5	147 ± 16**	2.2 ± 0.2**	17.0 ± 2**

Values are expressed as mean ± SEM. *Significant versus BL. **Significant versus T90

P165 Monitoring initial volume therapy after coronary bypass surgery by gastric tonometry

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Crit Care 1999, **3 (suppl 1)**:P165

Introduction: Gastric tonometry is a very sensitive, non-invasive method to detect hypovolemia in critical care patients. Several studies document the predictive value of tonometry for patients' outcome. Especially a widened arterial to gastric-intramucosal PCO_2 difference ($aiDCO_2$) warns of complications. This study demonstrates the use of tonometry as a monitoring device for actual aspects of volume status and tissue oxygenation in patients after cardiac surgery.

Methods: After IRB approval we studied 24 patients admitted to the ICU after aorto-coronary bypass surgery. In addition to standard monitoring each patient received a nasogastric tube (TRIP, NGS catheter; Tonometrics, Helsinki, Finland), a fiberoptic pulmonary artery catheter (CCO catheter for Vigilance monitor; Baxter Healthcare Corp., Irvine, USA) and a polarographic intramyocardial oxygen catheter (Licox; Kiel, Germany). Documentation of standard parameters followed every 15 resp. 60 min. intra- and postoperative until extubation. Retrospectively patients were devided into two groups (2×12) by the amount of postoperative colloid volume replacement: Group 1: <750 ml colloids during the first 3 postoperative hours; Group 2: >1000 ml colloids during the first 3 postoperative hours. Statistics were done by using Mann-Whitney-U and Friedman-test.

Results: There were no significant differences between group 1 and 2 with regard to age, ejection fraction, duration of extracorporal circulation, number of bypasses, arterial or mixed venous blood gas analyses, arterial or pulmonary arterial hemodynamics, lactate, heart rate and central venous pressure. Regional oxygenation differed significantly between the groups. Group 1 (<750 ml/3 h) showed a small $aiDCO_2$ during the first 5 postoperative hours. Afterwards splanchnicus perfusion impaired ($aiDCO_2$ >20 mmHg). In group 2 (>1000 ml/3 h) an initially higher $aiDCO_2$ was lowered by volume therapy. Group 2 developed a significantly lower postoperative increase in intramyocardial oxygen then group 1. More than 5 h after extracorporal circulation there was a significantly increasing need of epinephrine in group 2 and cardiac index was lower in group 2 without reaching significance.

Conclusion: Volume replacement after coronary bypass surgery should be monitored by gastric tonometry since hemodynamic parameters are less sensitive. High volume replacement without need ($aiDCO_2$ <20 mmHg) can improve splanchnicus perfusion but might impair myocardial oxygenation and myocardial function.

P166 Evaluation of intestinal perfusion monitoring techniques

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Introduction: Persistent hypoperfusion of the intestinal mucosa is considered important for the development of systemic complications during critical illness. The mucosal circulation is however not readily accessible to quantitative measurements of perfusion. Measurements of systemic perfusion are often extrapolated clinically to reflect regional perfusion, including the gastrointestinal organs. This extrapolation may introduce errors in the evaluation of hemodynamic status. Furthermore, the complex variable of perfusion involves movement of blood and erythrocytes as well as the exchange of carbon dioxide and oxygen.

Aims: To investigate the relationship between clinically available techniques of measuring mucosal perfusion in relation to mesenteric and central blood flow during acute circulatory failure.

Materials and method: Thirteen fasted, anesthetized (pentobarbital) mechanically ventilated, normovolemic pigs (28-35 kg) were instrumented to monitor cardiac output (CO), portal blood flow (QPV, Transonic Systems), jejunal, mucosal laser-Doppler flowmetry (LDF, Perimed AB), jejunal CO_2-tonometry (TONO, Tonocap, Datex Instr) and jejunal, mucosal oxygen tension (tO_2, Licox, GMS). Acute reduction of CO by 40% from baseline was

established by intrapericardial infusion of dextran and maintained for 90 minutes. Correlations between monitored variables were analyzed by ANOVA and linear regression (*$P < 0.05$) and differences were analyzed by Wilcoxon's test (§$P < 0.05$).

Results: The best regressions coefficients were found between variables relating to measurements of movement of volume (QPV) or erythrocytes (LDF). Second to best regressions were obtained for TONO (measuring the exchange of CO_2). Notably, tPO_2 (measuring the exchange of O_2) did not correlate to variables of flow or CO_2 exchange.

Conclusion: In the setting of acute circulatory failure in pigs, cardiac output approximates mesenteric as well as intestinal mucosal perfusion. Importantly, the mucosal oxygen tension might vary independent from flow, which probably reflects the complexity of the counter current circulation within the mucosa. Oxygenation, being the pivotal variable determining tissue function, is thus not assessed even by techniques specifically directed towards the mucosal circulation.

	CO	QPV	TONO	LDF	tPO_2
CO	–	0.81*	0.45*	0.53*	0.28 ns
QPV	–	–	0.34*	0.57*	0.15 ns
TONO	–	–	–	0.41*	0.05 ns
LDF	–	–	–	–	0.31 ns

P167 Jejunal mucosal NO production and substrate dependency during mesenteric hypoperfusion in pigs

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Background and aims: Intestinal NO production has been attributed a central role in the maintenance of the intestinal mucosal barrier. Hypofunction of this barrier has been suggested to be one important factor behind the initiation of the multiple organ dysfunction syndrome. Jejunal NO formation, as we previously have reported, has been shown to be impaired during mucosal hypoperfusion [1]. This study was undertaken to investigate if the impaired jejunal NO levels could be due to restricted mucosal availability of NO-synthase substrates, i.e. oxygen and/or L-arginine.

Methods: Chloralose-anesthetized pigs ($n = 18$) were prepared for jejunal intraluminal perfusion with 150 mM NaCl or 3 mM L-arginine solution and then subjected to cardiac tamponade. Jejunal mucosal NO formation was measured with a tonometric technique. Mesenteric blood flow was measured as portal blood flow and mucosal perfusion was measured by laserdoppler flowmetry. Regional oxygen consumption was calculated from blood samples.

Results: Cardiac tamponade reduced jejunal NO formation (–52%), mesenteric oxygen delivery (–75%), oxygen consumption (–39%) and mucosal laser doppler flow (–43%). Oxygenation of the jejunal intraluminal perfusate completely restored the intestinal NO levels within 30 min. Presence of L-arginine was without effect.

Conclusion: The study indicates that oxygen rather than L-arginine is the rate limiting factor for mucosal NO production during reduced splanchnic perfusion.

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P168 *In-vitro* evaluation of the neonatal tonometer

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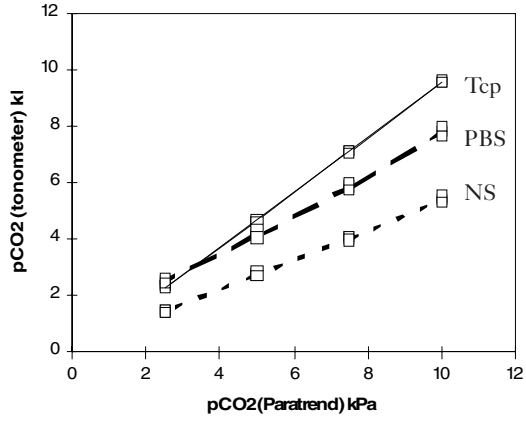
Objectives: A Neonatal Tonometer (5 French) using saline capnometry has been developed. We compared these tonometers in-vitro, using 0.9% saline (NS) and phosphate buffered saline (PBS) as the CO_2 vehicle, along with a Tonocap (14 F) against a set of known PCO_2's in a saline solution.

Method: A sealed equilibration chamber containing 0.9% Saline was maintained at 37°C and the dissolved CO_2 was kept at constant pCO_2's of 2.5, 5, 7.5, 10 kPa using a Paratrend 7 probe (Biomedical Sensors). Two Neonatal Gastric tonometers (Tonometrics) were positioned in the chamber along with a Tonocap monitor (Datex). NS was the CO_2 vehicle in the first tonometer, PBS (pH 6.0) in the second, and recirculating gas tonometry in the Tonocap. 20 consecutive measurements were taken, each after 60 min equilibration periods, from each of the tonometers at pCO_2's of 2.5, 5, 7.5, 10 kPa and processed in the IL BGE blood gas analyser. Data was analysed by linear regression and Bland-Altman plots.

Results: The Figure overleaf shows the known pCO_2 against the mean pCO_2 (95% CI) for Tonocap (Tcp), PBS and NS. The calculated Tonometer pCO_2 ($TpCO_2$) is derived from the linear regression equation.

Conclusion: Recirculating gas tonometry is undoubtedly the best mode of tonometry. Whilst we await its development for neonates either NS or PBS may be used. We suggest that correction factors specific to each unit's blood gas analyser should be calculated before appropriate comparison can be made between the arterial pCO_2 and the Neonatal tonometer's pCO_2.



$TpCO_2 = (Tonocap+0.13)/0.97$
$R^2 = 0.99$

$TpCO_2 = (PBS–0.74)/0.70$
$R^2 = 0.97$

$TpCO_2 = (NS–0.16)/0.53$
$R^2 = 0.98$

Bias + precision:

1. Tonocap: –0.31 kPa ± 0.25 kPa

2. PBS: –1.13 kPa ± 1.13 kPa

3. NS: –2.80 kPa ± 2.64 kPa

P169 Automated gas tonometric measurement of gastric tube carbon dioxide gap following oesophageal resection predicts post-operative complications

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Background: Gastric mucosal perfusion can be assessed tonometrically by measuring the gastric intra-mucosal pH (pHi) and its ability to predict outcome in the critically ill and following major surgery has been demonstrated by several previous studies. It has been suggested that the CO_2 gap (tonometer pCO_2) may provide a more sensitive measurement of mucosal hypoxia than pHi. Post-operative anastomotic leak and stricture following oesophageal resection and restoration of gastrointestinal continuity with a pro-peristaltic gastric tube has a multi-factorial aetiology. However, gastroplasty involves division of short gastric, left gastric and left gastroepiploic vessels and the consequent hypoperfusion and tissue hypoxia at the gastric end of the oesophago-gastric anastomosis is thought to be the most important causative factor. This study employed the new technique of automated gas tonometry to measure both gastric CO_2 gap and pHi following oesophagectomy to test the predictive ability of the technique for anastomotic complications.

Method: Gastric tonometers (Tonometric Division, Instrumentarium Division Helsinki, Finland) were placed in the gastric tube of 30 consecutive patients undergoing oesophageal resection and pro-peristaltic tubular gastroplasty based upon the right gastroepiploic and right gastric arteries. These were connected to a 'Tonocap' analyzer (Datex-Engstrom Division, Instrumentarium Corporation, Helsinki, Finland) which automatically samples gas from the tonometer balloon and measures the CO_2 concentration within it. In conjunction with simultaneously taken arterial blood samples the gastric CO_2 gap and pHi were calculated at 12 hourly intervals up to 48 h post-operatively. Those patients who survived were followed for 3 months and all post-operative complications recorded. Statistical comparison was made using the Mann–Whitney test for non-parametric data.

Results: Eleven patients suffered an anastomotic leak or benign stricture post-operatively, whilst five others suffered a life threatening complication not related to the anastomosis, of whom two survived. Because of balloon failure or re-operation within 48 h of initial surgery data was not available for one patient from each of the complication and no complication groups. Mean (SD) CO_2 gap and pHi over the first 48 post-operative hours were 1.7 kPa (0.8) and 7.26 (0.06) in the no complication group and 3.5 kPa (1.4) and 7.18 (0.09) in the complication group, respectively. The difference in CO_2 gap between the two groups was more significant than in pHi ($P < 0.005$ and $P < 0.05$). A mean CO_2 gap of 2.5 kPa or above had a sensitivity of 82% and a specificity of 70% for predicting anastomotic complications. The CO_2 gap was a better predictor of outcome than the pHi (<7.22 for predicting complications), with areas under their respective ROC curves of 0.847 and 0.684.

Conclusion: Gastric tube CO_2 gap and pHi are easily measured post-operatively using recirculating gas tonometry. Mean CO_2 gap was higher and pHi lower over the first 48 h following surgery in those patients in whom an anastomotic complication subsequently developed than in those in whom it did not. The CO_2 gap proved to be a better predictor of complications than the pHi. These findings confirm the suggestion that the CO_2 gap may be a more useful clinical tool than the pHi and that measures to improve gastric tube CO_2 gap post-operatively might reduce the incidence of anastomotic failure.

P170 Enteral nutrition via a jejunostomy decreases both jejunal and gastric tube intra-mucosal pH following oesophagectomy

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Crit Care 1999, **3 (suppl 1)**:P170

Background: Many animal and human studies have demonstrated that gastrointestinal intra-mucosal pH (pHi) which is usually measured using a gastric tonometer is partly dependent upon

mucosal perfusion, and that its measurement can predict for poor outcome in the critically ill. There is increasing evidence that not only in this group of patients but also following upper gastrointestinal surgery that the early introduction of enteral nutrition may reduce morbidity and mortality and increase enteric mucosal tissue perfusion. Theoretically this effect may be especially desirable following oesophagectomy and oesophagogastric anastomosis as gastric blood flow is compromised following gastroplasty. However, the measurement of gastric pHi using the tonometric method is thought to be confounded during infusion of enteral feed by the release of carbon dioxide from the feed itself following enzymic digestion. This study assessed the effect of a standard enteral feed upon both gastric and jejunal pHi measured using gas tonometry when delivered via a feeding jejunostomy.

Method: Nineteen patients undergoing oesophageal resection for carcinoma and reconstitution of gastrointestinal continuity using a gastric tube were studied. During surgery tonometer balloons (Tonometric division, Instrumentarium Division, Helsinki, Finland) were placed 5 cm distal to the anastomosis within the stomach and 10 cm from the duodeno-jejunal flexure within the jejunum. The jejunal tonometer was placed alongside a standard 8 F Foley feeding jejunostomy tube. The tonometers were connected to separate 'Tonocap' analysers (Datex, Helsinki, Finland). Five days following surgery all the patients had left the intensive care unit and had returned to the surgical ward and were being fed (Fresubin Standard, Fresenius Ltd, Runcorn, Cheshire, UK) via the jejunostomy tube (mean rate 108 ml/h). The feed was stopped for a minimum of 6 h and then both jejunal and gastric pHi was measured using a simultaneously taken arterial blood gas sample. The feed was then recommenced and after 2 h the measurements were repeated. The results were analysed using the Mann–Whitney test for non-parametric data.

Results: Prior to the commencement of feeding mean (SD) jejunal and gastric pHi were 7.44 (0.06) and 7.37 (0.08) respectively. Following 2 h of enteral nutrition jejunal and gastric pHi had fallen to 7.26 (0.09) and gastric pHi to 7.29 (0.12). These falls were both significant ($P < 0.005$ and $P < 0.05$, respectively).

Conclusion: Standard enteral nutrition delivered via a feeding jejunostomy appears to cause a fall in tonometrically measured jejunal pHi. That this may at least in part reflect a fall in mucosal blood flow rather than have been caused by the release of carbon dioxide from the feed is supported by the finding that gastric pHi also falls despite the fact that no feed was introduced into the stomach. That an enteric reflex may be responsible for this finding seems likely although its significance with regard to its effect upon anastomotic perfusion remains unknown.

P171 *In vitro* evaluation of a fast response, modified pH-Glass electrode designed for continuous measurement of the pCO_2 in the gastric lumen

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Introduction: The intramucosal pH (pHi) is a sensitive and early parameter of various shock states. Its prognostic and therapeutic value has been demonstrated. Tonometry relies on the measurement of intragastric pCO_2 via a nasogastric probe and the arterial bicarbonate. There are several shortcomings of the tonometric method (e.g. handling and measurement errors, and the need for a long equilibration time (30–90 min)). Therefore, we evaluated a modified pH-glass electrode for fast and continuous pCO_2-monitoring in the stomach.

Methods: Our *in vitro* measurements were performed using a special designed pH-metry glass electrode with an outer diameter of 4.5 mm (GK2801C;Radiometer) covered with a thin gas permeable teflon membrane. Thus, CO_2 may easily diffuse through the membrane and induces changes of the pH of an interspersed electrolyte solution. At first, the membrane and the membrane covered electrode were tested for chemical and mechanical stability in aggressive and acidic fluids. Secondly, the precision of two one-point calibrated electrodes to measure the pCO_2 in the range of 20 to 250 mmHg was tested. For each of five given pCO_2-levels a set of five measurements was done. Thirdly, the response time of two electrodes to reach 90% of the maximum (t_{90}) was tested by exposing the electrodes rapidly to two different solutions with a pCO_2 of 28.9 and 85.9 mmHg, respectively.

Results: The teflon membrane has proved to be stable against 0.1N hydrochloric acid, gastric and biliary secretions adjusted to pH 1, and mechanical irritations. In acidic fluids a linear relationship between the measured pCO_2 and the defined pCO_2 for both electrodes was observed. The slope of the regression line was $y=24.43x+7.64$ ($r=0.99$, $n=25$) and $27.57x+4.64$ ($r=0.99$, $n=25$) respectively. The deviation from the line of identity was only caused by the one point calibration. The reponse time t_{90} of the electrode was 19.5 ± 1.38 s and 25.5 ± 2.42 s (± SD), respectively.

Conclusion: This teflon membrane covered modified pH-glass electrode offers a fast, real time, and continuous measurement of the pCO_2 in the acidic environment of the gastric lumen.

P172 Investigation into the effects of enteral feeding on gastric tonometry monitoring using the saline technique and the Tonocap

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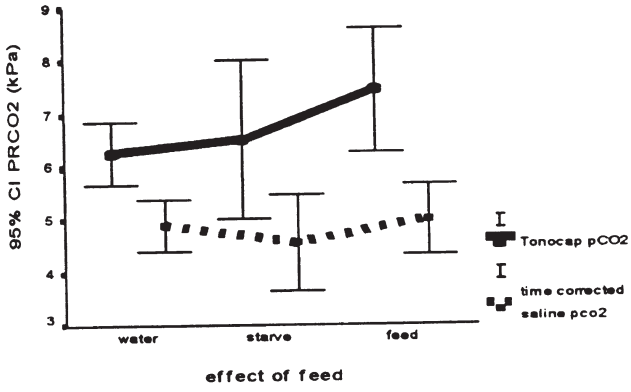
Aims of study: A prospective study of gastric $PrCO_2$ in ventilated neurosurgical patients when given enteral feed comparing two techniques: time corrected saline (TCS) tonometry and air tonometry (Tonocap).

Methods: After Ethical committee approval and patient assent, two tonometric catheters were inserted into patients who after an overnight fast, were given 30 ml per hour of water for 4 h and following a 1 h rest, 30 ml per hour of enteral feed for 4 h. All patients received iv ranitidine. The $PrCO_2$ was measured hourly using both techniques.

Results: Eight neurosurgical intensive care patients were studied (mean age 52 years, SD 15.3 years). All patients were stable and had no significant changes in cardiovascular or blood gas parameters during the study.

There was a significant difference between the TCS and Tonocap $PrCO_2$: 4.84 (± 2.78) kPa compared to 6.74 (± 4.46) ($r^2 = 0.36$). Bland–Altman analysis showed the mean bias between TCS and Tonocap $PrCO_2$ and –1.85 kPa with a precision of ± 3.49 kPa.

There was no significant difference between the effects of feeding with the two techniques.



Conclusion: Enteral feeding has no effect on $PrCO_2$ in neurosurgical patients. Saline tonometry under reads compared to the Tonocap similar to that of general intensive care patients.

P173 Does enteral feeding potentially alter the PCO_2 gap and pHi?

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Introduction: Measurement of pHi or the mucosal–arterial PCO_2 gap is advocated to detect splanchnic ischaemia and covert shock. Nasogastric feeding may significantly affect these measurements. We used a previously described animal model [1] to evaluate the effect of enteral feeds on the luminal PCO_2 response to intermittent splanchnic ischaemia.

Methods: Adult male Wistar rats (285–425 g) were anaesthetised with sodium pentobarbitone 60 mg/kg i.p. and ventilated with 100% oxygen and isoflurane via tracheostomy to a $PaCO_2$ of 30–40 torr. Distal aortic pressure was monitored continuously. A sensor (Paratrend 7, Diametrix Medical Inc., Bucks, UK) was inserted into the ileal lumen to record PCO_2 measurements every 2 s. Four rats received no feeds (controls) whilst in another four rats an ileal cannula was inserted and feed (Nutrison, Nutricia, Zoetermeer, Holland) infused at 3 ml/h. In each rat, five two-minute episodes of aortic hypotension were induced to a mean pressure of 30 mmHg by intermittent elevation of a silk sling placed around the proximal aorta.

Results: See Table. Feeds significantly elevated the mean baseline luminal PCO_2, and delayed and blunted the PCO_2 increases (ΔPCO_2) in response to transient ischaemia.

	Baseline PCO_2 (torr)	Time to onset of response (s)	Time to peak response (sec)	Peak ΔPCO_2 (torr)
Control	55 ± 4	47 ± 15	180 ± 12	28 ± 8
Feed	67 ± 9*	51 ± 18	196 ± 16*	23 ± 4*

Data are mean ± SD. *$P < 0.05$

Conclusion: Assuming no differences in $PaCO_2$ in both groups, the data suggest that enteral feeding increases the baseline mucosal–arterial PCO_2 gap and reduces baseline pHi. It may also impair the detection of splanchnic ischaemia by delaying and blunting the responses of these indices to reduced mucosal perfusion.

Reference

Morgan TJ, Venkatesh B, Endre ZH: *Crit Care Med* 1997, **25**:1575-1578.

P174 Enteral feed delays response times of a tissue PCO_2 sensor

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Crit Care 1999, **3 (suppl 1)**:P174

Introduction: Real time assessment of gut luminal PCO_2 is possible with rapidly responsive tissue CO_2 sensors [1]. The impact of the presence of feeds in the gut on the rapidity of response of the sensor to a change in mucosal CO_2 tension has not been evaluated.

Methods: The speed of onset of response and the 90% response time of a commonly used tissue gas sensor the Paratrend 7 (Diametrics Medical, UK) to a change in ambient CO_2 tension were compared in normal saline (control) and an enteral feed solution (Nutrison, Nutricia, Zoetermeer, Holland). Probe onset and 90% response times were determined for a step up and step down change in CO_2 tensions in saline and feed solutions by bubbling the following three pairs of gases A) 2% CO_2 and 10% CO_2 B) 10%

CO_2 and 5% CO_2 and C) 5% CO_2 and 2% CO_2 through these solutions maintained at 37°C in a bubble tonometer. After calibration, the sensor was equilibrated in saline bubbled with the first gas of each pair. After equilibration the second gas of each pair was bubbled through the solution. This was repeated for a total of six equilibrations between each pair of gases. The experiment was then repeated with the feed solution.

Results: See Table

Conclusion: The presence of enteric feed significantly slows down the onset time and response time of the sensor to a change in ambient CO_2 tension. Altered viscosity and CO_2 binding by the feed are possible mechanisms for the altered response of the sensor. The reduction in response time may impact on the ability of tissue CO_2 sensors to provide accurate real time data in clinical practice.

	Onset time (s)		90% response time (s)	
	Saline	Feed	Saline	Feed
Step up	39 ± 9	65 ± 10*	188 ± 25	307 ± 42*
Step down	30 ± 6	52 ± 9*	191 ± 18	297 ± 20*
Overall	34 ± 8	59 ± 11*	189 ± 21	302 ± 32*

The data are presented as mean ± SD (*$P < 0.001$)

Reference

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P175 Splanchnic and haemodynamic data as prognostic indexes in MODS patients

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Crit Care 1999, **3 (suppl 1)**:P175

Introduction: The aim of this prospective non intervention study is to evaluate if the analysis of some perfusional indexes, as gastric intramucosal pH (pHi, U) and plasma disappearance rate of indocyanine green (PDR dye, %/min), may be useful for prognostic evaluation in patients with MODS.

Material and methods: Eighty-four medical or surgical patients, with MODS (mean age 51, SD 17; mean SAPS II (1st day) 56, SD 9), were studied. After 6 h of ICU stay, a gastric tonometer, a 7.5 pulmonary artery catheter and a 4 F femoral artery catheter were inserted. The vascular catheters were connected to 'COLD System', an integrated monitoring system which uses the double indicator technique and studies hepatic perfusion, by analysis of PDR. All patients were in CMV and received ranitidine. The haemodynamic management was realized in order to optimize cardiac output (CO, l/min/m² BS) and systemic oxygen delivery (DO_2, ml/min/m² BS). All data were recorded at the beginning of the study (T0) and after 6 (T1), 12 (T2), 24 (T3) and 36 (T4) hours. Statistical analysis of data was performed using Manova Test, considering the significant differences in the times of study between survivors (S) and non-survivors (NS) and analysing the variance of repeated measures. Levels of $P < 0.05$ were accepted.

Results and conclusions: 40 (47.6%) patients died. Some data are shown in the Table (as mean and (SD); S vs NS: *$P < 0.0001$; $^{\$}P < 0.005$; T vs T0: $^{\S}P < 0.05$).

In this group of patients, a precocious splanchnic hypoperfusion seems to be the main prognostic factor. In NS group, gastric intramucosal acidosis is present in the early period of study and it is possible to notice a continuous worsening of liver perfusion. According to this point of view, perfusional parameters may give more prognostic informations than systemic data.

	Time 0	Time 1	Time 2	Time 3	Time 4
CO	S 4.5 (1.5) NS 4.7 (1.9)	5 (1.6) 4.6 (1.9)	(1.6) 4.9 (2.1)	(1.6) 5 (2.3)	5 (1.5) 4.6 (1.7)
DO2	S 656 (202) NS 631 (273)	723 (219) 628 (274)	713 (186) 670 (288)	672 (199) 679 (351)	697 (207) 614 (228)
PHi*	S 7.45 (0.07) NS 7.32 (0.1)	7.41 (0.09) 7.29 (0.21)	7.39 (0.14) 7.25 (0.24)§	7.40 (0.13) 7.24 (0.19)§	7.41 (0.1) 7.25 (0.18)§
PDR$	S 13.3 (6) NS 9.2 (6.1)	13.1 (7.2) 8.9 (5.5)	13.4 (6.2) 8.7 (4.8)	13.3 (6.3) 8.5 (4.2)	13.8 (6.8) 8.6 (5.7)

P176 Major abdominal surgery and complications: is air gastric tonometry predictive of outcome?

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Crit Care 1999, **3 (suppl 1)**:P176

Introduction: Gut mucosal ischemia can initiate a systemic inflammatory response sometimes leading to multiple organ failure. The adequacy of splanchnic perfusion during major abdominal surgery

can be evaluated by an easy, non invasive, new method : gastric air tonometry. Air tonometry is an important technical advance which eliminates errors involved in saline tonometry.

The aim of our study was to investigate wether there was a relationship between a perioperative tonometric parameter and clinical outcome.

Methods: 27 patients, ASA 1–3, admitted for major abdominal surgery (hepatectomy, pancreatoduodenectomy, colorectal resection) were prospectively studied between March 98 and October 98. After induction of anesthesia, intramucosal PCO_2 ($PrCO_2$) was measured by a gastric tonometer placed in the stomach and then connected to a TONOCAP® (Tonometrics-Datex-Engstrom). PCO_2 gap was measured immediately after tracheal intubation and until discharge of the SICU at H24 postoperatively. Post operative complications were recorded during the entire hospital stay. Statistical analysis used FISCHER's Exact Test.

	Complications	No complication
Gap ≥15	15	1
Gap <15	4	7

Results: 19 out of 27 patients suffered complications (bleeding, SIRS, sepsis, MOF, pancreatitis, wound infection, hepatic failure, anastomotic leakage) leading to death for two of them. Fifteen out of these 19 patients had a PCO gap >15 mmHg during surgery. The FISCHER's Exact Test ($P < 0.002$) was conclusive for both group. According to these results, PCO_2 gap can predict complications with a sensibility of 78.5% and a specificity of 88%.

Conclusion: During abdominal surgery, the assessment of splanchnic perfusion can be easily achieved with air tometry ; a PCO_2 gap >15 mmHg seems to be predictive of postoperative complications.

P177 Hemodynamic changes and cytokine trends during abdominal stop-flow

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Background: The stop-flow is a therapeutic technique to treat local splanchnic malignant neoplasm, especially of the liver. The rational of this technique is to reach and maintain high concentration of antiblastic drugs in the site of the tumor. This is made positioning two intravascular devices to stop both the arterial in-flow and the venous out-flow of the site where the tumor is localized. In this way a decreased vascular flow with consequent hypoxia is created to increase the efficacy of some antiblastic drugs. The aim of this work is to verify the hemodynamic changes due to the splanchnic hypoxia and the trend of TNFa, interleukin 1B, 6 and 8.

Material and methods: We have examined three patients: two with metastasis from carcinoma of colon-rectum and another with not operable carcinoma of pancreas. Before the stop-flow a pulmonary catheter to measure the cardiac output on-line (Vigilance, Baxter), a gastric tonometer and a radial artery were positioned. After the induction of anesthesia (fentanyl, thiopental, vecuronium) a venous device in vein cava and an arterial device in aorta artery, both with a balloon in the top, were positioned just under diaphragma muscle and inflated. In this way the aortic and caval flows were interrupted for 20 min and in this time antiblastic drugs were administred in the hypoxic and isolated splanchnich area. After 20 min the baloons were deflated, splanchnic area was revasculated and a dyalisis started to eliminate as soon as possible the drugs. At 5 times (after the induction of anesthesia, after 10', 20' of stop flow and after 15' and 40' of the end of stop-flow) all hemodynamic and oxyphoretic parameters, pHi and blood lactate were measured and sierum to detect cytokine TNFa, Il-1B, Il-6, Il-8, was stored at –60°C.

Results: In all three patients there was an increase of more 100% and a decrease of systemic vascular resistance after the stop flow and these changes were still present after 40 min from the revascularisation. At the same time blood lactate increased and pHi decreases below 7.32. Among the cytokines only Il-6 showed an increase of more 100% after the stop-flow, while the others had no significant movements.

Discussion: Decreasing tissue perfusion causes hypoxia and then acidosis that provokes a cellular damn, increasing of cellular permeability with loss of barrier function of gut mucosa. This induces the liberation of some substances, such as endotoxins, which start the inflammatory cascade of TNFa, Il-1, Il-6, Il-8. Moreover, another way to induce the formation of toxic substances, in the presence of ischemia followed by riperfusion, is the activation of purine metabolism with activation of xantine-oxydase (XO) and consequent production of the anion superoxydodismutasis, that, in the presence of iron (Fenton reaction) causes the formation of ossidryl ion, very dangerous for the organism. The hemodynamic response of these two cases (high CO, low SVR, pHa, pHi and increased blood lactate) and the increasing of Il-6 are not explanable only in terms of hypoxia and it could be supposed that these changes probably are due to a septic state, caused by the substances liberated from the hypoxic splanchnic tissue. This experimental model could be useful in the comprehension of physiopathology of hypoxia and perhaps of septic shock and, in some way in the experimentation of new drugs against the effects of hypoxia.

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P178 Continuous assessment of colonic perfusion during abdominal aortic reconstruction using a modified Paratrend 7™

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Crit Care 1999, **3 (suppl 1)**:P178

Background: Colonic ischaemia may initiate multiple organ dysfunction syndrome following abdominal aortic reconstruction. Most methods available to detect colonic hypoperfusion are not ideal for continuous intraoperative and postoperative monitoring.

Objective: Prospective evaluation of the use of a modified intra-arterial fiberoptic probe (Paratrend 7™) for continuous perioperative monitoring of colonic luminal pH, P_{CO2} and P_{O2} in patients undergoing abdominal aortic reconstruction.

Study design: Fourteen consecutive patients scheduled for infrarenal abdominal aortic reconstruction were recruited. Preoperative bowel preparation was partially performed in the first six patients and completely performed in the last eight patients. Under general anaesthetic, a modified Paratrend 7™ probe was inserted transanally to the rectosigmoid junction. Continuous intraoperative analysis was compared to intermittent intraoperative inferior mesenteric vein (IMV) sampling for pH, P_{CO2} and P_{O2} was observed on aortic cross clamping and declamping. The 95% limits of agreement with IMV pH, in patients with complete bowel preparation were 0.16 and –0.1 for the calculated intramucosal pH and 0.72 and –0.48 for the luminal pH. The estimated bias for the calculated pHi was –0.03. Results were directly affected by the condition of bowel preparation

Conclusion: The modified Paratrend 7™ effectively detects changes in colonic perfusion during abdominal aortic reconstruction. However, complete bowel preparation is essential and modifications may be required to increase its precision.

P179 Effect of endotoxemia on hepatic portal and sinusoidal blood flow in rats

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A decrease of liver blood flow leads to a dysfunction of hepatocytes and Kupffer-cells with subsequent local and systemic liberation of proinflammatory mediators [1] that may maintain SIRS and may lead to MODS [2]. There is only limited knowledge about the hepatic micro- and macrocirculation during sepsis or endotoxemia. Therefore, aim of our study was to investigate alterations in hepatic portal (PBF) and sinusoidal blood flow (SBF) during endotoxemia.

In male Wistar rats endotoxemia was induced by continuous infusion of 2 mg/kg/h lipopolysaccharides (LPS) from *E. coli* 026:B6 immediately after baseline measurements (LPS group; $n = 10$). The control group ($n = 10$) received an equivalent volume of Ringer's solution. MAP, HR, CO, PBF and SBF were measured at baseline, and 60 min, and 120 min after induction of endotoxemia. PBF was measured using a laser-doppler flow probe that was positioned around the portal vein. SBF was detected by *in vivo* videomicroscopy of the left liver lobe. Statistical analysis was performed using Mann-Whitney's U-test.

MAP and CO remained at baseline values in both groups. In the LPS-group HR significantly increased. During endotoxemia PBF and SBF significantly decreased (Table).

		0 min	60 min	120 min
Cardiac output (ml/min)	Control ($n=10$)	127 ± 12	150 ± 14	135 ± 24
	LPS ($n=10$)	124 ± 20	143 ± 30	131 ± 22
Portal blood flow (ml/min)	Control ($n=10$)	24 ± 4	22 ± 4	22 ± 3
	LPS ($n=10$)	23 ± 3	15 ± 4*	16 ± 3*
Sinusoidal blood flow (10^3 µm³/s)	Control ($n=10$)	37.3 ± 9.2	37.1 ± 8.5	36.3 ± 7.1
	LPS ($n=10$)	39.4 ± 8.1	27.0 ± 5.6*	22.5 ± 3.7*

Data are expressed as mean ± SD. * $P < 0.01$ vs. control

Our results demonstrate that during early endotoxemia hepatic macro- and microcirculatory perfusion is significantly decreased despite unchanged MAP and CO. This early reduction of hepatic perfusion might be caused by an increased hepatic vessel resistance as a consequence of liberation of vasoconstrictive mediators (e.g. endothelin) or/and by a decrease in intestinal perfusion.

Reference

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P180 Multiple organ disfunction, surgical techniques and prognostic markers in acute pancreatitis

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Introduction: Multiple organ dysfunction (MOD) is the leading cause of morbidity and mortality in patients admitted to an intensive care unit (ICU).

Objective: To study the relationship between MOD and mortality in severe acute pancreatitis (SAP) together with bacterial infections, surgical techniques as well as clinical and biological markers.

Material and method: A prospective study of clinical results and laboratory testing and image techniques made in 100 patients treated in the ICU over 6 years, from 1991–96.

Results: See Table.

Conclusion: MOD score higher than 2 is related to serious pancreatitis. It is important to preserve different organ functions together with nosocomial vigilance with the support of biological markers just to indicate specifif antibiotherapy if sepsis is present, and surgery in early phase as a last resort.

	Survival						
	Yes			No			
Variables	*n*	Average	SD	*n*	Average	SD	*P**
Age	72	61.7	13.8	28	69.8	11.3	0.005
RCP 48 h	34	25.7	22,4	10	68	43	0.05
S. Calcium 48 h	67	7.6	1.4	24	5.7	1.4	0.000
Albumin 1 Week	34	2.1	1.5	13	1.6	1.1	ns
N. Dysfunction Organ	68	0.98	0.71	27	3.1	1.03	0.000
MOD Score#	68	2	1.5	26	7.8	3.2	0.000
N. Bacteria Inf. Abdom.	26	1.3	0.98	15	2.9	1.9	0.04
N. Surgery	52	0.8	0.4	22	1.3	0.86	0.01
Days onset surgery	40	12	4.7	18	3.6	2.1	0.003
	n	%	N Group	*n*	%	N Group	*P***
Biliar etiology	46	66	72	15	60	28	ns
Sepsis	18	27	69	14	64	24	0.008
Marsupialization***	9	22	40	7	38	18	0.002

t* Test. **Chi Square. N., number; RCP, reactive C protein, S., serum. ***Included if is biliar colechistectomy. #*Crit Care Med* 1995; **10:1638-1652.

P181 Outcome prediction for patients with chronic liver disease requiring medical intensive care

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Introduction: To determine the outcome and prognostic factors of patients with cirrhosis of the liver requiring medical intensive care

Patients and methods: All patients with chronic liver disease and cirrhosis admitted to the medical ICU between 7/95 and 6/97 were enrolled in the study. Prospectively the reason for ICU admission, acute diagnoses, presence of co-morbid illness, stage of liver disease, number and length of organ failures, daily APACHE II and TISS classification and outcome were documented. Laboratory values were drawn retrospectively from the charts. Patients with multiple ICU treatments were reviewed only for the initial admission. Contingency tables were analysed using χ^2 test, continuous variables were compared using Mann–Whitney U test.

Results: One hundred and two patients met the study criteria; mean age was 51 ± 12 (± SD) years, median 50, range 28–78 years, 67% were male. Mean ICU length of stay was 8.6 ± 14.7 days. Mean APACHE II score (first 24 h) was 20 ± 11, range 5–48. Mean TISS score (first 24 h) was 30 ± 14, range 0–69. ICU mortality was 38%, a significant association was seen between ICU mortality and the following variables: sepsis ($P = 0.000001$), pneumonia ($P = 0.00027$), elevated serum lactate ($P = 0.00003$) and CRP ($P = 0.00001$) on admission, respirator, renal replacement or catecholamine therapy (all $P = 0.00001$), Child–Pugh ($P = 0.19$) and APACHE II score ($P = 0.00001$) within the first 24 h. No significant association was noted between ICU mortality and age ($P = 0.89$), length of stay ($P = 0.12$), gastrointestinal bleeding ($P = 0.15$), spontaneous bacterial peritonitis ($P = 0.31$), and the etiology of liver disease (alcohol, viral, both combined, others $P = 0.68$).

Conclusion: Among critically ill patients with cirrhosis of the liver ICU mortality was 38%, in comparison, the mortality for all ICU admissions in this period of time was 23%. APACHE II score and variables describing single or multiple organ dysfunction and pulmonary infection are excellent predictors of mortality.

P182 Outcome of chronic liver disease in a specialist liver intensive therapy unit

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Background: Decompensated chronic liver disease (CLD) is associated with high morbidity and mortality. Intensive therapy unit (ITU) admission in this clinical setting consumes significant resources and remains of unproven benefit.

Methods: We examined the records of all patients with chronic liver disease who were admitted to the Liver ITU at King's College Hospital between 1/9/97 and 30/9/98.

Results: One hundred and nine patients were admitted with CLD (M:F 70:39, median age 47 years, range 18–72, aetiology: alcoholic liver disease (ALD) 67%, viral hepatitis 12%, ALD+viral hepatitis 9%, other CLD 12%). Fifty-four (50%) patients survived (including two who underwent liver transplantation) and 55 died. There was no difference in age between survivors and non-survivors ($P = 0.5208$, unpaired t-test). Seventy-eight patients (72%) were ventilated, of whom 51 (65%) died. Forty-six patients (42%) were treated with renal support, of whom 42 (91%) died. Of the 4 survivors from the renal supported group 2 underwent liver transplantation. 44 patients (40%) needed both ventilation and renal support, of whom 40 (91%) died.

Conclusion: Patients with decompensated CLD needing ITU care have a high mortality. Single organ support in the form of mechanical ventilation is a reasonable use of resources as there is a good chance of recovery. The need for renal support is a bad prognostic indicator. Unless there is an acute reversible component to renal failure or liver transplantation is contemplated, the use of renal support in this patient group may not be a good use of resources.

P183 Association between interleukin-10 (IL-10) gene promoter polymorphisms and outcome in acetaminophen induced acute liver failure requiring admission to a liver intensive care unit

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Background: The outcome of severe hepatic necrosis following acetaminophen overdose is unpredictable and may have up to a 90% mortality. IL-10 is an anti-inflammatory cytokine which plays a pivotal role in inflammation and potentially in multiorgan failure. Elevated plasma levels of IL-10 are found in patients with acute liver failure. Polymorphisms in the promoter region of the IL-10 gene have recently been described comprising three single base-pair substitutions at positions (–1082, –819, –592) resulting in three common three haplotypes GCC, ACC and ATA. The GCC/GCC genotype is associated with higher IL-10 production, and ATA haplotype with lower production.

Patients and methods: 96 patients with severe acetaminophen hepatotoxicity requiring intensive care were studied. IL-10 gene polymorphisms were determined by sequence-specific oligonucleotide probing using a standard PCR based technique. Haplotype frequencies were compared with those of 71 racially and geographically matched controls.

Results: See Table.

Patients (no)	No. haplotypes	GCC	ATA	ACC
Controls (71)	142	47%	25%	28%
All patients (96)	192	56%	19%	25%
Survivors (60)	120	57%	20%	23%
Non survivors/Tx (36)	72	54%	18%	28%
ARDS (25)	50	56%	20%	24%
ARF (47)	94	61%	18%	21%
Hypotensive/ vasopressors (32)	64	56%	20%	24%

ARF, acute renal failure: creatinine > 300 μmol/l and/or oliguria requiring haemofiltration; ARDS, acute respiratory distress syndrome: PaO_2 (kPa)/FiO_2 <20, PEEP >5 cmH_2O; Tx, liver transplant. Haplotype frequencies were compared using χ^2 test with Yates correction.

Conclusion: There is no significant association between outcome or incidence of multiorgan failure in patients with acetaminophen induced acute liver failure and these three common IL-10 gene promoter haplotypes.

P184 A reproducible rabbit model of acetaminophen induced acute hepatic failure (AHF) and multi-organ failure (MOF)

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Background: Acetaminophen overdose is the commonest cause of AHF in the UK. Patients may require liver transplantation and intensive care for support for MOF. Acetaminophen (APAP) metabolism is catalysed by cytochrome P450 (CYP450). This leads to formation of the toxic metabolite *N*-acetyl-*p*-benzoquinnone (NAPQI). NAPQI detoxification requires glutathione. Both prior CYP450 induction and glutathione depletion exacerbate hepatic damage.

Aim: To develop a reproducible rabbit model of AHF and MOF paralleling, clinical, biochemical and histological patterns of human disease.

Method: CYP450 was induced in New Zealand White Rabbits ($n = 8$) using 20-methylcholanthrene (80 mg/kg i.p.) dissolved in corn oil. The glutathione synthetase inhibitor buthionine sulphoxime (2 mmol/kg i.v.) was administered just prior to APAP administration, (500 mg/kg s.c.) 4-hourly for 24 h.

Clinical observations were recorded and arterial blood sampled over 48 h.

Results: *Clinical:* Grade I-III encephalopathy (modified from Zimmerman *et al.*) occurred at 8–12, 12–18, 18–36 h, respectively. Mortality was 75% at 48 h, preceded by a short period of grade IV encephalopathy.

Biochemistry: Expressed as mean values $\pm s_{(n-1)}$

	24 h	36 h
AST (24–40 iu/l)	6470 ± 1310	4321 ± 750
NH3 (<75 N-µg/dl)	148 ± 22	164 ± 12
Lactate (0.6–1.8 mm/l)	8.1 ± 1.3	11.1 ± 1.0
PT (10–12 s)	8.2 ± 0.97	11 ± 0.44
Creatinine (60–100 µmol/l)	214 ± 31	312 ± 52

Histology: Liver: Centrilobular necrosis was prominent on the surface of the liver at 24 h, with extensive severe coagulative necrosis at 48 h. Kidney: Acute tubular necrosis at 24 h.

Conclusion: Preliminary data suggests that we have developed a reproducible rabbit model of AHF and associated MOF, however, further characterisation is required.

P185 Monitoring in liver transplantation

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Introduction: Despite the overall acceptable results obtained in liver transplantation during the last 15 years infection and the appropriate management of the immunosuppressive treatment remains a major issue in the follow-up and outcome after liver transplantation.

Patients and methods: One hundred liver transplants with a 1 year survival rate of 81% were performed at the university of Leipzig since December 1993. Patients were monitored beside the routine laboratory parameters by Procalcitonin (PCT), soluble IL-2-receptor (s-IL2-R) TNF alpha, Interleukin 6 (IL-6) and Interleukin 8 (IL-8). The postoperative complications were differentiated whether a gram– or + sepsis or a fungal infection occurred.

Results: See Table.

	Gram+ sepsis	Gram– sepsis	Fungal infection
PCT	↑↑	↑↑	↑
IL-6	↑	↑	↑(↑)
IL-8	↑	↑	(↑)
TNF alpha	↑	↑	↑↑↑
s-IL-2R	↑↑↑	(↑)	↑↑↑

Conclusion: These qualitatively summarized results indicate the potential role of an advanced monitoring for the differentiation of infectious complications. Elevated PCT, IL-6 and s-IL-2 R levels are found in severe bacterial infections, whereas very high levels of TNF alpha and s-IL-2 R seem to be more specific for fungal infections. These findings may be a useful guide for the initiation of a specific diagnostic work up, for the induction of an adequate treatment and/or for an appropriate modification of the immunosuppressive treatment.

P186 Rare fatal complications of acute fatty liver of pregnancy

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Background: Acute fatty liver of pregnancy (AFLP) and the syndrome of haemolysis, elevated liver enzyme levels, and low platelet count (HELLP) are rare but major disorders of the third trimester of pregnancy and are maybe related to pre-eclampsia. Mortality of 9–24% has been reported and complications include pulmonary oedema, adult respiratory distress syndrome, abruptio placentae, disseminated intravascular coagulation, ruptured liver haematomas, and acute renal failure increasing mortality to 50–90%. Multi-organ failure may result requiring full intensive care support. Perinatal mortality is equally high, ranging from 79 to 367 per 1000 live births, and neonatal complications correlate with the severity of maternal disease. Most presentations of AFLP and HELLP require monitoring and supportive care, however, early recognition of rarely associated complications and their appropriate treatment is of paramount importance to the survival of the mother and child.

Case reports: We report five patients referred to the Liver Intensive Care Unit (LITU) with mild AFLP in 3 years. Their disease progressed rapidly to acute hepatic failure with associated multi-

organ failure(1 ± 2 days post admission to LITU). Patients (age 26.4 ± 5.2 years) presented in the third trimester of pregnancy (33 ± 3 weeks) with proteinuria, hypertension (systolic 186 ± 27.1, diastolic 103 ± 10.1 mmHg), and deranged liver function consistent with AFLP and evidence in four patients of HELLP syndrome. Maternal deterioration and foetal distress required emergency caesarean section. Following uncomplicated caesarean section, reduced conscious level (Grade I–II encephalopathy) was associated with severe hypovolaemic shock (systolic 60 ± 5 diastolic 40 ± 7 mmHg). Haematological investigations demonstrated a fall in haemoglobin (8.6 ± 1.4 g/dl), worsening thrombocytopaenia (platelets 42 ± 20 $\times 10^9$/l), rising coagulopathy (prothrombin time 23.2 ± 5.6 s),and disseminated intravascular coagulopathy. Biochemical investigations revealed, metabolic acidosis (pH 7.09 ± 0.15), hyperlactataemia (10.16 ± 4.5 mmol/l), severe transaminitis (AST 4050 ± 599 iu/l), increasing total bilirubin (194 ± 75 µmol/l) and oligo-anuric renal failure (creatinine 353 ± 156 µmol/l). Patients were resuscitated, intubated and mechanically ventilated. Intra-cranial transducers were inserted to monitor intracranial pressure. Vaso-active agents were used to maintain haemodynamic stability and continuos venous-venous haemofiltration initiated. Intravenous *N*-acetylcysteine, antibiotics and anti-fungals were commenced. Ultrasound, helical computer tomography and angiography confirmed extensive subcapsular haematomas suggestive of liver rupture in three patients, massive hepatic necrosis in the fourth patient and abnormal aorto-portal shunting suggestive of veno-occlusive disease in the fifth patient. Patients were listed for liver transplantation.

Of the five, patient one did not survive long enough for transplantation, however, the others successfully received liver transplants (7.4 ± 6 days post caesarean section). Unfortunately patient two developed hepatic artery thrombosis and was re-transplanted, but died soon after.

The other three patients remain alive and well. Patients have been investigated for pro-thrombotic disorders, evidence of which is not present.

Conclusion: We describe potentially fatal complications in five patients initially presenting with mild AFLP and or HELLP associated with pre-eclampsia with a mortality of greater than 90%. These rare complications include hepatic rupture, hepatic infarction and necrosis and veno-occlusive disease. Clinical suspicion must be high if there is evidence of hypotension, altered conscious state, metabolic acidosis, hyperlactataemia and deranged liver function. The early recognition of the changing clinical parameters of disease, multidisciplinary support, and specialist intensive care is required for the survival of this rare group of patients and their children.

P187 Treatment of acute hepatic failure and encephalopathy with extracorporeal *ex vivo* pig-liver perfusion in the critical care unit

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Patients with fulminant hepatic failure have a higher mortality rate after orthotopic liver transplantation than patients with chronic liver disease. Due to the shortage of cadaveric livers for transplantation, the concept of perfusion through a liver outside the body has recently been reintroduced in the clinical setting.

We describe a venovenous perfusion circuit with two Biomed pumps and one oxygenator connected to the patient's venous system via two hemodialysis catheters. The circuit provided adequate flow during *ex vivo* pig-liver perfusion in a critically ill patient with a stage 5 coma. The procedure lasted 4.5 h and was terminated when the oxygen extraction and bile production decreased, and the total bilirubin level went back up. During the period of *ex vivo* perfusion the patient moved all four extremities spontaneously within 30 min of perfusion, serum total bilirubin, and the serum ammonia level decreased by 50% and 60% respectively. The patient eventually developed sepsis and the therapy was discontinued.

Conclusion: For patients with acute hepatic failure and encephalopathy associated with cerebral edema in whom cadaveric liver transplantation is not an immediate option, extracorporeal *ex vivo* pig-liver perfusion is a reasonable alternative in the critical care setting.

P188 Increased prevalence of *Helicobacter pylori* infection in critically ill patients with stress ulceration

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Introduction: *H. pylori* is known for its causative role in gastric and duodenal ulcer disease. However, it is unknown whether *H. pylori* plays a role in the formation of stress ulceration in critically ill patients. Therefore we studied the presence of *H. pylori* infection in critically ill patients on admission to the intensive care and the relation to gastric and duodenal mucosal injury.

Methods: Inclusion criteria were admittance to the intensive care unit for emergency reasons and the need for mechanical ventilation. *H. pylori* was detected by the Laser Assisted Ratio analyser-^{13}C-urea breath test (UBT). Upper gastro-intestinal endoscopy was performed in all patients by the same endoscopist who was blinded for the results of the *H. pylori* test. Breath test and endoscopy were performed within 6 h after admission. Gastric and duodena mucosal injury were assessed according to the so called Brown scoring system [1]; grade 0, normal mucosa; grade 1, 1 to 5

erosions or submucosal hemorrhages; grade 2, 6 to 20 erosions or hemorrhages; grade 3, more than 20 erosions or hemorrhages.

Results: Fifty consecutive patients were included. In seven patients the UBT was unable to be processed ($n = 6$) or endoscopy was inadequate ($n = 1$). Of 43 eligible patients 21 were *H. pylori* positive and 22 were *H. pylori* negative. Of 28 patients who had a mucosa injury grade 0 or 1 nine were *H. pylori* positive (32%) and mean APACHE II score was 25.6. Of 15 patients who had a mucosal injury score 2 or 3, 12 were *H. pylori* positive (80%) and mean APACHE II score was 25.5. *H. pylori* infection was significantly associated with mucosal injury gradation 2 or 3 ($P = 0.003$, Pearson Chi-square, odds ratio 8.4 and relative risk 4.2).

Conclusion: The severity of gastric and duodenal mucosal injury in critically ill patients during mechanical ventilation is significantly related to the presence of *H. pylori* infection.

Reference

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P189 Effects of spinal sympathicolysis on gastrointestinal motility in critically ill patients

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In surgical ICU patients many causes provide a gastrointestinal atony, i.e. shock, systemic analgesia + sedation. Due to this atony, early enteral nutrition and a normal function of the gut is often prevented. Translocation, ileus or endotoxine transmission and their complications are pretended. Most of the seriously injured polytrauma patients and those after major abdominal surgery are concerned. Even intensive and prolonged conservative efforts for stimulation of gastrointestinal motility (i.e. laxatives, contrast agent, metoclopramid, neostigmin, ceruletid, enteroclysis, erythromycin, systemic sympathicolytics) are not always successful. In the last 2 years, we performed in unsuccessful cases after excluding all contraindications a central neuraxial block with local anesthetics as an ultima ratio approach.

Methods: Spinal sympathicolysis was performed if critically ill ICU patients in spite of prolonged and repeated conservative efforts did not defecate within 6 days. After the decision conservative efforts were continued for 24 h. If the patients did not defecate, we carried out spinal or epidural anesthesia. Sepsis, coma and coagulation abnormalities were contraindications. In presence of leucocytosis without septic symptoms, the local anesthetic (3 ml bupivacaine 0.25%) + 0.5 mg morphine was injected intrathecally. In other cases we placed a lumbar epidural catheter with an initial dose of 10 ml bupivacaine 0.25% + 3 mg morphine. If necessary, the dose was repeated within 12 h.

Results: We report about 26 patients, which were treated with spinal sympathicolysis, in 10 cases as single shot spinal anesthesia and in 16 cases as epidural anesthesia. In all patients gastrointestinal motility improved significantly within the first 12 h. Twelve (46%) patients defecated within 12 h and 9 (35%) within 24 h. Four of the remaining patients, all with epidural anesthesia, defecated during the second day after the beginning of the sympathicolysis. One patient with intrathecal single shot sympathicolysis without defecation within 48 h received a second intrathecal treatment with success. As an accompanying and important side-effect, in most patients systemic analgesia and sedation could be reduced significantly and weaning could be initiated. None of the 26 patients had an untoward effect.

Conclusion: In our patients spinal sympathicolysis was a successful method to stimulate gastrointestinal motility in critically ill ICU patients. Regarding to the possible complications of a prolonged intestinal atony (translocation, ileus operation, endotoxine transmission) and after trying all conservative efforts spinal sympathicolysis can be considered as an acceptable approach in spite of the possible untoward effects. By the good results we now more often decide for this method because of the good effects and side-effects.

P190 Gastro-intestinal bleeding in 1211 ventilated trauma patients: a multivariate analysis of the risk factors

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Aim: Anti-acid therapies are described as potential risk factors for acquired pneumonia in ICU patients. The aim of this prospective study is to assess the incidence and risk factors of gastro-intestinal bleeding (GIB) in a level 1 trauma ICU, in order to better define the populations of patients likely to benefit from such a preventive treatment.

Methods: 5 year prospective study (May 1st 1993, April 30th 1998). All trauma patients admitted to ICU and ventilated for more than 2 days were included. All patients were submitted to the same diagnostic and therapeutic procedures. None of them received systematic anti-acid therapies except in the case of documented history of GIB. GIB patients (confirmed by endoscopy) were compared to all others patients (GIB–).

Results: 1211 patients (age*: 38.6 ± 19.3 years, ISS**: 31 (24–41), GCS**: 7 (3–15), Coma (GCS = 8): 52%, SAPS II**: 30 (19–37),

Table 1

	n	AIS Head**	Coma**	ARF	UGIT	Septic shock	SDRA
GIB +	28	2(0–5)	32%	32%	57%	25%	21%
GIB –	1183	5 (2–5)	52%	6%	9%	8%	5%
P	–	<0.001	0.05	<0.001	<0.001	0.005	0.003

AIS head, Abbreviated injury score, Coma: GCS = 8, ARF: Acute renal failure, UGIT: unavailability of the gastro intestinal tract, *mean, standard deviation, **median, centils 25–75

Table 2

	Coefficient	Odds ratio	Confidence limits	*P*
UGIT	2.366	10.65	5.53–25.00	<0.001
Acute renal failure	1.18	3.253	1.24–8.49	0.01
Spinal cord injury	1.288	3.624	1.23–10.68	0.02

ventilation: 13.5 ± 11 days) were included. The incidence of GIB is 2.3% ($n = 28$). Table 1 summarizes the only significant risk factors after univariate analysis, Table 2 the final model after stepwise logistic regression.

All patients were successfully treated (medical treatment: 22, surgical treatment: 6) and the occurrence of GIB resulted in no additional mortality.

Conclusion: Unavailability of the gastro-intestinal tract, acute renal failure and spinal cord injury are important risk factors for GIB. These results emphasize the importance of early enteral feeding which certainly represents the best prevention from the occurrence of GIB.

P191 Emergency treatment of hemorrhagic gastric and duodenal ulcer

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Crit Care 1999, **3 (suppl 1)**:P191

Introduction: Hemorrhage is one of the most common serious complication of gastric and duodenal ulcer even so, the knowledge and the usage of new anti-ulcer drugs (H_2-receptor antagonists and inhibitors of the proton-pump enzyme such as omeprazole) and the success of therapy of *Helicobacter pylori* infection of gastric and duodenal mucosa, have changed the role of surgical treatment of ulcer disease.

Our aim is to describe the evaluation of bleeding peptic ulcer, the indications for surgical treatment and the type of operative procedure or method that it has to be performed.

Patients and methods: From 1987–1992 we had in our clinic 416 patients with severe gastric-duodenal hemorrhage (312 males and 104 females). The average age of the patients was 63 years (range: 20–85 yrs). Analytically we had: 251 (60.3%) patients with duodenal ulcer, 72 (17.3%) with gastric ulcer, 58 (13.9%) with gastric cancer, 27 (96.5%) patients had acute hemorrhagic gastritis and 4 (1%) patients had gastric benign tumors.

Results: In 84 patients we could not manage to control the bleeding (severe hemorrhage) by conservative methods (transfusions of blood, anti-ulcer medication) or/and by using the method of endoscopy. These patients have been operated. The surgical procedures that have been undertaken were: vagotomy and pyloroplasty 43 (51.1%), vagotomy and gastrojejunostomy 23 (27.5%) and gastrectomy 18 (21.4%).

From these patients 78 have cured and 6 died because of the high severity of the bleeding in association with their old age (age >80 years) and their general health status (2 of them had coronary disease and another one was diabetic with respiratory deficiency).

Conclusions: Bleeding as complication of peptic ulcer remains up today very serious factor that increases the morbidity and the mortality. The aim is to avoid operating on all patients who would recover on medical treatment, but to operate on all patients who if treated medically would bleed again to a dangerous extent. Furthermore, if surgical treatment is undertaken, it should be performed at the optimal time and the safest operative procedure should be used, by a highly skilled surgeon. The age and general condition of the patient are important factors to consider. The amount of hemorrhage and the rate of hemorrhage are of prognostic significance.

P192 Probiotics in critical illness

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Crit Care 1999, **3 (suppl 1)**:P192

Introduction: Critically ill patients are commonly treated with broadspectrum antibiotics. This brings about a major impact on the delicate microbiological balance in the gut, often causing diarrhoea and overgrowth of resistant pathogens and fungi.

Many potentially pathogenic bacteria adhere to enterocytes via a mannose-specific adhesin. This mechanism has also been found in *Lactobacillus plantarum 299v (L p 299v)* both in the jejunum in the rectum. It is when bacteria are adhered to the mucosa that they interact with the enterocytes, both in negative and positive fashions.

Given in fermented oatmeal soup to healthy subjects, *L p 299v* was detected even 11 days after termination of intake.

In patients with persisting *Clostridium difficile* infections this fermented oatmeal soup containing *L p 299v* has also been effective in normalising gutflora and function.

Objectives: The prime objective was to study if *L p 299v* could survive and colonise on the mucosa in the intestine of patients treated in an ICU. Stool consistency and frequency were among other parameters studied.

Method and materials: In a randomised prospective trial 8 patients received 200 ml daily for 3 days and then 100 ml of an oatmeal soup containing 10^9 cfu/ml of *L P 299v* through out their stay in the ICU. Enteral nutrition as well as the oatmeal soup was started within 24 h after admission to the ICU. Control-patients (7) were treated in the same fashion except for the fermented oatmeal soup. The rectal mucosa was biopsied after admission and then twice a week. Biopsies were analysed blindly for bacterial content and species.

Results: Four of the control patients were colonised with *L p 299v* on admission, but at the second biopsy they were all negative. Of eight treated patients none had positive cultures for *L p 299v* on admission but from the second sample and through their ICU-stay three of them had the bacteria adhered to the mucosa confirmed by cultures from homogenised biopsies.

Bacterial analyses revealed a reduction of sulphite-reducing *clostridia* in the treatment group. In treated patients *lactobacilli* increased while they remained at the original level in controls.

Diarrhoea was less frequent in treated patients.

Discussion: The initially positive biopsies in four of the control patients were probably due to that these patients had ingested *L p 299v* through the commercial *L p 299v*-containing 'Proviva', which is sold in almost all grocery-shops in southern Sweden. The use of antibiotics leads to a level of *L p 299v* below the limit of detection in those that were colonised from the beginning.

In the treatment group the *L p 299v* adhered to the mucosa in 3/8 patients although they as well were treated with antibiotics. It seems that repeated administration is essential if the bacteria should remain in sufficient numbers adhered to the mucosa. Our study shows that antibiotic treated patients in an ICU environment can benefit from probiotics. Less diarrhoea means less impact on the gutflora.

By the repeated administration of the oatmeal soup fermented with *L p 299v* it is concluded that the bacteria can adhere to the gut mucosa in antibiotic treated critically ill patients. Further studies with larger numbers of patients are needed to evaluate other effects.

P193 A simple and safe bedside method of transpyloric feeding tube placement in critically ill patients

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Background Early enteral nutrition is an accepted gold standard in the treatment of critically ill patients. The major limiting factor is depressed gastric motility. However, while small bowel function usually remains intact, the placement of postpyloric feeding tubes increases the number of patients absorbing a sufficient volume of enteral nutrition early in their ICU course. To eliminate the need of invasive and expensive interventions, many bedside techniques have been proposed. Recently one effective way has been described in critically ill children [1]. We modified this method and used it in 27 adult patients.

Methods: Thirty-one postpyloric feeding tubes were placed blindly in 27 consecutive ventilated postsurgical ICU patients using a bedside protocol. The feeding tube was considered to be postpyloric when following the insufflation of 20 ml of air an amount less then 5 ml could be reaspirated. The explanation is the immediat collapse of the narrow small intestine lumen, when air is reaspirated. The tube position was confirmed by abdominal radiography .

Results: In all 31 cases the enteral feeding tube was placed successfully. The average placement time was 14 min. Nineteen tubes (61.2 %) were positioned in the duodenum and 12 tubes (38.8%) in the jejunum. The inability to reaspirate insufflated air correctly predicted transpyloric position in all cases. Initially the administration of enteral feeding was in 100% successfully possible. After 2 days of continous enteral nutrition, we observed duodeno-gastric reflux in one patient. No further complications occured.

Conclusion: A simple bedside placement protocol enables the positioning of postpyloric feeding tubes in adult ventilated critically ill patients. The inability to aspirate insufflated air from the tube confirmed the correct position in every case. This approach leads to a cost effective and early initiation of enteral feeding in the critical care setting without requiring extensive methods.

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P194 Peritoneal ventilation in volume controlled hemorrhagic shock: outcome model in rats

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Introduction: Peritoneal ventilation was studied few years ago [1,2] to be a successful auxiliary extrapulmonary method for improving oxygenation and CO_2 elimination in laboratory animals with experimental ARDS. Bowel ischemia during hemorrhagic shock is known to cause, after initial fluid resuscitation, late hazardous remote effects with multiple organ system failure and high mortality rate [3].

Hypothesis: In severe volume controlled hemorrhagic shock, peritoneal ventilation with oxygen would: 1) improve local oxygenation of the abdominal viscera, preventing later multiple organ failure, and 2) increase survival rate.

Methods: (Figure) The study included three groups (10 rats each), using light anesthesia (N_2O/O_2 and Halothane) during preparation and the first 120 min of the study. Group I = PEV-O_2 (Peritoneal ventilation with 100% oxygen), Group II = PEV-RA (PEV with room-air), Group III (control, no PEV). In groups I & II, a 14 F catheter was surgically introduced into the peritoneal cavity, before hemorrhagic shock (HS). *Phase I – HS:* All rats underwent blood withdrawal of 3 ml/100 g body weight within 15 min, causing HS lasting up to 60 min. Starting at 15 min, Group I & II were terated by peritoneal ventilation (oxygen vs. room-air), rate = 40/min, tidal volume = 6 ml, until the end of resuscitation phase. *Phase II - Resuscitation* - lasted 60 min (from 60 to 120 min), at the beginning of which 3–4 ml of blood transfusion increased MAP to >80 mmHg within 2–3 min. The rest of the blood was transfused over the next 15 min. *Phase III - observation* – lasted 7 days. Surviving rats were scarified (high dose halothane). Necropsy of abdominal organs was performed in all rats.

Results: *Survival* to 7 days was achieved by 10 of 10 rats in PEV-O_2 Group I, 9 of 10 in PEV-RA Group II, and 5 of 10 rats in the Control Group III. Survival rate in the PEV-O_2 group (100% survival) was significantly higher than that of the control group, but not significantly higher than that of the PEV-RA group. The survival rate of the PEV-RA group (90%) was not significantly higher than that of the control group (50%). *Morbidity* evaluation of all rats during the observation phase, as reflected by their daily neurological deficit scores, showed significant difference between all groups. *Necropsy* examination of the rats who died during the observation phase showed marked, diffuse pathology of abdominal organs, mainly gut perforations and necrosis. Necropsy of the rats who survived the 7 days of observation, showed marked macroscopic abnormalities in all survivors of the Control Group III, moderate changes in most of the rats of the PEV-RA Group II, and normal examination in all 10 rats of the PEV-O_2 Group I.

Conclusion: Peritoneal ventilation with oxygen during and after hemorrhagic shock, seems to help to preserve viability of the intestine and may significantly decrease morbidity and mortality.

Acknowledgement: The study was supported by the US Navy MRDC-ONR)

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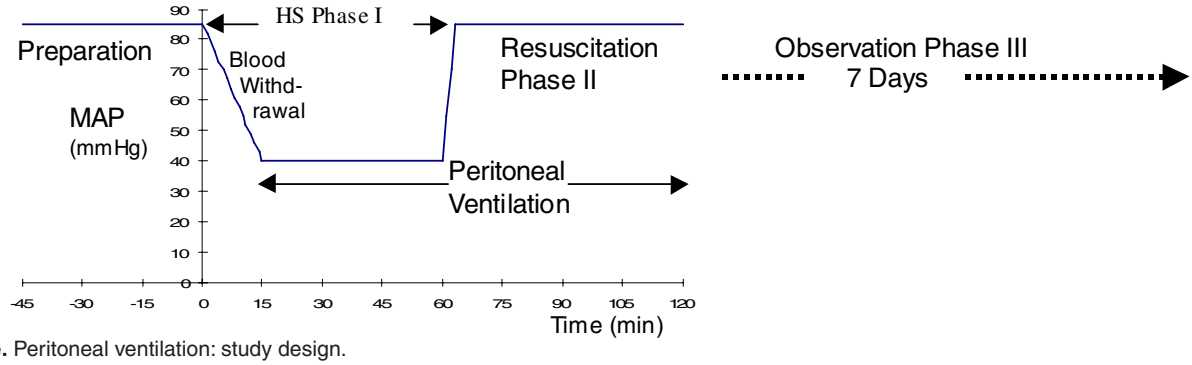

Figure. Peritoneal ventilation: study design.

P195 The Paracetamol Absorption Test (PAT): an obligatory addition to the enteral nutrition algorithm?

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Enteral nutrition (EN) is beneficial for critically ill patients. The simplest and most convenient way of providing EN is via a nasogastric (NG) tube. Feeding is often stopped because of increased

volumes of NG aspirate, thought to reflect inadequate intestinal function. However, this has been shown to be an unreliable indicator of gastric function. We assessed whether the PAT (absorption of paracetamol in the small intestine depends on the rate of gastric emptying) could provide more reliable information in patients with a large NG rest.

Methods: We studied 14 consecutive patients receiving continuous EN via NG tubes who had large gastric residues (>120 ml or 2× the hourly rate) on routine aspiration. EN was stopped and gastric emptying using the PAT was assessed immediately thereafter. The test was considered normal if the area under the concentration curve from 0–60 min (AUC_{60}) after giving 1 g of paracetamol through the NG tube was >600 mg/min/l. Results of the test were obtained within 4 h and EN was resumed in those patients with a normal result.

Results: See Table; expressed as median ± SD. EN was successfully restarted in all group 2 patients

Conclusions: This study showed that 6/14 patients (43%) with an abnormal NG aspirate had a normal PAT; these patients continued to receive EN without untoward effects. We suggest that the PAT be performed in all patients receiving EN with a large NG aspirate; if the test was normal, EN should be continued; if the test is abnormal, use of prokinetic agents should be considered.

	Total group	Group 1 (AUC_{60} <600)	Group 2 (AUC_{60} >600)	*P* value (Gp 1 versus 2)
Number	14	8	6	
AUC_{60} (ml/min/l)	314.25 ± 356.81	118.12 ± 123.14	711 ± 174.96	<0.001
NG aspirate (ml)	245 ± 247.11	350 ± 296.9	180 ± 55.50	0.109

P196 Enteral versus parenteral nutrition: no difference in the incidence of fungal infections in critically-ill patients on mechanical ventilation with selective digestive decontamination

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Background: Infections are an important cause of morbidity and mortality in patients in the intensive care units (ICUs). Fungal infections have increased substantially over recent years and fungi have become one of the important pathogens in intensive care patients. This study was undertaken to test the hypothesis that the incidence of fungal infections is lower in critically-ill patients under mechanical ventilation receiving enteral rather than parenteral nutrition.

Methods: By using a prospectively-built database, we analyzed retrospectively the charts of 110 critically-ill, intubated patients hospitalized in surgical and medical ICUs and receiving selective digestive decontamination (SDD). SDD is the prophylactic use of topical, nonabsorbable antibiotics to reduce the incidence of respiratory tract infections in critically-ill patients. It is known that this therapy significantly reduces the incidence, but not the mortality rate of pneumonia in ICU patients. In this study the SDD for all patients comprised of a PNV solution (polymyxin B, neomycin, vancomycin) at a dosage of 15 ml administered six times daily. Seventy-nine patients received enteral nutrition and 31 patients parenteral nutrition.

Those patients without contraindications, and expected to be intubated for more than 72 h, received enteral nutrition which was started within 24 h after intubation. Patients with contraindications for enteral nutrition received parenteral nutrition which was discontinued when the criteria for enteral nutrition were met. We compared the incidence of fungal infections in both subgroups of patients, i.e., enteral versus parenteral nutrition.

Results: The two subgroups were similar with regard to their APACHE II score, in age, sex distribution and comorbidities at the time of study entry. The rate of fungal infection was seen to be higher in the parenteral nutrition group, 5 out of 29, as compared to 7 out of 71 in the enteral nutrition group. However, this difference was not considered to be statistically significant.

Conclusion: No significant difference is observed between enteral vs. parenteral nutrition in the incidence of fungal infections in critically-ill patients receiving SDD.

P197 Hyperglycemia predispose to catheter-related sepsis in diabetic patients receiving Total Parenteral Nutrition

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Hyperglycemia is encountered during nutritional support in diabetics and in patients with stress-related glucose intolerance. Aim of this study is to determine the incidence of central venous catheter-related sepsis (CRS) and its relationship with the serum glucose levels in diabetic patients treated with Total Parenteral Nutrition (TPN).

Methods: Medical records of 123 surgical patients (median age 68.1 years) treated with TPN in our Department between 1/1/1990 and 31/12/1997 were reviewed. They received TPN for a median duration of 14.3 days (range 2–65) by the method of 'all-in-one'. Out of these, 27 patients were diabetics. Two units of regular insulin were added in the TPN-bag for each 20 g of glucose contained, in each diabetic patient. The nutrient admixture was volumetrically delivered over 24 h through a subclavian

vein catheter. The parameters measured were lenght of TPN therapy, serum glucose levels (measured every 6 h) during the nutritional support, and the incidence of CRS which was defined by local or systemic signs of sepsis, positive culture of the catheter tip, concurrent positive blood cultures and defervescence of the clinical signs of sepsis following catheter removal. Data analysis was done using the Fisher's exact test. Values $P < 0.05$ were considered statistically significant.

Results: There was no difference to the lenght of TPN therapy between diabetics and non diabetics. In 20 diabetics the serum glucose levels remained <200 mg/dl, and in 7 were constantly high (>200 mg/dl) in all measurements during TPN administration. Eleven out of the 96 non diabetics (11.4%) and 3 out of the 20 'euglycemic' diabetics (15%) presented CRS, but this difference was not significant ($P = 0.8$); however, CRS was presented in 5 out of the 7 diabetics whom serum glucose levels were >200 mg/dl during TPN therapy ($P = 0.01$).

Conclusion: The results of out study suggest that CRS is serious risk in diabetics receiving TPN if good control of glycemia is not maintained; in adverse, the incidence of CRS doesn't seem to be significantly increased in well-controlled diabetics.

P198 Dysregulation of glucose metabolism in enterally fed patients with acute pancreatitis

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Introduction: Dysregulation of glucose metabolism is one of Ranson's criteria for prognostic scoring in acute pancreatitis. Aim of this study was to evaluate the impact of gastric and jejunal access of enteral nutrition on glucose metabolism in patients with mild and severe acute pancreatitis.

Patients and methods: Eighty-two non-diabetic patients admitted to a medical ward for acute pancreatitis entered the study. All patients were treated with total parenteral nutrition, and subsequently with total enteral nutrition administered into the jejunum. The jejunal tube was placed into the stomach at the end of the study period. Glycaemia was monitored 48 h after onset of acute pancreatitis (G1), on the last day of jejunal nutrition (G2) and on day 2 of gastric nutrition (G3).

Results: In patients with mild acute pancreatitis ($n = 56$), G1 was above the normal range in 10 patients (17.9%), G2 in 2 patients (3.6%), and G3 in 3 patients (5.4%).

In patients with severe acute pancreatitis ($n = 26$), G1 was above the normal range in 22 patients (84.6%), G2 in 5 patients (19.2%), G3 in 5 patients (19.2%). Secondary diabetes mellitus was present in 3 patients of this group (11.5%). No significant difference of serum insulin levels was found between both groups.

Conclusion: Dysregulation of glucose metabolism in mild acute pancreatitis is transient and usually does not require therapeutic intervention. Hyperglycaemia in severe acute pancreatitis is clinically relevant and manifestation of secondary diabetes mellitus is frequent. Type of enteral nutrition does not represent a significant impact on glucose metabolism.

P199 Energy consumption rate of critically ill patients: a prognostic factor?

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Introduction: Energy consumption of critically ill patients is increased in relation to basic metabolic rate due to post aggression metabolism. The aim of the present study is to assess the effect of various energy consumption rates in critically ill patients referring to the outcome of these patients.

Materials and methods: 40 critically ill patients on a surgical intensive care unit were included in a prospective clinical trial (6 female and 34 male patients). The following criteria for these patients were fixed: mechanical ventilation for at least 3 days, clinical criteria of MODS or SIRS, APACHE-II-score >10, TISS-score >20, total parenteral nutrition for at least 6 days, FiO_2 >40%, informed consent. The basic metabolic rate was calculated daily (Harris-Benedict). Current metabolic rate was measured by indirect calorimetry using a Deltatrac II(Datex-Engström) in the respiratory mode. Data aquisition (oxygen consumption VO_2 and CO_2 production VCO_2) was performed in 6-h periods over average 5.7 days. Energy consumption was determinated by calculation of respiratory quotient. We compared the energy consumption rates with the patients outcome during the trial (14 days).

Results: 30 patients survived the first 14 days, 10 patients died due to multi organ failure. The mean calculated basal metabolic rate in the group of survivors was 1662 kcal/24 h, the measured energy consumption was 2109 kcal/24 h. The mean increase was 26.9% in relation to basal rate. Non-survivors had a basal rate of 1653 kcal/24 h, a measured rate of 2097 kcal/24 h. That is a mean increase of 25.4%. The increase in both groups was statistically not significant (t-test, $P < 0.05$). Energy consumption rates of critically ill patients show no significant differences between survivors and non-survivors during 2 weeks. Deviations of energy consumtion in these patients could not use as a prognostic factor.

P200 Alterations of metabolic and hemodynamic parameters during whole body hyperthermia on the ICU

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Introduction: Whole body hyperthermia (WBH) has received renewed interest for the treatment of metastatic cancer [1]. Using a radiant heat device for induction and maintenance of WBH has been shown to have little toxicity [2]. However, the acute cardiovascular and metabolic changes during the treatment are pronounced [3].

Methods: After informed consent, in 12 ASA II patients with metastatic malignant disease who were eligible for WBH hemodynamic, metabolic parameters, lactate and catecholamine plasma concentrations were studied over a 24 h period. The heating device was a RHS-7500, Enthermics Medical Systems, Inc., Menomonee Falls, WI, USA. Target temperature was 41.8°C, time at target was 60 min. Anaesthesia was total intravenous anaesthesia by TCI using propofol (4–6 µg/kg/min). Patients were intubated and mechanically ventilated with an FiO_2 of 0.4 after induction with sufentanil (0.3–0.4 µg/kg), propofol and rocuronium (0.8 mg/kg). Measurements were taken at baseline, during heating, at plateau, after reaching baseline temperature and at 24 h post plateau. Hemodynamic data consisted of HR, MAP, CVP, PAP, PCWP, CI, SVR. Metabolic data were obtained by indirect calorimetry (Puritan Bennett 7250 Metabolic Monitor, Puritan-Bennett-Hoyer GmbH, Bremen, Germany) and consisted of VO_2, VCO_2, RQ and energy expenditure (EE).

Results: During heating and plateau at 41.8°C an increase of cardiac index from baseline of up to 140% could be observed, which was due to a decrease of SVR and MAP. HR increased to 138 ± 27 bpm. CVP, PCWP and PAP did not change significantly. VO_2 increased from 176 ± 23 ml/min to 372 ± 62 ml/min, EE from 1232 ± 51 kcal/day to 2214 ± 62 kcal/day and VCO_2 from 156 ± 21 ml/min to 303± 33 ml/min. The values remained elevated after the patients had returned to baseline core temperature. Lactate plasma concentrations did not change significantly. Plasma levels of noradrenaline changed from 156 ± 140 µg/l after induction of anaesthesia to 699 ± 302 µg/l during plateau, adrenaline levels increased slightly from 40 ± 48 µg/l to 67 ± 64 µg/l. Arrhythmia, myocardial ischemia or left ventricular failure were not observed. Pulmonary and renal function remained undisturbed.

Discussion: During WBH, the changes of cardiovascular and metabolic parameters are severe but in our patients did not compromise cardiac, pulmonary or renal function. However, great care must be taken to exclude patients with cardiorespiratory pathology. Elevation of the body temperature to 41.8°C was accompanied by a fourfold rise in plasma noradrenaline, reflecting high sympathetic nerve activity. Plasma adrenaline remained almost unchanged during plateau. The pronounced heat-induced hypermetabolism and the endocrine response to heating were not abolished by general anaesthesia and were present throughout the observation period. Lactate levels did not rise significantly, suggesting that metabolism remained aerobic. To compensate for the massive loss of peripheral vasomotor tone, aggressive fluid replacement guided by invasive monitoring is recommended for management of patients undergoing WBH. Further studies will determine what type of anaesthetic management should be preferred.

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P201 GH and cortisol secretion in patients with burn on day 7 after thermal injury

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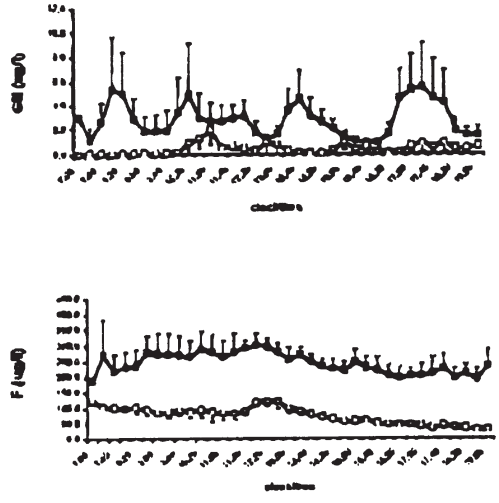
Objectives: Hormonal and nutritional changes occur in burns patients, in whom low IGF-I and high cortisol levels are commonly reported during the first 2 weeks after the burn event. However, conflicting data about GH secretion are still present. In fact, high GH levels have been reported by some but not by other authors. Aim of this study was to define growth hormone (GH) and cortisol (F) secretion during a 12-h period on day 7 after a major burn in man.

Methods: In 5 patients with major burn injury (BURN, age, mean ± SEM: 35.5 ± 5.4 years; BMI: 27.1 ± 2.3 kg/m²; burn area: 36.5 ± 5.5%; ROI score: 0.3 ± 0.1) serum GH and cortisol levels were evaluated every 20 min from 7.00 am to 7.00 pm on day 7 after burn unit (BU) admission, during parenteral and/or enteral nutrition and dopamine infusion (5–10 µg/kg/min). The same hormonal evaluation was performed in six normal fed adult subjects (NS, age: 30.2 ± 2.5 years; BMI: 22.3 ± 2.6 kg/m²). IGF-I levels were also evaluated at 7.00 am on day 7 after BU admission in BURN and basally in NS.



Results: On day 7 after BU admission, IGF-I levels in BURN were lower than in NS (90.5 ± 12.3 vs 210.6 ± 12.8 µg/l, $P < 0.05$). On the contrary, mean serum GH levels in BURN (solid circles) were higher than in NS (open circles) (mean GH levels: 2.8 ± 1.5 vs 0.4 ± 0.1 µg/l, $P < 0.001$; AUC: 85.7 ± 41.9 vs 21.7 ± 6.7 µg/l/h, $P < 0.001$). Particularly, GH secretion in BURN was normally pulsatile with elevated baseline GH levels. Also mean F levels BURN were elevated and higher than in NS (mean F levels: 241.7 ± 39.9 vs 84.4 ± 17.1 µg/l, $P < 0.001$; AUC: 15093.3 ± 3112.4 vs 5048.6 ± 1030.8 µg/l/h, $P < 0.001$), with high levels even in the late afternoon and loss of circadian rhythm.

Conclusion: Our data show that in burns patients on day 7 after BU admission, GH as well as cortisol secretion are markedly higher while IGF-I levels are clearly lower than in NS. These findings confirm the existence of peripheral GH resistance in critical illness together with adrenal axis hyperactivity. Peripheral GH resistance and hypercortisolism could likely contribute to impair recovery from the catabolic state in the early phase after thermal injury.

Acknowledgement: This study has been supported by Fondazione Piemontese per gli Studi e le Ricerche sulle Ustioni and Fondazione SMEM, Italy

P202 Magnetic stimulation of the phrenic nerves to assess diaphragm strength on the Intensive Care Unit

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Traditional methods of assessing respiratory muscle strength in the critically ill rely on some degree of co-operation from the patient, and are of limited use. We performed bilateral magnetic stimulation of the phrenic nerves, using two 43 mm magnetic coils placed anteriorly on the neck [1]. The transdiaphragmatic pressure change (TwPdi) was recorded using oesophageal and gastric balloon catheters in the conventional manner. Twitch endotracheal tube pressure (TwPett) was also recorded, which reflects twitch oesophageal pressure (TwPoes). The pressure readings, Poes, Pgas and Pett were displayed and recorded on a computer together with the calculated value for Pdi (Pgas–Poes).

Twenty critically ill patients were studied (12 male, eight female), with a mean age of 59 years. Average length of ICU stay prior to the study was 27 days. The mean TwPdi was 9.5 cmH_2O (range 1.0–29.3), mean TwPocs was 6.6 cmH_2O (range 0.5–22.9), and mean TwPett was 70 cmH_2O (range 0.0–26.3). The mean difference between TwPett and TwPoes was 0.4 cmH_2O, and the correlation of the means of TwPett to TwPoes was 0.93.

Diaphragm contractility can be assessed in the sedated ICU patient, by magnetic stimulation of the phrenic nerves. This technique is non-volitional and is reasonably well tolerated. Our data shows that diaphragm conctractility in the critically ill patient is considerably less than in the laboratory based control subject [1]. Also, we report a good correlation between TwPoes and TwPett, leading to the possibility of further simplification of the technique.

Acknowledgement: Funded by the Wellcome Trust

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P203 Assessment of adductor pollicis muscle function in critically ill patients

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Skeletal muscle wasting is a recognised finding in the critically ill, but few data exist concerning the strength of peripheral skeletal muscles in patients on the Intensive Care Unit (ICU). This may be because previously available techniques involved measurement of force during a maximal voluntary contraction (MVC) and on ICU this type of test may be unreliable since it is effort dependent. We therefore used a novel, non-volitional technique, supramaximal magnetic stimulation of the ulnar nerve (Harris *et al.*: *AJRCCM* 1998, **157**:A359), to measure adductor pollicis twitch tension (Tw AP) in 14 patients (10M 4F), mean age 44 (range 24–73) years, with a range of diagnoses. Severity of illness was scored within 24 h of admission to ICU and median (95% CI) Apache II score was 19.5 (14–28). Median length of stay (95% CI) (at the time of testing) was 11 (5–17) days. Fourteen healthy volunteers (10M 4F) mean age 44 (21–78) years, served as controls. Median (95% CI) Tw AP in the patients was 3.6 (23–5.9) N and in the controls 7.9 (5.3–9.9) N ($P < 0.01$, Mann Whitney U Test). Our data show that patients with critical illness are weaker than ambulant controls. The reasons for the observed differences in strength are likely to be multifactorial; further studies are therefore warranted to elucidate the specific causes of this weakness and the relationship between skeletal muscle weakness and failure to wean from mechanical ventilation.

Acknowledgement: NHS Executive Grant No RDF 028

P204 Skeletal muscle strength in critically ill patients

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Crit Care 1999, **3 (suppl 1)**:P204

Measurement of peripheral muscle strength in the Intensive Care Unit (ICU) has been seldom documented. The purpose of the study was to determine whether quadriceps twitch tension (Tw Q) could be measured in a range of critically ill patients in the ICU using a novel non-volitional technique, supramaximal magnetic stimulation of the femoral nerve (Polkey *et al.*: *Muscle Nerve* 1996,

19:549-555) and to determine the magnitude of weakness. Measurements were made in 20 patients (12M 8F), mean age 59 (range 24–81) years, with varying diagnoses. Median (95% CI) length of stay (at the time of testing) was 18 (7–29) days. 20 healthy elderly volunteers (12M 8F), mean age 59 (range 25–80) served as controls. Median (95% CI) Tw Q in the patients was 3.5 (2.6–5) kg compared with 9.5 (7.8–11.7) kg in controls ($P < 0.01$, Mann Whitney U Test) and weakness was not correlated with length of ICU stay. The data demonstrate that profound quadriceps weakness can occur in critically ill patients. This weakness may influence mobilisation and rehabilitation. It is likely that other skeletal muscles are similarly affected, including the muscles of respiration. If so, this would in part, determine weaning outcome.

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P205 Ultrasonographic quantification of muscular mass thickness in patients of intensive care unit

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Purpose: The aim of this study is to assess the degree of change of upper-arm skeletal muscle thickness in patients of Intensive Care Unit (ICU) and to propose a new method for quantifying this change.

Methods: The thickness of upper-arm biceps was measured twice in 16 female patients (mean age 61.63 ± 8 years) and in 27 male patients (mean age 50.7 ± 9 years) during an ultrasonographic scan by the same ultrasonographer. A 10 MHz frequency, linear high resolution transducer was held longitudinal to the biceps muscle in the place of maximum thickness. All subjects were patients of ICU (13 with multi trauma, 4 with brain injuries, 11 with cerebral sroke, 8 with respiratory insufficiency, 3 with tetraparesis C3–C4 fracture, 3 with hypoxemic engephalopathy and 1 with septic shock) hospitalized for 18.88 ± 3 days. Throughout hospitalization all patients were in parenteral nutritional support with 1800–2400 Kcal/day intake and were also under physical therapy for 60 min/day. Creatine phosphokinase (CPK), Aldolase (Ald) and Albumin (Alb) levels were recorded twice. First measurement was done when patients entered the study and second when they left ICU. Ultrasonographic scans were performed at the same periods of time. Ten of our patients were not under muscle relaxant or drug depression muscle treatment, meanwhile all the others were under muscle relaxant treatment for 4 ± 2 days and under drug depression muscle treatment for 7 ± 3 days.

Results: During the period of our study CPK levels decreased from 2301.26 U/l (mean value, with maximum level 20 000 U/l and minimum level 20 U/l) to 251.21 U/l (mean value, with maximum level 850 U/l and minimum level 30 U/l), Ald levels decreased from 10.39 U/l (mean value, with maximum level 21.15 U/l and minimum level 3.5 U/l) to 7.59 U/l (mean value, with maximum level 18.6 U/l and minimum level 3 U/l), Alb levels decreased from 33.07 g/l (mean value, with maximum level 41.15 g/l and minimum level 26 g/l) to 29.56 g/l (mean value, with maximum level 35 g/l and minimum level 24 g/l). Fifteen patients showed an increase of 2.714 g/l of the Albumin levels and 28 other patients showed a decrease of 7 g/l of the Albumin levels. Muscle thickness decreased from 2.51 cm (mean value, with maximum level 3.75 cm and minimum level 1.48 cm) to 2 cm (mean value, with maximum level 2.19 cm and minimum level 1.19 cm)

Conclusion: We conclude that long term ICU hospitalization is associated with a gradual decline (0.03 cm/day) in muscular mass. This decline is not CPK, Ald, Alb or physical therapy-dependent.

P206 The influence of aldosterone and angiotensin II on the diuretic effects of atrial natriuretic peptide in the isolated perfused rat kidney

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Background: The diuretic effects of atrial natriuretic peptide (ANP-99-126) are reduced in patients with advanced cirrhosis of the liver and severe myocardial dysfunction. These patients also often display an increased acitivity of the renin–angiotensin–aldosterone system (RAAS) resulting in high plasma concentrations of aldosterone (ALD) and angiotensin II (AII).

Objective: To study the effects of ANP in isolated perfused rat kidneys after pretreatment with AII or ALD to determine which hormone causes ANP unresponsiveness in this setting.

Materials and methods: Three groups of kidneys were perfused for 3 h with a constant perfusion pressure of 100 mmHg.: a control group ($n = 5$), a AII/ANP group ($n = 6$; 0.1 nmol/l AII in the second hour; 3.25 nmol/l hANP in the third hour) and an ALD/ANP group ($n = 4$; 27.7 nmol/l ALD in the second hour; 3.25 nmol/l hANP in the third hour). We determined urine flow (VU), urinary excretion of sodium ($V_{Na}U$) and potassium (V_KU), inulin-clearance (GFR) and renal vascular resistance RVR.

Results: *AII/ANP group*: treatment with AII decreased VU, $V_{Na}U$,V_KU and GFR and increased RVR. ANP restored renal function to control levels ($V_{Na}U$, V_KU, GFR) or above (VU, RVR). *ALD/ANP group*: treatment with ALD induced an increase of V_KU. Subsequent treatment with ANP further increased V_KU and slightly decreased RVR. No effects on GFR, VU or $V_{Na}U$ were observed.

Conclusion: Our findings suggest that blunted ANP effects during increased RAAS-activity are mainly determined by ALD. Interestingly, this is not only due to a blunted increase of sodium excretion (tubular mechanism) but also due to a blunted increase of glomerular filtration rate (altered glomerular vascular reactivity).

P207 Urinary excretion of urodilatin is increased during pressure natriuresis in the isolated perfused rat kidney

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Background: Treatment with urodilatin (URO; ANP-95-126), a kidney derived natriuretic peptide, may be beneficial in patients with incipient acute renal failure after cardiac surgery [1]. The findings about mechanisms regulating endogenous production and renal excretion of URO are controversial. Recent evidence suggests that urinary excretion of urodilatin ($V_{URO}U$) is increased in patients after uncomplicated cardiac surgery and positively correlated with blood pressure [2].

Objective: To determine the effects of different perfusion pressures on urine flow (VU), urinary excretion of sodium ($V_{Na}U$), potassium (V_KU) and urodilatin ($V_{URO}U$) and the concentration of urodilatin in the perfusate (P_{URO}) in isolated perfused rat kidneys.

Materials and methods: Kidneys from Sprague-Dawley rats were perfused for 180 min with constant perfusion pressures (80 mmHg ($n = 4$); 120 mmHg ($n = 4$)) in a closed circuit system. Samples were taken every 30 min. The concentration of urodilatin in urine and perfusate were determined by a radioimmuno-assay for rat-urodilatin (rURO: Immundiagnostik, Bensheim, Germany) not cross-reacting with rBNP, rCNP,rCDD/ANP-99-126 or hURO.

Results: Mean VU, $V_{Na}U$, V_KU and $V_{URO}U$ were significantly higher with a perfusion pressure of 120 mmHg than with 80 mmHg (all: $P < 0.05$); P_{URO} did not change significantly.

Conclusion: Our data suggest that renal perfusion pressure and consequently mean arterial blood pressure are determinants of $V_{URO}U$. Additionally, our data underline the importance of perfusion pressure for adequate renal function; this may be especially relevant for patients at risk to develop acute renal failure after cardiac surgery.

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P208 Urine output in the first twelve hours after cardiopulmonary bypass does not predict the development of renal impairment

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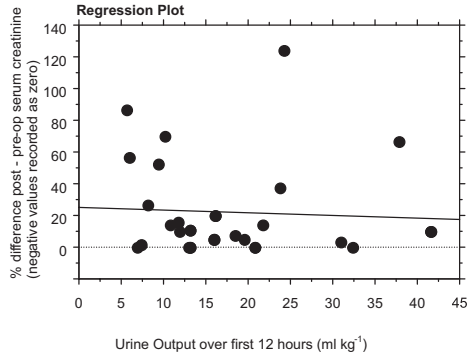
Hourly urine output is one of the foremost indices which are monitored in patients who have undergone cardiac surgery. Traditionally, a urine output of less than 0.5 ml/kg/h triggers intervention [1]. However, renal failure may supervene in patients who have seemingly adequate renal function according to conventional monitoring. In this pilot study we analysed urine output and alterations in serum creatinine in 31 consecutive patients in the first 12 h following coronary artery bypass and valvular surgery. We found that an 'adequate' urine output alone is an unreliable predictor of subsequent renal impairment (indicated by a rise in 24 h post-operative serum creatinine by more than 50%). Six patients demonstrated such a rise in serum creatinine despite their producing urine outputs of greater than or equal to an average of 0.5 ml/kg/h. Of these, five subsequently required renal replacement therapy. This finding may have implications for the monitoring of cardiac patients who return to low-dependency patient care areas within 12 h of surgery.



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P209 Homeostatic indications for the administration of diuretics

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The authors monitored the effects of the different diuretics upon the natrium and water homeostasis and acid–base balance. The aim of the study was to clarify the exact mechanisms of their action and possible ways of monitoring of their homeostatic effects. The effects of furosemide (18 patients), hydrochlorothiazide (eight patients), spironolactone (14 patients), acetazolamide (10 patients), amiloride (four patients) and manitol (eight patients) were monitored in critically ill patients using computer pro-

gramme utilizing 17 routinely monitored input values and calculating creatinine clearance, tubular resorbtion , excretion fractions of sodium, potassium, water and osmotically active substances, clearance of the osmotically active substances, clearance of solute free water, electrolyte clearance, electrolyte free water clearance, urine outputs of sodium, potassium and urea, urea concentration index and serum and urine anion gaps. The development of parameters typical for each diuretic was evaluated using Student's *t*-test comparing the values before and during the treatment with the agent.

Main results: The natriuresis caused by furosemide is less important than the disturbing of the kidney concentrating ability. It is indicated in hyponatremia. Any of the evaluated parameters except serum potassium levels were not typical for the treatment with spironolactone. Hydrochlorothiazide reduces adverse effects of furosemide upon the kidney concentrating ability. It is useful in hypernatremia especially in the secondary nephrogenic diabetes insipidus and it is indicated in the secondary renal tubular acidosis. Amiloride was proved as the ideal therapy of chloride resistant metabolic alkalosis and hypokalemia. In comparison to acetazolamide it is potassium sparing drug and it seems to be less natriuretic. The indication for the use of acetazolamide is metabolic acidosis with the need for quick correction. Hyponatremia and hypoosmolality were not proven as the homeostatic indications for manitol.

P210 The effect of intraoperative Lasix on sodium excretion following cardiac surgery

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Objective: To determine the effect of intra-operative Lasix on sodium excretion (NaEx) in children following cardiac surgery after cardiopulmonary bypass (CPB).

Methods: Thirty-six children (median age 5.9 months, range 0.06–182 months) underwent corrective cardiac surgery for congenital heart disease (CHD). The patients were divided into two groups, Group A ($n = 12$) received 1 mg/kg of intravenous Lasix at the end of the surgical operation, Group B did not receive Lasix and acted as the control group. Urine samples were collected over the 1st (t = 0) and 16th (t = 16) postoperative hour and sent with paired blood samples for electrolyte measurements. Sodium excretion (NaEx) and urine volume (ml/kg/h) was compared between the two groups at t = 0 and t = 16 using the Mann-Whitney test. NaEx was calculated by multiplying urine volume by urine Na concentration and expressed as mmoles/kg/h.

Results: There were no significant differences in age, weight, preoperative renal function, CPB times or underlying heart disease (cyanotic vs acynotic) between the two groups.

NaEx and urine volume were significantly greater at t = 0 in the group that received Lasix ($P = 0.013$ and $P = 0.001$ respectively). These differences were no longer present at the 16th postoperative hour ($P = 0.67$ and $P = 0.38$ respectively). In both groups sodium excretion correlated with urine volume ($r = 0.98$).

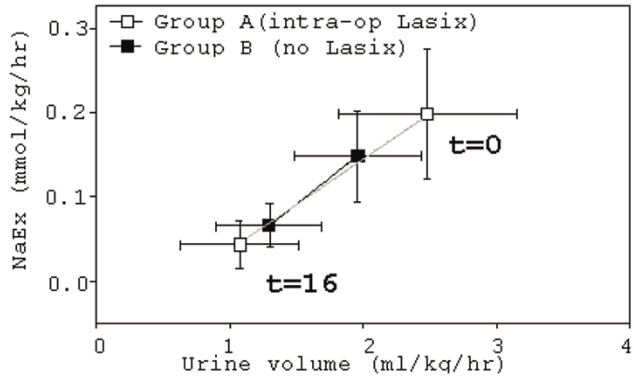

Figure. NaEx plotted against urine volume at t = 0 and t = 16. Blocks indicate median values, whiskers indicate 95%CI.

Conclusion: Although intraoperative Lasix transiently increases sodium excretion and therefore urine volumes in the immediate post operative period it does not appear to offer any advantage by the 16th postoperative hour, a time when renal water and sodium conservation is maximal.

P211 Treatment and prognosis of patients with nontraumatic rhabdomyolysis

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Introduction: Nontraumatic rhabdomyolysis is not frequent in an internal-neurological ICU and there are few reports of aetiology, clinical course, therapy and outcome of patients with severe rhabdomyolysis. We analyzed our patients with nontraumatic rhabdomyolysis to evaluate therapeutic strategies and prognostic parameters.

Methods: In a retrospective study we analyzed the hospital reports of patients with nontraumatic rhabdomyolysis admitted to our internal-neurological ICU during a 12-year period (1986–1997).

Results: Thirty-four patients were admitted during the study period (incidence 1: 416). The average age of the patients was 35.2 years (27 male, 7 female patients). The most frequent causes for nontraumatic rhabdomyolysis were drug intoxication (35.3%), strenuous exercise (26.5%), infections (17.6%) and seizures (11.7%). The average level of creatine phosphokinase (CK) was 16234 U/l. All patients were treated by intravenous fluids for volume repletion and by alkalinization of the urine, dialysis was required in six patients (17.6%) for control of uremic symptoms. Seven patients (20.5%) were treated by plasma exchange to reduce rapidly excessive CK-levels in order to prevent acute renal failure. Two patients died in septic MOF after drug-induced rhabdomyolysis and delayed hospital admission (mortality 5.9%). After

ICU-stay three patients showed peripheroneural lesions, all other patients (85.3%) recovered without sequelae.

Conclusion: Nontraumatic rhabdomyolysis has a good prognosis if the patients are admitted early to the hospital for treatment. Plasma exchange seems to be an effective therapy to prevent acute renal failure. Septic MOF after rhabdomyolysis has a poor prognosis.

P212 High-volume continuous veno-venous haemofiltration in hyper-acute liver failure: a pilot study

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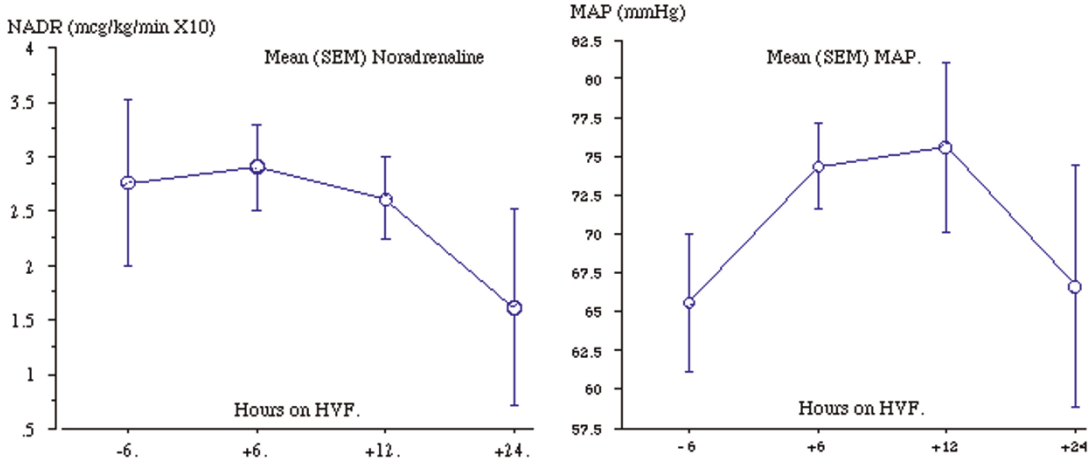
Background: Once defined clinical criteria are fulfilled in hyper-acute liver failure (ALF) mortality without liver transplantation (OLT) approaches 90%. Patients' clinical condition may deteriorate whilst awaiting a graft, such that transplantation becomes impossible due to the rapid progression of multiple organ failure. There is need for therapies that may stabilise the patient and thus provide a 'bridge to transplantation'. Animal studies suggest that high-volume continuous veno-venous haemofiltration (HVF) in septic shock is associated with improvements in haemodynamic stability and a reduction in the requirement for vasopressor support. We report findings of a pilot study of HVF in patients with ALF.

Patients and methods: Eight patients fulfilling transplantation criteria with acetaminophen induced ALF were studied. Median age was 28 years (range 19–51), INR 4.6 (1.9–15), pH 7.23 (7.1–7.42), lactate 9.4 mmol/l (6.7–17) and APACHE II 24 (22–34). Six patients (75%) were receiving vasopressor support with noradrenaline at 0.29 µg/kg/min (0.03–0.5) and all were in anuric renal failure. Five patients were already established on conventional veno-venous filtration. HVF (Baxter system) was commenced 2 days (1–4) after admission using buffer-free dialysate at 4000 ml/h (3500-6000) with concurrent $NaHCO_3$ infusion and filter surface area 1.25 m^2 for a median of 34 h (22–72).

Results: HVF resulted in a rapid correction of pH and significant reductions in both serum lactate and base deficit within 24 h. Mean arterial pressure was increased after 6 and 12 h of HVF ($P < 0.13$) without corresponding increases in vasopressor support (Figure). After 24 h of HVF four (50%) patients required noradrenaline at 1.45 µg/kg/min (0.025–0.4). Two patients underwent OLT and survived, and 1 patient survived without transplantation.

Conclusions: HVF effectively corrects acidosis in patients with ALF and is associated with improvements in haemodynamic stability. Its use in the support of patients awaiting transplantation deserves further investigation.



P213 Continuous hemodiafiltration with bicarbonate- and lactate-buffered replacement fluids in septic shock

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Introduction. Acid–base imbalances are an important aspect while using continuous renal replacement techniques in critically ill patients. The quality of replacement fluid needs to be considered regarding to the acid–base requirements especially in septic patients. Commonly used replacement fluids contain lactate as buffer. Whereas lactate has to enter the Cori- or Citrate-Cycle to become effective as a buffer, bicarbonate can act immediately. The metabolism of lactate in addition is depending on the impaired liver function of patients with septic shock and represents an oxygen consuming process.

Methods: We investigated the metabolic effects of lactate- and bicarbonate-buffered hemofiltration substitution fluids in a clinical follow-up design in 13 patients (mean age 67 ± 9 years [± SD]) with acute renal failure during septic shock. All patients received continous veno-venous hemodiafiltration (*CVVHDF, Prisma® Hospal*). Seven patients have been treated with bicarbonate- (*Schiwa Combi-Pac®, Schiwa*) and 6 patients with conventional lactate-buffered

replacement fluid (*Biosol®, Hospal*). We evaluated individual course of pH, HCO_3^-, BE and lactate levels within the first 5 days after start of CVVHDF by linear regression analysis (*Excel® regression-procedure*). The slopes of the regression equations for bicarbonate- and lactate-buffered hemodiafiltration were compared by *t*-test (*SPSS®*).

Results: The use of bicarbonate replacement fluids for CVVHDF leads to a significant improvement of acid-base balance in the course of acute renal failure in septic shock. Linear regression equations for bicarbonate- and lactate CVVHDF are shown in the folllowing table (mean ± SEM):

Discussion: Lactate buffered CVVHDF leads to the removal of large amounts of endogenous bicarbonate per day (600–1.000 mmol). Its impact on the acid–base balance in septic shock is considerable. The approach with bicarbonate replacement flluid for the treatment of acute renal failure in septic shock seems to be advantageous to normalize an impaired acid–base balance.

	Bicarbonate-buffered ($n=7$)	Lactate-buffered ($n=6$)	P
pH	$Y = [0.039 \pm 0.002] \times X + [7.254 \pm 0.006]$	$Y = [-0.004 \pm 0.001] \times X + [7.431 \pm 0.005]$	<0.05
HCO_3^-	$Y = [1.369 \pm 0.035] \times X + [18.627 \pm 0.177]$	$Y = [0.585 \pm 0.032] \times X + [26.658 \pm 0.107]$	<0.05
BE	$Y = [1.951 \pm 0.025] \times X + [-8.129 \pm 0.084]$	$Y = [0.012 \pm 0.051] \times X + [4.399 \pm 0.168]$	<0.05
Lactate	$Y = [0.354 \pm 0.074] \times X + [4.800 \pm 0.245]$	$Y = [0.202 \pm 0.008] \times X + [3.940 \pm 0.025]$	n.s.

P214 Changes in C-type natriuretic peptide (CNP) levels in the plasma and cerebrospinal fluid of the patients with subarachnoid hemorrhage

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Objectives: This study was conducted to clarify the role of C-type natriuretic peptide (CNP) in the plasma and cerebrospinal fluid (CSF) in patients with subarachnoid hemorrhage (SAH).

Subjects and methods: The subjects were 10 patients with subarachnoid hemorrhage, who were admitted to our ICU, and received clipping operation within 48 h after the disease onset. Patients who had heart or renal diseases were excluded from this study. CNP levels in the plasma and CSF were measured at 6.00 on days 1, 3, and 7 of hospital admission by radioimmunoassay (RIA). As a control, CNP levels in CSF were measured in patients who received spinal anesthesia for orthopedic surgery. Differences between the measured levels on Day 1 and that on Day 3 or Day 7 were analyzed with Student's *t* test, and values less than 0.05 were considered statistically significant.

Results: Plasma CNP levels in the subject and control patients were within normal range, and there were no significant group differences. Mean CNP levels ± SD in the CSF was 13.1 ± 2.4 pg/ml in the controls and 15.5 ± 2.8 pg/ml on Day 1 in the subjects and there were also no significant group differences. However, CNP levels in the CSF of our subjects was significantly different between Day 1 (15.5 ± 2.8) and Day 7 (10.6 ± 3.6) ($P < 0.05$).

Discussion: CNP levels is known to be highest in the brain, and that is thought to regulate the local cerebral blood flow, because some studies demonstrated that CNP induced relaxation of cerebral arterioles through cGMP in rat brain. Our findings show that CNP in the CSF acts as an inhibitor of vasospasm on Day 1, and 3 because CNP levels in the CSF decreased significantly on Day 7.

Conclusion: Any specific role of CNP was not indicated from our findings, but we presume that CNP in the CSF could function as a vasodilator when vasospasm occurs in the brain.

P215 Prevention of infective complications of penetrating injuries to the head

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Infective complications often occur after craniocerebral wounds caused by explosive fragments. These dangerous sequelae are, in our experience, the chief cause of delayed death after injury. Initial contamination. The presence of retained bone and metal fragments acting as a nidus for micro growth,and disturbances in cerebrospinal fluid (CSF) circulation, especially when the ventricular system is involved, are challenging problems in the management of missile wounds of the brain. The analysis covers 53 penetrating craniocerebral wounds, treated in ZhuHai and ZhoungShan in the period from 1988 to 1996. In 35 cases the head injuries were produced by explosive fragments and in the remaining 18 cases by low-velocity bullets. We have analysed the significance of these factors in cases undergoing operation within 24 h, the incidence of infection was 12.6%. Rising to 29.3%when delay in execess of 72 h after injury was unavoidable. We formed the opinion that the risk of infection was not significantly increased by failure to remove small inaccessible bone chips. The most formidable complication was CSF leakage which often resulted in infections of the central nervous system. This implies that successfully addressing the risk of infection is, potentially, the most powerful method of improving outcome from penetrating injuries to injuries to brain.

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P216 Should endovascular therapy for cerebral vasospasm coincide with hypervolemic-hypertensive therapy (HT) in aneurysmal subarachnoid hemorrhage (SAH)?

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Crit Care 1999, **3 (suppl 1)**:P216

Introduction: In patients suffering from SAH, cerebral vasospasm is a major cause of morbidity and mortality from multifocal cerebral infarction. Hypervolemic-hypertensive therapy is considered the cornerstone of the medical management and generally the first line approach. The therapeutic role of intra-arterial infusion of papaverine and balloon angioplasty has been established as an alternative therapy. The timing of neuroradiological intervention is unknown.

Methods: We retrospectively analyzed the charts of 537 patients with SAH, admitted in our institution between January 1987–December 1997. Of those, 156 (29%) received HT therapy, for clinically neurologic deficits attributable to cerebral vasospasm, after surgical aneurysm repair. Symptomatic vasospasm was defined as decrease in the level of consciousness or the appearance of new focal neurologic signs. Clinical and angiographic improvement, after HT alone, or in combination with neuroradiological intervention was studied.

Results: Of the 156 patients, 92 (58%) showed neurologic improvement with HT alone. Of the remaining 64 patients (42%), 37 (57%) underwent intra-arterial papaverine infusion and/or balloon angioplasty, as an adjunct treatment, after failure of medical therapy. 30 patients (81%) improved clinically, whereas 34 patients (89%) had angiographic amelioration alone. Twenty-seven patients (17%) failed medical therapy but did not receive intervention due to early death.

Conclusion: Our results indicate that endovascular therapy for symptomatic vasospasm contributes to significant clinical improvement. Medical therapy fails in almost half of the patients, of which a large proportion can additionally benefit from neuroradiological intervention. These results underscore the need for future studies on timing of both therapeutic modalities for cerebral vasospasm.

P217 Application of near infrared spectroscopy in the ICU for follow-up of patients with subdural haematomas

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Background: Secondary haemorrhage is an important cause of brain injury following initial therapy of subdural haematoma (SDH). Early identification and treatment of secondary haemorrhage improve neurologic outcome. Nearinfrared light at a wavelength of 760 nm shows a high absorption for haemoglobin. In a previous study we were able to show the potential of Near Infrared Spectroscopy (NIRS) as a noninvasive tool to detect intracranial haemorrhage. Aim of our study was to analyse the capabilities of NIRS for follow-up of SDH patients.

Methods: We prospectively studied 21 patients with the CT diagnosis of SDH using NIRS (RunMan™, NIM Inc.). The difference in absorbance of light (ΔOD) at a wavelength of 760 nm between both hemispheres was measured at three different measuring points. The first measurement was performed upon hospital admission. Measurements were repeated on day 1, 2, 3 and at discharge. Additional measurements were performed in case the patients' neurological conditions had changed.

Results: 17 patients showed unilateral SDH at admission, 16 of these were correctly identified by NIRS; four patients showed bilateral SDH at admission. All patients received neurosurgical treatment. At day 1 after surgery NIRS measurements identified 3 patients with complete drainage of the haematoma, 4 patients were identified at day 2 and 5 patients were identified at day three. At discharge there were no pathologic NIRS findings in 13 patients, indicating the complete resorption of the haematoma. CT scans at discharge proved these findings. In 8 patients we found pathologic NIRS values at discharge, indicating an incomplete resorption of the haematomas. CT scans prior to discharge demonstrated residual SDH in all of these 8 patients.

Conclusion: Our results showed that repeated NIRS measurements in patients with SDH help to document the clinical course after surgical treatment. As a non-invasive, easily transportable diagnostic device, the RunMan™ helps to avoid time delay in diagnosis of secondary haemorrhage and facilitate early treatment, thus possibly saving time and reducing secondary injury as well as treatment costs.

P218 Correlation of transcranial doppler (TCD) parameters with intracranial pressure (ICP)

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Crit Care 1999, **3 (suppl 1)**:P218

Introduction: Intracranial Pressure (ICP) is an important factor in providing adequate cerebral blood flow and oxygen delivery to the brain. The use of ICP monitoring techniques has a lot of surgical risk factors, it is expensive, and is not readily available. On the other hand, transcranial doppler ultrasonography (TCD), is a non invasive bedside technique, which measures the velocities of the great cerebral arteries and may detect cerebral ischemia. The aim of our study was to test the hypothesis that, in head trauma patients, a correlation exists between ICP and TCD findings.

Methods: 59 patients (37 ± 19 years) with severe head trauma (Glasgow coma scale below 8) were included in our study. We assessed ICP and jugular bulb venous oxygen saturation ($SjvO_2$). All patients were under mechanical ventilation and ICP measurements were carried out using an intracerebral or intraventricular catheter. Intracerebral hypertension management was based on CPP and $SjvO_2$ findings. During the first three crucial ICU days, multiple TCD examinations (total 108) were performed. Simultaneous measurements of ICP, CPP, $SjvO_2$, as well as TCD values were recorded. The TCD parameters used were: Maximum velocity (Vmax), minimum velocity (Vmin), time average mean velocity (tamV), and pulsatility index (PI). [PI =(Vmax–Vmin)/tamV]. The findings obtained from TCD were compared with ICP using the multiple regression analysis method.

Results: In our study, the best correlation was demonstrated between ICP and the PI index as well as Vmin. The correlation of PI with ICP was exponential ($P = 0.028$), while the correlation of Vmin with CPP was a linear regression ($P = 0.022$). Using the multiple regression method, the elevation of ICP was demonstrated by the PI index in only 10 per cent ($R^2 = 0.10934$). With this same method, Vmin was unable to provide more information.

Conclusion: Pulsatility index (PI) can predict the elevation of ICP. However, this is not applicable in all cases. At a prior study [1], we found that the reduction of CPP was demonstrated by the PI index in 50% ($R^2 = 0.50$) and we suggested that this was due to factors which can influence the pulsatile arterial waveform (impaired vascular contractility, tachycardia, etc.). At this study we found that the elevation of ICP is demonstrated by the PI index in only 10% ($R^2 = 0.10$). We suggest that this is due to the suppression of the cerebral autoregulation at head trauma patients.

Reference

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P219 Transcranial Doppler sonography and cerebrovascular CO_2-reactivity during whole body hyperthermia

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Introduction: Disturbance of neurologic function is common in heat stroke patients. Loss of thermoregulatory response is associated with high mortality due to progressive brain edema. However, during whole body hyperthermia (WBH) for the treatment of metastatic cancer temperatures of above 41.8°C are intentionally applied [1]. Monitoring cerebral blood flow velocity therefore is a non-invasive method that may be useful in the detection of acute and potentially harmful alterations of the cerebral circulation.

Methods: After informed consent, in 10 ASA II patients with metastatic malignant disease who were eligible for WBH mean blood flow velocity (Vm) of the M1-segment of the middle cerebral artery was studied using a 2 MHz pulsed TCD device (TC 2–64, EME) with the probe fixed to the temporal window. The heating device was a RHS-7500 (Enthermics Medical Systems, USA). Target temperature was 41.8°C, time at target was 60 min. Anaesthesia was total intravenous anaesthesia by TCI using propofol (4–6 μg/kg/min). Patients were intubated and ventilated with an FiO_2 of 0.4 after induction with sufentanil (0.3–0.4 μg/kg), propofol and rocuronium (0.8 mg/kg). After induction of anaesthesia, three sequential measurements for Vm and Gosling's pulsatility index (PI) (systolic-diastolic/mean blood flow velocity) were taken during normo- and hypercapnia at baseline and at plateau and were averaged for each point of measurement. A two channel EEG was continuously recorded above the prefrontal cortex (Aspect Monitor A1000, Aspect Medical Systems). EEG data were processed online to yield bispectral index (BIS) values throughout the course of anaesthesia.

Results: During baseline, Vm at normocapnia ($PaCO_2$ 40.1 ± 0.99 mmHg) was 39.26 ± 11.81 cm/s. At hypercapnia ($PaCO_2$ 47.4 ± 2.08 mmHg), Vm was 55 ± 20.84 cm/s. CO_2 reactivity ($\Delta Vm/\Delta PaCO_2$) was 2.39 ± 0.9 cm/s/mmHg. During hyperthermia, Vm at normocapnia was 54.07 ± 21.19 cm/s, and almost doubled to 106.07 ± 40.43 cm/s at hypercapnia. CO_2 reactivity increased to 6.11 cm/s/mmHg. The PI under normocapnia significantly increased from 1.05 ± 0.2 (normothermia) to 1.49 ± 0.3 (hyperthermia). BIS readings remained below 35 during anaesthesia. During heating and plateau at 41.8°C an increase of cardiac index from baseline of up to 140% could be observed, which was due to a significant decrease of SVR and MAP. HR increased to 138± 27 bpm. None of the patients showed general or focal signs of CNS toxicity at 24 h after the treatment.

Discussion: During WBH under general anaesthesia a profound increase of cerebral blood flow velocity can be observed. This is partially due to the changes of systemic hemodynamic parameters, especially to increases of heart rate and cardiac index and to the decrease of MAP [2]. EEG data suggest that the observed effect is of primarily vascular origin and not due to increased CMRO2, although cerebral metabolism was not measured. Under WBH cerebrovascular reactivity was preserved and showed a marked positive dependency on baseline flow, as described previously [3]. Hyperventilation only slightly decreased Vm during hyperthermia, suggesting that patients with intracranial space-occupying lesions should be excluded from WBH treatment.

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P220 Serum sodium is inversely proportional to intracranial pressure in acute liver failure

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Crit Care 1999, **3 (suppl 1)**:P220

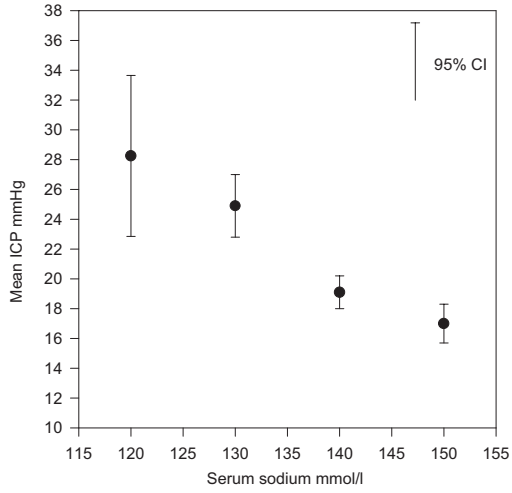
Objectives: Is there a correlation between serum sodium and intracranial pressure (ICP) in patients with acute liver failure.

Methods: All patients with ICP monitors inserted for suspected intracranial hypertension since 1991 treated on the liver unit of King's College London were identified. Indications for ICP monitoring included pupillary abnormalities, low jugular venous saturation and abnormal posturing. Eighty-two of the149 ICU charts were available for data collection. ICP, charted hourly, was averaged for every 6 h. Serum sodium, measured approximately 4 hourly was paired with the averaged ICP for the entire period of monitoring. Paired data was placed into four groups. Serum sodium less than 120, serum sodium less than 130, less than 140 and less than 160.

Results: See Table and Figure.

	Serum Na	Number	Mean ICP	SD	95% CI
Group 1	≤120	36	28.2	16.0	5.4
Group 2	≤130	177	24.9	14.3	2.1
Group 3	≤140	402	19.1	11.5	1.1
Group 4	>141	388	17	13.5	1.3

ICP vs Serum sodium



Conclusion: From the data examined there is a significant inverse correlation between serum sodium and intracranial pressure in acute liver failure. The sole use of electrolyte free fluids should be avoided in these patients.

P221 Gastric injuries: a rare surgical event due to blunt abdominal trauma

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Background/aims: Gastric rupture from blunt abdominal trauma is rare occurrence. The purpose of this paper was to evaluate the results of surgical treatment of patients with blunt trauma to the stomach.

Materials and methods: In a retrospective review of hospitals records of two trauma-admitting hospitals, 10 patients were identified. The main cause of blunt gastric injury was motor vehicle accident.

Results: All patients presenting usually with clinical signs warranting early laparotomy. There were six full-thickness, and two partial thickness gastric injuries located in the anterior wall in eight cases. All injuries could be managed with simple surgical techniques without resections. Two patients exsanguinated on the operating table from associated injuries. All but one of the survivors had postoperative complications with a mean hospital length of stay of 18.4 ± 7.6 (range 10–30) days.

Conclusion: Blunt gastric injury is usually diagnosed at laparotomy for associated injuries but occasionally may be suspected from specific clinical findings. In most cases the injury is on the anterior wall. Simple repair is usually sufficient and the prognosis depends on the severity of the associated injuries.

P222 Protein S100 as a marker for cerebral outcome after cardiopulmonary resuscitation

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Crit Care 1999, **3 (suppl 1)**:P222

Introduction: S100 is a CNS-specific protein, derived from the cytosol of glial cells, that can be detected in peripheral blood after structural brain damage. We prospectively examined the prognostic value of S100-levels after cardiopulmonary resuscitaton (CPR).

Patients and methods: In 17 consecutive patients admitted to a medical intensive care unit (ICU) after primary successfull cardiopulmonary resuscitation blood specimens were collected during the 7 days following CPR in a certain scheme, starting 1 h after the onset of CPR. On admission pH, base excess, serum lactate, time from cardiac arrest until onset of CPR, duration of CPR and dose of

catecholamines used were recorded. Blood samples were centrifugated and sera stored at –20°C. Levels of protein S100 were measured using a commercial immunoluminometric assay (Sangtec 100®, Byk Sangtec Diagnostica, Dietzenbach, Germany) according to the guidelines of the manufacturer. Reference level was <0.3 µg/l. Cerebral recovery was evaluated by the five-point cerebral performance category (CPC) on ICU demisson [1].

Results: Mean age was 66 yrs, median 67, range 35–78 years, 9/17 (65%) were male. 14/17 (82%) survived and were evaluated by the CPC. 5/13 (38%) met Category 1 criteria (conscious and alert/normal function), 2 met CPC 2 (conscious and alert/moderate disability, 2 met CPC 3 (conscious with severe disability), 4 met CPC 4 (comatose), 1 met CPC 5 (brain death). In 16/17 patients an elevated S100 was measured with a mean value of 5.13 µg/l, range 0.5–15.4, median 3.8 µg/l, with a maximum 1 h after CPR in 13/16 patients. In all patients of category 1 normal or slightly elevated levels (0.1–0.7 µg/l) were found, returning to normal within a few hours. In category C the highest S100 values (8.8/12.1 µg/l) of surviving patients were found, in contrast to category D with moderate elevated levels (1.7–5.4 µg/l). Patients who died had S100 values of 4.7–15.4 µg/l. No correlation was seen between pH, base excess, serum lactate on admission, catecholamine dosis needed during CPR and neurological outcome.

Conclusion: S100 seems to be a sensitive marker of cerebral injury due to diffuse hypoxia after CPR. Normal S100 values excluded severe cerebral damage. Normal or slightly elevated levels of S100 (≤0.7 µg/l) are correlated with good neurological outcome, but high S100 values do not necessarily predict an unfavourable prognosis.

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P223 Serum S100 as a marker of cerebral injury in acute liver failure (ALF) and during orthotopic liver transplantation (OLT)

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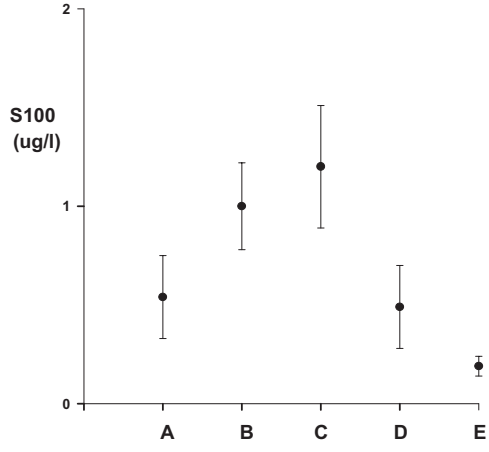
Crit Care 1999, **3 (suppl 1)**:P223

Introduction: Encephalopathy and irreversible cerebral injury may occur in ALF. S100 is a CNS-specific protein that is a marker of cerebral injury [1,2]. We investigated S100 protein in patients with ALF who underwent OLT.

Methods: After IRB approval blood samples were taken in 10 patients age 20–51 years with ALF. Blood was taken before OLT (A), during the anhepatic phase (B), 30 min after reperfusion (C), and on days 1 (D) and 4 (E) post-OLT. The blood was centrifuged and serum stored at –70°C. S100 was analysed using an immunoluminometric assay.

Results: Serum S100 (X ± SEM) was elevated prior to OLT (normal <0.12 µg/l). By day 4 post-OLT S100 had fallen in all patients except one. This patient subsequently died.

Conclusion: Serum S100 is elevated in ALF and encephalopathy. We observed a rise in S100 during OLT in these patients. The role of S100 as a marker of neuronal injury in ALF and OLT warrants further investigation.



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P224 S_{100}: a potential marker of cerebral trauma

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Crit Care 1999, **3 (suppl 1)**:P224

Introduction: Head injuries are associated with a high level of morbidity and mortality. The aim of this study was to examine if S_{100}, a calcium binding protein localised in astroglial cells of the central nervous system, can be used as a marker of head injury and to predict survival outcomes from severe head injury.

Methods: After informed consent and local ethics approval, 12 severe head injured patients (GCS ≤8) were included. All patients were treated according to standardised head injury protocols. Serial serum samples were taken over a period of 48 h together with various other physiologic measurements. Plasma concentrations of S_{100} were analysed using a radioimmunometric assay — Sangtec®S_{100}IMRA.

Results: The mean S_{100} in patients who survived was 1.1 µg/l and in those who died 0.79 µg/l. Six of the 12 patients in the study died.

Conclusion: Plasma S_{100} concentrations increase in severe head injuries. The reference value is less than 0.2 µg/l and this was exceeded in both patients who survived and those who died. Serum S_{100} levels could not be correlated with mortality.

Serum S_{100} (µg/l) after severe head injury

Time after admission (h)		0	2	6	12	24	48	72
S_{100} (µg/l)	Mean	0.417	0.5	1.25	1.06	2.49	0.7	0.35
	Std deviation	0.59	0.74	2.68	1.72	6.54	1.16	0.64
	No. of patients	12	12	12	12	12	12	6

P225 The effect of tracheostomy and vasoconstrictor therapy on outcome in neurosurgical patients requiring intensive care

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Crit Care 1999, **3 (suppl 1)**:P225

Aims of study: A retrospective review of the treatment and outcome of neurosurgical patients admitted to the ICU in the years 1990 and 1996 to assess the effect of the introduction of the routine use of percutaneous tracheostomy and vasoconstrictor therapy.

Results: See Table.

Discussion: The use of tracheostomies and vasoconstrictors has increased during this period of study. Tracheostomy has no effect on mortality whereas vasoconstrictor usage appears to result in an increase in mortality.

	1990	1996	*P* value
Total patients admitted	86	129	–
Mean age (years)	31.2	43.4	<0.001
Median GCS	8.4	8.7	NS
Days on ICU	4.2	3.4	NS
Tracheostomies performed (%)	26	44	<0.001
Days until tracheostomy	6.0	3.0	<0.001
Use of vasoconstriction (%)	16	38	<0.001
Mortality (%)	30	55	NS

Logistic regression on mortality (odds ratio):

Tracheostomy	Exp (B) = 0.76	95% CI (0.40–1.46)
Vasoconstrictor	Exp (B) = 5.46	95% CI (2.87–10.41)

P226 Effects of continuous flow insufflation of oxygen on arterial gazometry during cardiopulmonary resuscitation

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Crit Care 1999, **3 (suppl 1)**:P226

Introduction: During experimental cardiac arrrest, precordial compression associated to the unique use for ventilation of constant flow insufflation of air at the distal end of a modified endotracheal tube provided the same ventilatory results but better hemodynamic effects than manual ventilation [1]. Because of these results and the simplicity of the technique, a study concerning humans beings and using oxygen during cardiopulmonary resuscitation (CPR) has been realized.

Methods: After ethic committee approval, adult out-of-hospital cardiac arrests (shocked arrests excluded) were randomized in two groups: control group (C) treated by conventional CPR with active compression-decompression (ACD) and manual ventilation after intubation, Constant Flow Insufflation group (CFI-CPR) treated with ACD and flow rate of 15 l/min through small capillaries of Boussignac tube (Vygon, Ecouen, France). CPR continued for 30 min at the most. As soon as spontaneous circulation returned (SCR), arterial gazometry was made and all patients were mechanically ventilated. Statistical analysis was performed by χ_2 and Mann-Whitney tests. A $P < 0.05$ was considered statistically significant. Results were expressed as mean ± SD.

Results: Thirty patients were included in C group, 34 in CFI-CPR group. There were no differences in mean age (65 ± 3 vs 62 ± 3 years) or delayed CPR activation (6 ± 2 vs 7 ± 3 min). SCR was observed in 8 patients of C group after 13 ± 6 min and in 6 patients of CFI-CPR group after 14 ± 6 min (NS). The results of arterial gazometries for both group are shown in the Table.

	PH	$PaCO_2$ (mmHg)	PaO_2 (mmHg)	HCO_3^- (mmol/l)	SaO_2 (%)
CFI-CPR	6.86 ± 0.08	103 ± 18	237 ± 80	18.2 ± 2.4	95 ± 3
Control	6.88 ± 0.05	81 ± 10	155 ± 37	14.2 ± 1.5	92 ± 3

Arterial gazometry, no statistically differences

Conclusion: Comparable values of arterial gazometry were observed after CFI-CPR or standard CPR. This easier technique is as efficient as manual ventilation in terms of oxygenation during the early phase of cardiac arrest. Further studies are required to determine if CFI-CPR improve prognosis.

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P227 Airway management during cardiopulmonary resuscitation (CPR) by training nurses

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A experimental model of a patient was designed to grade the success of ventilation using the Guedel airway/face mask (GA/FM), Laryngeal mask (LM) or Combitube (CT) in CPR. It consisted of a manikin head, training lung (Dräger®: compliance 50 ml/cmH_2O, resistance 16 cmH_2O/l/sec), lower esophagial sphincter pressure (LESP) 7 cmH_2O and a simulated stomach [1]. Sixteen training nurses were shown the correct use of each device. The volunteers than used each device for a 2-min ventilation. For a successful ventilation a tidal lung volume of >200 mls had to be achieved within 180 s. Peak pressures in the esophagus, lung and gastric 2-min volumes were recorded. Each volunteer was graded from 1 (excellent) to 4 (bad), on the success of airway insertion, quality of the seal and visible adequacy of ventilation. The volunteers could deliver an adequate tidal lung volume with the GA/FM in 7–102 s (median: 24 s); LM in 18–92 s (median: 37 s), and 46–180 s (median: 74 s) with the CT. In the GA/FM group there were three failures, and two in the CT group. Analysis of the success of airway insertion, sealing and adequacy of ventilation shows a significant advantage with the LM or CT ($P < 0.0001$) against the GA/FM. There was no difference between the LM and CT. The 2-min lung volume delivered with the GA/FM ranged from 4.2–13.4 l (mean: 8.0 l), with peak LESP of 9–27 cmH_2O (mean: 16.4 cmH_2O) causing a gastric inflation of 2.5–13.6 l (mean: 6.6 l). The 2-min lung volume with the LM was 11.7–44.1 l (mean: 25 l), peak LESP of 0–22 cmH_2O (mean: 7.9 cmH_2O) and gastric inflation of 0–6.2 l (mean: 1.4 l). For the CT the 2-minute lung volume ranged from 12.3–41.5 l (mean: 27 l), peak LESP of 0 and without gastric inflation. Our results show the significant risk of gastric distension when using the GA/FM. Adequate lung ventilation of >5 l/min delivered with the GA/FM could be achieved only by 4 volunteers. The LM might provide the best alternative for airway management during CPR by nursing staff with a 100% success rate on adequacy of ventilation. A training program on the LM might further reduce the risk of gastric inflation.

Reference

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P228 Does emergency transportation induce a stress-response in probationers

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Introduction: Common opinion is that emergency transportation is a stressful event for patients. The question is if simulated emergency transportation might be a useful model to measure the levels of stress-responsive with a high ecological validity.

Methods: After approval by the local ethical committee 32 male probationers (age 18–40) were randomized into two groups ('strain', 'control'). The following values were taken: plasma-hormones (epinephrine E, norepinephrine NE, cortisol C) and CVS-values (BP, MAP, HR). The 'strain'-group was carried downstairs from a third floor flat and taken into an ambulance for an emergency transport. Blood samples were taken in the flat after informing the probationer (A), at the ground-floor (B) and at the end of a 15 min emergency transportation under defined conditions (C). The CVS-values were recorded continuously . The 'control'-group had to sit on a chair for 5 min and afterwards to lay on a stretcher for 15 min. The blood samples were done at equivalent times. The results were evaluated by a two-factor variance analysis with repetition of the values for the factor measuring time.

Results: Our study shows that a simulated emergency transportation induces stress. Differences in stress-responses depending on the period of the simulated emergency transport were found. The increase of E, NE, C and HR during the transport of the probationer down the stairs was significant ($P < 0.001$); no significant alterations could be shown in the 'control' group. The emergency transport in the ambulance appears to be clearly less of a strain to the patient. This was shown by a significant decrease of HR, E and NE levels ($P < 0.001$) compared to the downstairs part.

Conclusion: More attention should be focused on the period of emergency transport from on-scene to the ambulance to influence positively the most stressing event. Further studies concerning sedation before transportation appear to be necessary.

P229 Road traffic accident related morbidity and mortality as seen in an emergency department

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Crit Care 1999, **3 (suppl 1)**:P229

Introduction: Trauma remains the leading cause of death in the first four decades of life. Trauma-related costs is accounted for by accident injuries and the resultant disabilities, lost wages, medical expenses, insurance administration costs and most importantly loss of life become a great national issue in Greece. The purpose of this study is to report in epidemiological manner certain official information regarding prenosocomial events of all traffic accidents in the Southern area of Athens (1 000 000 inhabitants) within a year. The records were a co-operative and cross-matched result from the following services involved : The Department of Surgery and Intensive Care, 'ASCLEPEION' Hospital of Voulas, Athens and Department of Hygiene and Epidemiology, Athens University Medical School.

Patients and methods: From January 1997 to January 1998, 3211 trauma victims were to 1300 traffic accidents. 2173/3211 (67.7%) were males and 1038/3211 (32.3%) females. The mean age of victims was 39 years (range 14–90 years). In more than 70% of the cases the cause of accident was reported as being 'human error' regarding the driver of vehicle.

Results: The two most common incidents of the casualties were collision and deviation. 57/3211 (1.8%) victims died either immediately or during transportation to our hospital. From the victims 43 (75.44%) were males and 14 (24.56%) females. The mean age of victims was 54 years (range 12–82 years). The most frequent fatal accident time were the hours between 14:00–24:00 (28 victims = 49.12%). April and July were the most fatal months (8 victims each = 14%).The primary use of Abbreviated Injury Scoring system (A.I.S.) on those who reached the Hospital alive classified 518 cases (16.13%) as having mild injuries and 2693 cases (83.87%) as having medium and/or severe injuries.

Morbidity and mortality among the population of Greece were 33238 and 2139 respectively within the above period.

Conclusion: Nevertheless newspapers, radio and TV pay more attention to the narcotic and other causes victims than that of the car accidents which is the main reason of deaths among the young.

We can conclude that the suitable prehospitalized care of the injured victims and the rapid assessment and resuscitation at the Trauma Centers are the cornerstones of the current treatment and improve the outcome of the injured significantly.

P230 Sports activity after severe polytrauma: results of a prospective study

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Crit Care 1999, **3 (suppl 1)**:P230

Background: There is only a small body of literature dealing with the problem of sports activity after survived severe polytrauma. Having in mind that most of these patients are in the age group between 18 to 40 years, sports activity after survived polytrauma is a decisive factor of their quality of life.

Materials and method: In a prospective trial we evaluated the sports activity and sports performance of a group of 50 polytrauma patients (ISS >15) after a minimum time of 6 months following their discharge from hospital. The characteristics of the group were as follows (mean values): age 28.5 years, follow-up time 18 months, sex: male 40, female 10 patients. The ISS was 50. Cause of injury was in 96% a MVA, in 4% a fall from great height. The APACHE II on the first day was 17. The patients' time on respirator was 7 days. The stay on ICU was 11, and the stay in hospital 26 days. The sports activity and performance were evaluated according to a standardized score in all patients who practiced sports before the trauma. In addition, a performance test with spiroergometry and serum lactate samples could be performed in seven cases.

Results: During the 6 months after discharge from hospital four patients died. The sports status of these patients could not be evaluated. Forty-six patients (92%) were available for further evaluation. The pre- and post-traumatic status of their sports is listed in Table 1. Sports performance and participation levels in difference activities were evaluated in the 36 patients who practised sport before the trauma. The results are listed in Table 2.

Table 1

Status of sports activity	Group 1 (sports)	Group II (no sports)	Group changes
Pre-trauma	36 = 78.2%	10 = 21.7%	
Post-trauma	25 = 54.34%	21 = 45.6%	1 = 2.1%

Table 2

	Activity level I	Activity level II	Activity level III	Activity level IV
Pre-trauma	0%	0%	3%	97%
Post-trauma	0%	42%	37%	21%

Conclusion: According to our results a decrease in activity and performance levels is obvious in the post trauma patient group. More than 70% of the patients practising sports before the trauma had to reduce their activity level. 23.86% had to quit their former activities. However, more than 50% of the patients were able to practice sports after their trauma.

P231 Discomfort, awareness and recall of patients in the intensive care: still a problem?

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Crit Care 1999, **3 (suppl 1)**:P231

Introduction: During surgery, anaesthetists take extra care to prevent awareness of any patient who is having any kind of operation done, mainly under general anaesthesia either by using inhalational or intravenous medications, but patients in the ICU, mainly those on ventilatory support, with intubation and sedation, pass through a lot of psychological stress and frustration, which most of the times is not documented in the genera intensive care, and has never been done in our unit.

Aim of this study: In this study at our general ICU, we tried to have a proper assessment of this problem in order to avoid it in the future, and to get a proper consensus regarding its existence and solution.

Methods: Seventy patients between the ages 20–60 years, were interviewed 1 day after discharge from the ICU, about their memory of events during their stay. Patients with head injury, CNS infection or those who were disoriented at the time of interview were excluded from the study. The remaining 55 patients were oriented to place and time.

Intravenous opiates (morphine, pethidine) were used for analgesia as required, while sedation was achieved using midazolam and morphine infusions in appropriate doses as decided by the attending doctors and nurses.

Questions asked were generally about patients' memory of events and about their distressing experiences regarding pain, anxiety, dreams, fear, noises, causes of discomfort and others which will be displayed in the results section.

The same questions were repeated 5 days later.

Results: The sample of patients were representative of our regular ICU admissions in their age group, APACHE II score and duration of stay.

The most distressing and commonest experiences recalled were: anxiety (68%), discomfort from endo-tube (60%), fear (54%), pain (52%), discomfort from N/G tube (48%), difficulty in communicating (33%), dreams and hallucinations (31%), discomfort from physiotherapy (24%), noise (15%), insomnia (13%), thirst (10%), some of these like anxiety, fear, dreams, hallucinations and insomnia had continued since discharge in 6% of patients. None of the studied experiences correlated with age, sex, or with the APACHE II score. On interviewing the patients 5 days later, there were no significant changes in their responses.

Conclusion: Our sedation and analgesia in the ICU is not enough to prevent unpleasant experiences, mainly those related to patient awareness.

More work is still needed, i.e. using sedation scores to improve our sedation and analgesia in the ICU.

P232 Sedation of patients in intensive care units by midazolam (MDZ): clinical and biological evaluation

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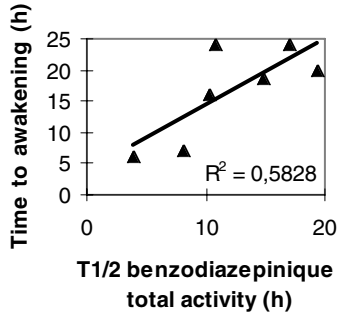
Aim: To assess if the clinical scoring of sedation (Ramsay scale), the administered dose of MDZ, the serum levels of MDZ from the beginning to the end of sedation are related to clinical parameters (body area), biological data (creatinine clearance, liver enzymes, protidemia), and pharmacokinetic parameters (elimination half-life $T_{1/2}$).

Patients and methods: The study was conducted with 31 patients (70 ± 10 year-old; IGS II = 41 ± 14). The objective was to reach a score of sedation of 2 up to 4. Sedation of patients was initiated with an intravenous bolus of MDZ (B = 0.1 mg/kg) and maintained with MDZ at the rate (H_1 = 0.08 mg/kg/h). If needed, the dose of MDZ was gradually increased: $H_2 = 1/2B + 1{,}5H_1$; $H_3 = 1/2B + 2H_1$ (if H3 was insufficient, sufentanil was added (0.17 µg/kg/h and 0.34 µg/kg/h)). Waking up of patients was monitored by the beginning of respiratory weaning. Liver enzymes, protidemia and creatinine clearance are evaluated every day and 24 h after the end of sedation.The serum levels of MDZ and its metabolites were measured by HPLC and RRA every 8 h during the first day; then every 24 h, before and after each change of posology and finally every 4 h after the end of sedation for 24 h. The correlations between the different parameters monitored were evaluated by a Pearson's test.

Results: No correlation between time to awakening (22 ± 21h) and duration of sedation (96 ± 57 h) or clinical parameters or biological data was observed. In a similar way, score of sedation, posology and serum levels of MDZ were not correlated. The pharmacokinetic parameters of MDZ were: T1/2 = 11.77 ± 4.8 h, clearance = 8.6 ± 4 l/h, Vd = 149 ± 98 l, concentration at steady state = 1008.7 ± 395 ng/ml. The unique parameter modulating the time to awakening was T1/2 of benzodiazepinique total activity (T1/2 = 12 ± 4.96 h) with 7 patients.

Conclusion: The clinical evaluation of sedation is sufficient to adjust the dose of MDZ required for sedation and efficient awake in intensive care units.



P233 Cardiovascular effects of dexmedotomidine for ITU sedation: UK results of a multi-centre study (St George's, University College, St Thomas's and Bristol Royal Infirmary Hospitals)

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Introduction: A multi-centre study examining the safety and efficacy of the novel sedative agent dexmedetomidine, a highly selective alpha-2 agonist, possessing analgesic and sympatholytic properties.

Methods: One-hundred and nineteen post-operative patients who required sedation and ventilation for at least 6 h on the ITU were enrolled. Ninety-eight completed the randomised, placebo-controlled, double-blind study (81 cardiac and 17 general surgical) in four centres in the UK, but all patient data was used in the safety analysis. Within 1 h of return from theatre, the study drug was started with a loading dose of 1 µg/kg for 10 min, followed by a maintenance infusion of 0.2–0.7 µg/kg/h to maintain a Ramsay sedation score of ≥3 and was continued for 6 h after extubation (maximum duration 24 h). Rescue sedation and analgesia was provided with midazolam and morphine respectively. Heart rate, systolic, diastolic pressures and central venous pressures were recorded at 10 min intervals for the first 30 min and then hourly.

Results: Patient demographics were comparable as were Ramsay sedation scores between the two groups. The average dexmedetomidine infusion rate was 0.35 µg/kg/h whilst intubated and 0.15 µg/kg/h after extubation (range 0–0.7 µg/kg/h). Data was collated for the initial 6 h of the infusion and for the period pre- and post-extubation ± 4 h, hence, allowing for the variation in the duration of intubation in the data analysis. Once adequately sedated the patients receiving dexmedetomidine achieved greater cardiovascular stability as compared to the placebo group, with a significantly lower and less variable heart rate ($P = 0.0001$), this was clearly demonstrated in the period around extubation when mean heart rate in the dexmedetomidine group was 75 (SEM ± 2.0), versus 92 (± 2.9) in the placebo group. Diastolic blood pressure showed a similar trend with a reduction of 5 mmHg in the dexmedetomidine group, but no sustained significant differences in systolic arterial pressure or central venous pressures. Of the 66 patients who received dexmedetomidine, 16 had transient episodes of hypotension (MAP <60 or >30% reduction from pre-infusion BP) and/or bradycardia (HR <50), mainly during the loading dose, of which three patients required temporary interruption of the infusion and three others required termination of the infusion.

Summary: Dexmedetomidine may improve cardiovascular stability.

P234 Ovarian hyperstimulation syndrome (OHSS) at a maternity hospital

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Background: Ovarian hyperstimulation syndrome (OHSS) is a clinically important entity due to assisted conception which occurs in about 1–10% of *in vitro* fertilization (IVF) cycles with serious complications such as deep vein thrombosis, hypovolaemia, haemorrhage, respiratory distress and hepato-renal failure.

Objective: The aim of this study was to describe our experience with OHSS at 'IASO' Maternity Hospital.

Materials and methods: The last year seven patients with age 30 ± 2.4 (X ± SEM) were admitted in our ICU due to severe ovarian hyperstimulation syndrome complications.

Results: Signs and symptoms (Table 1) and labs (Table 2) were due to third space fluid shift (increased capillary permeability) with evidence of hypovolaemia, haemoconcentration and dehydration.

Ultrasound examination of the abdomen showed ascites, pelvic fluid and enlarged ovaries (in our patients >11 cm in diameter) in all patients and chest X-ray revealed hydrothorax in five patients (71%). Ovarian hyperstimulation syndrome clinical feature is due to exaggerated ovarian response characterized by marked elevation of serum oestradiol levels and the presence of a large number of follicles (>20).

Management and outcome: All patients had bed rest, fluid input–output control, adequate fluid intake, high protein oral intake, human albumin solutions iv and LMWH sc (nadroparin

Table 1. Signs and symptoms on admission

Generalized edema	100%
Ascites	100%
Weight gain	100%
Chest discomfort	71%
Thirst sensation	71%
Nausea-vomiting	71%
Hydrothorax	71%
Abdominal distension or pain	43%
Anxiety	28%

Table 2. Labs on admission and discharge

Laboratory examination	Admission (X ± SEM)	Discharge (X ± SEM)
Ht (%)	45 ± 1.97	33 ± 1.67
Na^+ (mmol/l)	133 ± 1.02	138 ± 1.29
Urea (mg/dl)	42 ± 4.6	32 ± 1.8
Alb (g/dl)	2.8 ± 0.12	4.25 ± 0.31
WBC × 10^3/µl	16.4 ± 1.35	10.7 ± 1.54
Oestradiol (pg/dl)	4735 ± 1658	

calcium 3000 iu). Two patients had paracentesis of hydrothorax because of dyspnea or discomfort. Hospital and ICU stay was 8 ± 3.3 and 5 ± 1.9 days, respectively. All patients recovered without developing any life threatening complications and were discharged in good condition.

Conclusions and discussion: Ovarian hyperstimulation syndrome is a serious clinical condition [1] which may be complicated by life threatening events in up to 0.5–2% [1,2]. Early recognition and management until normalization of oestradiol serum levels provide good outcome with mortality rate 0.0025% [1].

Reference

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P235 Anticoagulation: hitting the target after cardiac surgery

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Introduction: A pharmacy led anticoagulant service has recently been introduced to dose and monitor warfarin in all cardiothoracic inpatients at the Leeds General Infirmary. This abstract presents an audit of locally produced guidelines for the induction of warfarin in cardiothoracic patients.

Aim: To improve the anticoagulant process for cardiothoracic patients by using the experience of clinical pharmacists to produce guidelines for induction of warfarin.

Results: An audit was undertaken and data was collected on 89 patients. Sixty patients (67%) received a warfarin loading dose according to the local guidelines. Fifteen (71%) of the 21 patients with mechanical valves had an acceptable INR on day four. Only one patient (5%) had a high INR, and 5 (24%) had a low INR. Of the 39 'low risk' patients (tissue valves, coronary endarterectomies and A.F), 21 (54%) were within the acceptable range on day 4 whilst four (10%) were high and 14 (36%) were low.

In a group of 29 patients where guidelines were not followed (dosing decisions were made by junior surgeons), only 8 patients (28%) had an acceptable INR on day four, 16 (55%) had a low INR and 5 (17%) had a high INR.

Discussion: This study has shown that the locally developed guidelines can be used to safely initiate warfarin in cardiothoracic patients immediately following cardiac surgery. In the future we intend to undertake an analysis to produce maintenance dose guidelines which are specific to cardiothoracic patients. A combination of these two guidelines should optimise the dosing of warfarin in cardiothoracic patients and contribute to an overall improvement in their care.

P236 A prospective study of thrombocytopenia and prognosis in intensive care

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Introduction: To study the incidence and prognosis of thrombocytopenia in an adult critically ill population, 329 patients consecutively admitted during a 5-month period to the medical intensive care unit (ICU) of a university hospital (212 patients) and a medical-surgical ICU of a regional hospital (117 patients), were prospectively surveyed. The primary outcome measure was ICU mortality.

Results: One hundred and thirty-six patients (41.3%) had at least one platelet count < 150×10^9/l. These patients displayed a higher APACHE (Acute Physiology and Chronic Health Evaluation) II, SAPS II (new Simplified Acute Physiology Score) and MODS (Multiple Organ Dysfunction Score) at admission, longer ICU stay (8 versus 5 days median (interquartile range)) and a higher mortality rate (crude odds ratio, OR = 5.0, 95% confidence interval, CI 2.7–9.1) than those who never developed thrombocytopenia ($P < 0.0005$ for all comparisons). Bleeding incidence rose from 4.1% in non-thrombocytopenic patients to 21.4% in patients with minimal platelet counts between 101 and 149×10^9/l ($P = 0.0002$), and to 51.9% in patients with minimal platelet counts $<100\times10^9$/l ($P < 0.0001$). 19.5% of the study population died in the ICU following the index admission. Eighteen of 193 patients (9.3%) who never became thrombocytopenic died, versus 31 of 89 patients who were thrombocytopenic at admission (OR = 5.2, 95% CI 2.7–9.8, $P < 0.0001$) and versus 15 of 47 patients (31.9%) who developed thrombocytopenia later on during ICU stay (OR = 4.6, 95% CI 2.1–10.0, $P = 0.0002$). In addition we found that a drop in platelet count to ≤50% of admission was associated with higher death rates (OR = 6.0, 95% CI 3.0–12.0, $P < 0.0001$). In a linear regression analysis, adjusting for admission APACHE II, SAPS II and MODS, admission thrombocytosis and the occurrence of bleeding, nadir thrombocytosis remained significantly related to ICU mortality.

Conclusion: Thrombocytopenia is a simple and readily available risk marker for ICU mortality, independent of and complementary to established severity of disease indices. Both a low nadir thrombocytosis and a significant fall of platelet count predict a poor vital outcome in adult ICU patients.

P237 Platelet function and inflammatory markers in septic patients

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Background: In septic patients disseminated intravascular coagulation is a severe complication whereby an altered platelet function appears contributory. Clinical outcome depends on an early diagnosis and sufficient therapy. In the present study the association of platelet function to inflammatory markers indicating disease severity was investigated.

Methods: Inflammatory markers C-reactive protein, procalcitonin, interleukin-6 and interleukin-10 were measured using standard methods in 18 patients fulfilling clinical, inflammatory and hemodynamic criteria of sepsis. Platelet activation marker P-selectin was flow cytometrically analysed *ex vivo* and after stimulation using 5 µmol/l ADP and 10 µmol/l TRAP-6.

Results: Flow cytometrically measured platelet function was tightly associated with inflammatory markers. Pre-activation of platelets in the circulation was significantly correlated to plasma levels of procalcitonin ($P < 0.023$), whereas in vitro induced reagibility after ADP- and TRAP-6 stimulation correlated well with the plasma concentration of the C-reactive protein ($P < 0.001$; $P < 0.012$). Furthermore, a close relation of IL-6, but not of IL-10, plasma levels to TRAP-6 stimulated P-selectin expression was observed ($P < 0.033$).

Conclusion: Platelet function was demonstrated to be tightly associated with the inflammation process in septic patients. Whether this finding may be a useful marker for disease severity and the development of a disseminated intravascular coagulation should be clarified in prospective studies.

P238 Retrospective study of patients with haematological malignancies admitted in an intensive care unit

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Introduction: The development of aggressive schemes of chemotherapy predisposes haematological patients to various life-threatening complications. The admission of neutropenic patients into an intensive care unit (ICU) is still controversial mainly if they have multiple organ dysfunction (MOD) and /or if mechanical ventilation is required.

Objective: Analyses from patients with haematological malignancies admitted in a medico-surgery ICU of an oncology hospital.

Patients and methods: Retrospective observational study on patients with haematological malignancies admitted in ICU from October/96 to October/98, coming from Paediatric Department (PD), Onco-Haematological Unit (OHU) and Bone Marrow Transplantation Unit (BMTU). We analysed the patient data, namely the underlying malignancy, the reason for admission, the type and number of organ dysfunction (including neutropenia and requirement of mechanical ventilation), the time in ICU, acute physiology, age, chronic health evaluation (APACHE II) and sepsis-related organ failure assessment (SOFA).

Results: Between October/96 and October/98, 46 onco-haematological patients were admitted in the UCI (56 inpatients) with ages from 9 months to 70 years old, 23 female/23 male: 6 came from PD (13%), 29 from OHU (63%) and 11 from BMTU (24%).

Underlying haematological malignancy: Non Hodgkin Lymphoma (34%), Acute Myeloid Leukaemia (21%), Chronic Myeloid Leukaemia (15%), Hodgkin Disease (15%), Acute Lymphoid leukaemia (11%), Multiple myeloma (4%). Six of the 46 patients were excluded because of the short time in ICU (≤12 h). Six patients were readmitted. The mean time of stay was 8.2 days. The reasons for ICU admission were: acute respiratory failure (54%), multi-organ dysfunction (MOD; 14%), post-surgery (14%), septic shock (8%), tumour lysis syndrome (6%), hypovolemic shock (2%) and neurological dysfunction (2%). The ICU mortality was 52.5%, being 76% of them neutropenic patients with MOD and requiring invasive ventilation. 89% of the patients coming from BMTU died.

Conclusion: The main risk factors to dead in an ICU are the number of organ dysfunction at admission, the requirement of invasive ventilation, BMT, APACHE II ≥20 and SOFA ≥15.

P239 Prognostic value of the bone marrow in severe sepsis/septic shock

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Introduction: Peripheral haematological changes are one of the sepsis diagnosis criteria. However, there are only a few studies concerning the effects of severe sepsis/septic shock in bone marrow of the adult patient.

Objectives: Characterise the bone marrow haematological changes in severe sepsis/septic shock patients and to evaluate the prognostic value of the marrow cell differential count (myeloid, lymphoreticular, erythroid series).

Materials and methods: Prospective study of 29 patients with the diagnosis of severe sepsis/septic shock of different etiologies. Age, SAPS II in the first 24 h, organ dysfunctions according to SOFA, organ failure according to Knaus and the final outcome were considered in the present study.

The bone marrow of each patient was studied and a differential count considering the myeloid, lymphoreticular and erythroid series was made. The patients were separated according to final outcome (dead and alive) and the bone marrow differential counts were compared between the two groups applying *t* Student test.

Results: See Table.

Conclusion: In the present study significant statistical correlation was found between lymphoreticular count and mortality. We can conclude that bone marrow evaluation has had a prognostic value in this patient group.

	Dead ($n=17$)	Alive ($n=12$)	*P*
Myeloid series (%)	67 ± 11.1	68 ± 11.1	0.81
Lymphoreticular series (%)	10.6 ± 4.5	15.98 ± 6.22	0.018
Erythroid series (%)	21.7 ± 11.7	15.1 ± 7.7	0.06
Age	52.6 ± 18.4	50.6 ± 21.1	0.79
SAPS II	55.7 ± 12.9	62.8 ± 16.6	0.24
SOFA	13.9 ± 2.6	10.9 ± 2.2	0.003
OSF	3.1 ± 1.3	1.9 ± 0.8	0.004

Mortality rate 58.86%

P240 Monitoring of plasma lipid peroxide level after abdominal aortic reconstruction in humans

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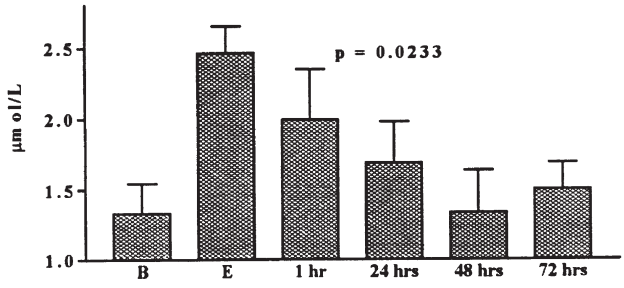
Aortic reconstructive surgery is associated with post-ischemic reperfusion and oxidative stress. It is expected that oxidative stress should be self-limiting during healing process in the postoperative period. Lipid hydroperoxides (LHP) are one of oxidative stress markers therefore we evaluated changes in LHP level in the course of uncomplicated healing in patients who underwent abdominal aortic reconstruction. Ten male patients, aged 56–74 years (mean 65.5 ± 6.01) with abdominal aortic aneurysm or aorto-iliac occlusive disease were submitted to aortic grafting operation. LHP concentration was measured in blood samples collected via central line prior to (P), at the end of (E) and 1 h, 24 h, 48 h and 72 h after surgery. The results are presented as mean ± SEM. *Nonparametric one-way ANOVA–Kruskal–Wallis test



LHP concentration was significantly increased at the end of surgery and started to decrease just after 1 h later reaching the initial level within 48 h. The obtained results indicate limitation of the oxidative stress in the course of uncomplicated healing. The results also suggest that LHP level can be used for monitoring of oxidative stress activity in humans.

P241 Deep leg veign thrombosis in multiply injured patients: an underestimated problem? Results of a prospective clinical study with 50 patients

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Introduction: Too little is still known about the incidence rate of thromboembolic complications in polytrauma patients after ICU treatment, as only a small amount of data is available on this topic. The majority of the studies published to date that have been performed to assess the incidence rate of thrombosis in multiply injured patients only refer to the clinical symptoms of a venous thrombosis. A systematic screening-examination for the assessment of the incidence rate of thromboembolic complications in the above-mentioned patient collective has not yet gained acceptance as a routine method in clinical practice.

Material and method: Between January 1996 and December 1997, 50 polytrauma patients were included in a prospective clinical study. Including criteria were: an initial ISS-score >16, a stay on the ICU of at least 72 h and a time on the respirator of at least 72 h. All patients were examined for a deep veign thrombosis by using a standardized protocol and by means of a colour-coded duplex (ccd) sonography. In cases in which the clinical or/and sonographic examination yielded results of a suspected veign thrombosis, a phlebography was performed. In cases of a suspected pulmonary embolism a pulmonary angiography was performed. The colour-coded duplex sonography was used before the patients were mobilized or transfered to an other ward (generally after 15 days).

Results: If not indicated otherwise numbers are given as median. The age of the 38 male and 12 female patients was 38.6 years. The severity of trauma was characterized by an ISS-score of 39.5 points. Eight patients died of a multiorgan-failure during their stay on the ICU. The autopsy findings reveal that no patient died of the of a veign thrombosis or a pulmonary embolism. Of the

remaining 42 patients, 8 patients (19%) showed deep leg veign thrombosis in the ccd. In three of these patients (7%) also a pulmonary embolism occurred.

Conclusion: Having in mind the results of our study the incidence rate of thromboembolic complications in polytrauma patients seems to be much higher as expected in comparison to the published results of other authors.

P242 Obstructive shock in pulmonary embolism: thrombolytic therapy and survival

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Study objectives: Shock due to massive pulmonary embolism (PE) shows a variable prevalence in literature, without general agreement about thrombolytic therapy effectiveness. Objective of the study was to appreciate prevalence and main clinical features of obstructive shock (OS) in patients with PE admitted to our departement, and to evaluate thrombolytic therapy effectiveness (BAPE regimen).

Methods and results: 236 PE cases were treated from March 95 until June 98; 24/236 suffered OS (10.2%, 14 F, 10 M, mean age 69 years). In 91.6% of OS we found one risk factor, at least, and in 62% two or more risk factors. 3/24 patients presented with cardiac arrest, 7/24 showed RBBB and 5/24 $S_1Q_3T_3$ pattern on EKG, 9/24 showed a normal EKG. Echocardiography, performed in 66% of patients, detected in all cases an enlarged and hypokinetic right ventricle; venous duplex ultrasound, performed in 70% of cases, detected DVT in 70.5%; perfusion radionuclide lung scan, performed in 70.5% of cases, showed a high probability pattern in 94%. D-dimer was altered in all cases; ABG analysis showed hypoxemia in all cases. 13/24 patients with OS were given thrombolysis according to BAPE regimen (rTPA 0.6 mg/kg over 15 min); 11/24 patients with OS were not given thombolysis because of absolute contraindications. Thrombolytic therapy decision-making rested on clinical data, on echocardiography in 38% of case and on echocardiography and lung scan in 61% of cases. Intra-hospital overall death-rate was 37.5% (9/24 patients); all 13 patients given thrombolysis were alive at discharge, whereas, 9/11 (81.8%) patients not given thrombolysis died in the hospital.

Conclusion: We found OS in 10.2 % of PE cases; 13 patients given thrombolysis all were alive and showed stable hemodynamic parameters at discharge, whereas 9/11 patients not thrombolysis given died during hospital stay. This outlines the need of an expeditious clinical and instrumental diagnosis as a tool of decision-making, especially about thrombolytic therapy. Moreover, we found a 100% sensibility of D-dimer, hypoxemia as detected by ABG analysis, echocardiography and perfusion radionuclide lung scan.

P243 Aortic valve replacement with 'stentless' versus mechanical prosthesis: what difference in postoperative ICU course?

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Introduction: Aortic valve prosthesis determine a transvalvular gradient (Δp) with changes in aortic flow that can affect left ventricular geometry and function, implanted prosthesis and aortic route. In order to improve prognosis a new prosthesis has been proposed , the so called 'stentless valve' (SV), whose main characteristic is the absence of the supporting ring. Aim of our study was to evaluate if such valve could influence early postoperative course in ICU.

Methods: Forty patients, age 67 ± 11 and EF 56 ± 14, undergoing aortic valve replacement were enrolled. Nineteen patients, 12 with aortic stenosis (AoS) and seven with insufficiency (AoI) underwent SV implantation (group S); 21 patients, 13 with AoS and eight with AoI, received mechanical valve (group M). Anaesthesia with remifentanil and propofol, moderate hypothermia (30°C) and anterograde blood cardioplegia were used. In all cases mechanical ventilation (MV) and intubation time, need for inotropic support and blood loss were registered during ICU stay.

Results: No differences were found in duration of MV (125 ± 30 min in group S versus 136 ± 12 min in group M, $P > 0.05$) and intubation (3 h in group S versus 3.4 h in group M, $P > 0.05$) in patients with aortic stenosis. In patients with AoI MV and intubation time was shorter in group S (respectively 140 ± 25 min versus 155 ± 18 min in group M, $P < 0.05$; 3.9 h versus 4.5 h in group M, $P < 0.05$). No differences were observed in blood loss between two groups, nor in dopamine dosage (5.4 μg/kg/min versus 6.6 μg/kg/min, $P < 0.05$).

Discussion: Our results show no differences in early postoperative outcome in patients with AoS when treated with mechanical or SV. Vice versa SV seems to improve ICU course of patients with AoI, with regard to duration of MV and intubation. Other studies with echocardiography are necessary to clear if these differences can be due to a lower aortic transvalvular gradient of SV.

P244 High risk patients in major thoracic surgery

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Lung resections are correlated to high mortality (4–6%) and morbidity (20–40%) that can increase in high risk patients. Objectives of this study is to analyze preoperative risk factors, in a group of high risk patients undergoing thoracotomy for lung cancer and to assess the relationship with postoperative complications.

Methods: From January 1996 to December 1997 43 patients, undergone pulmonary resection for lung cancer, were considered at high risk and enrolled in this study according to one or more of the following including criteria: age older than 70 years; previous cardiovascular disease; poor pulmonary function (FEV1 <65% predicted values, PaO_2 <65 mmHg or $PaCO_2$ >42 mmHg); chronic systemic disease. Patients clinical data are reported in the Table. Anesthetic technique was the same for all patients. All the patients were monitored with EKG, pulse oxymetry (Nellcor N200), invasive arterial pressure, pulmonary artery catheter when necessary and in-end expiratory gas analysis. Preoperatively an epidural catheter was inserted in T6-T11 space. Anesthesia was maintained with isoflurane 0.5% vecuronium and fentanyl combined with epidural analgesia (bupivacaine 0.5% and fentanyl). A continuous infusion through the epidural catheter of morphine 20 mg in 250 ml normal saline 0.9% at 5 ml/h was used for postoperative pain relief. Surgical procedures included: 33 lobectomy, 4 bilobectomy, 3 sleeve resections, 2 pneumonectomy. Relationship among different preoperative risk factors and postoperative complications were performed with χ^2 test and corrected with Fisher's exact test.

Results: Mean age was 69 yrs (range 50–83 years). All patients were extubated in the operative room at the end of surgical procedures.

Complications occurred in 25.5% of patients (11/43): 3 arrhythmias, 2 myocardial infarctions, 2 pulmonary edema, 2 acute renal failures, 2 pulmonary complications (prolonged air leakage) (Table). The perioperative mortality rate was 4.6% (2/43). The mean length of staying in hospital was 11 days for all patients, 12.5 for respiratory group, 9.6 for cardiac group, 10.9 for age group.

Conclusion: In our experience lung resections in high risk patients have low mortality and morbidity. Therefore, age over 70 years alone has no longer to be considered a limiting factor in patients undergoing surgery for lung cancer. High risk patients need a very careful preoperative evaluation of cardiovascular and pulmonary function in order to avoid perioperative complications and to reduce the morbidity. An appropiate surgical and anesthetic technique, and postoperative pain relief improves outcome in high risk patients.

Table. Preoperative risk factors and perioperative complications

Risk factors	No. patients	Complications
Age	9	
Cardiovascular	4	1 MI
Respiratory	8	3 arrhythmia, 1 PE, 1 resp
Age + cardiovascular	8	1 MI (died), 1 resp
Age + respiratory	4	
Age + other	1	
Age + cardiovascular + other	1	2 RF (1 died)
Age + respiratory + other	1	1 PE
Age + cardiovascular + respiratory + other	2	
Age + cardiovascular + respiratory	2	
Cardiovascular + other	2	
Respiratory + cardiovascular	1	

MI, myocardial infarction; PE, pulmonary edema; RF, renal failure

P245 Outcome of systemic rheumatic disease patients admitted in intensive care unit

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Objective: The aim of this study was the determination of short and longterm outcomes and prognostic factors for patients with systemic rheumatic diseases (SRD) admitted to intensive care units (ICU) in a retrospective case series study of SRD patients admitted in six French ICU in community and teaching hospital between January 1992 and July 1996.

Main results: A total of 60 SRD patients were included with diagnostic of infection (40%), acute exacerbation of SRD (16.7%), iatrogenic complication (16.7%), cardiovascular complication (15%), and miscellaneous (11.7%). The death rate in intensive care units was 26.7% (16/60). Multivariate analysis (Cox model) identified two factor predicting poor MICU outcome: age above 65 years (relative risk [RR], 3.3; 95% confidence interval [CI], 1.9–5.8) and Tran organ failure indices (RR, 2.2; 95% CI, 1.7–2.8). The mean overall survival time after admission to ICU was 18.8 months. The 1-year survival rate was 61.1%, and the 2-years 58.8%. Multivariate analysis (Cox model) identified two factors predicting poor long term outcome: age above 65 years (RR 4.0; 95% CI 2.7–6.0), and need of mechanical ventilation (RR, 6.5; 95% CI, 4.2–10.1) (Fig).

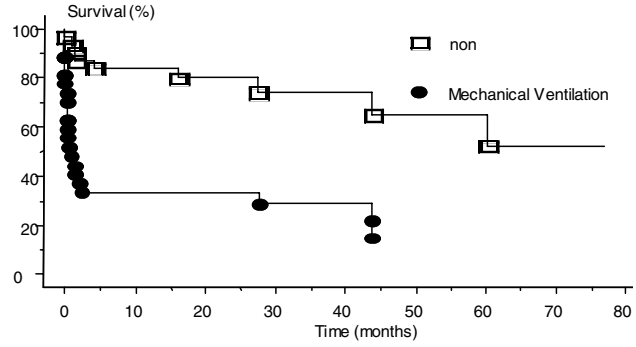

Figure. Survival of patients with SRD in intensive care unit, influence of mechanical ventilation.

Conclusion: We conclude that this SRD patients should be admitted to the ICU on the same basis as other patients. In this population neither the diagnostic of the underlying disease, nor the use of immunosuppresive therapy did influence the short and long outcome. Long-term survival depended only on the age and the need of mechanical ventilation.

P246 Abdominal sepsis in the surgical intensive care unit: a follow up study on quality of life, morbidity and mortality

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Surgical intensive care consumes considerable facilities and the associated costs are high. The present study aimed at evaluating longterm outcome of patients treated due to abdominal sepsis in the surgical intensive care unit from January 1983 to December 1995 by a follow-up from June to August 1997 of patients surviving the hospital stay. The patients were interviewed by telephone and also completed a 'quality-of-life' form. Out of 210 patients (mean age 65 years) 151 survived the hospital stay. At follow-up, another 45 patients were deceased, 41 patients were not reached and another 17 patients declined to participate. Thus, the follow-up included 48 patients. At discharge from hospital, 54% of the patients returned directly home and 67% returned to their regular work after a median sick-leave of 10 weeks. When comparing a quality-of-life score, an impairment of median scores ($P < 0.01$) was found, although the patients subjectively appreciated quality of life not to have changed significantly. 49% claimed full recovery. Hospital mortality was 28% attributable to multiple organ dysfunction and total mortality over the time period was 50% and rarely associated with abdominal sepsis. Thus, recovery following abdominal sepsis treated in the surgical intensive care unit is good and motivates efforts performed during the acute phase.

P247 Time and type of admission to a surgical intensive care unit

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Crit Care 1999, **3 (suppl 1)**:P247

Introduction: Duke University Medical Center (DUMC) is a tertiary care hospital with a Level 1 (USA) Trauma Center Designation. Increasing level of patient acuteness, high census levels, decreasing resident staffing and financial concerns have led to intensive care unit (ICU) organization and staffing changes. ICU care is being redefined at DUMC via pursuit of a multidisciplinary approach to the treatment of critically ill patients. As part of this initiative, analysis of Surgical Intensive Care Unit (SICU) admissions was performed for January through March 1998. This analysis showed that 45% of admissions occurred when there was no attending in house. To fulfill the missions of patient care, education, research, cost-containment, optimal bed utilization and appropriate reimbursement for services, we instituted around-the-clock board-certified intensivist coverage in the SICU. Continuing analysis of admission distribution confirms that half of admissions occur at night and breakdown of type of admission indicates that these admissions are the patients most requiring active resuscitation and supervision of resident management.

Methods: To determine time and type of SICU admissions we retrospectively reviewed the SICU database from July through November 1998. Time of arrival was divided into 12-h blocks beginning at 6 AM and 6 PM. Patients were divided into four categories: postoperative, direct admission, trauma and floor transfer.

Results: There are approximately 115 admissions per month to this 16 bed ICU for a total of 575 admissions for the study period. From 6 PM to 6 AM, 276 (48%) admissions occurred encompassing 88% of trauma patients and 79% of floor transfers. The time distribution was constant for each month and the incidence of postoperative, direct admission, and floor transfer was also constant from month to month, while the incidence of trauma admissions was higher in July and August.

Admission	6 am–6 pm	6 pm–6 am	Total
Postoperative	261 (70%)	114 (30%)	375 (65.2%)
Direct admission	12 (48%)	13 (52%)	25 (4.4%)
Trauma	13 (12%)	99 (88%)	112 (19.5%)
Floor transfer	13 (21%)	50 (79%)	63 (10.9%)
Total	299 (52%)	276 (48%)	575 (100%)

Conclusion: Fifty percent of admissions to the DUMC SICU occur during off-hours when traditionally there has been no attending level in-house supervision. The high percentage of trauma and floor transfers during off-hours validates this reorganization of ICU staffing and around-the-clock supervision.

P248 Preliminary data: PIM and Prism in infants and children post cardiac surgery in a UK PICU

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Objective: To describe the predictive and calibration capabilities of PIM and PRISM in infants and children following cardiac surgery.

Design: Between December 1997 and November 1998, 250 consecutive infants and children were studied. No child died in theatre. There were; 53 patients <1 month, 75 from 1 month–1 year and 122 >1 year. Median age 11.43 months (range 0.02–229). Survivors were defined by ICU discharge.

Results: Crude mortality was 6% (15/250) all deaths occurred in children <1 year old. Median age of death (range) was 0.33 months (0.02–11.83). Median time (range) to death was 53 h (2–264).

Table. Observed vs (predicted) deaths and area under the ROC curve for PRISM and PIM

Mortality%	<1	1–4.99	5–14.99	15–29.99	>30	Total	ROC
PRISM	0 (0.42)	0 (2.8)	5 (3.22)	4 (3.96)	6 (5.78)	15 (16.1)	0.93
No.	73	113	33	19	12	250	(0.88-0.97)
Mean risk	0.58	2.52	9.78	20.88	48.22		
PIM	0 (0.24)	3 (3.79)	4 (1.99)	4 (4.64)	4 (3.19)	15 (13.8)	0.87
No.	30	177	22	22	8	250	(0.77-0.99)
Mean risk	0.79	2.14	8.68	21.08	39.8		

Calibration using the Hosmer-Lemeshow goodness of fit test, showed a χ^2 16.15, df 8, significance 0.04 for PRISM and χ^2 17.05, df 8, significance 0.03 for PIM. Using a cut off at $P = 0.5$, sensitivity and specificity for PRISM was 98.3% and 33.3%, and 99.2% and 26.7% for PIM.

Conclusion: Neither PRISM, nor the new scoring system PIM are well calibrated for predicting individual mortality. However, despite the small numbers, the area under the ROC plot for PIM compares favourably with the original work by Shann *et al.* [1] (0.87 vs 0.83). Therefore we would concur with their conclusion that PIM is accurate enough to describe the risk of mortality in *groups* of children, and has the added advantage of needing less data collection than PRISM.

Reference

1. Shann *et al.*: *Intensive Care Med* 1997; **23**:201-207.

P249 Does intensive care improve outcome?

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Crit Care 1999, **3 (suppl 1)**:P249

Introduction: 'Does intensive care improve outcome?' is a question of fundamental importance. It is unlikely to ever be answered conclusively, because of ethical constraints on performing a controlled study of two groups randomised to ICU admission or no ICU admission. It is possible however, to assess ICU admission as an independent predictor of survival when considered alongside other possible predictors.

Method: Prospective cohort study of all adult patients referred for emergency admission to the only adult ICU of a university hospital during a 3-month period. Because of the limited number of alternative ICU beds patients refused admission are not transferred to an ICU in another hospital. Exclusion criteria were: direct ICU transfers from other hospitals, patients referred when the ICU was full, patients with acute burn injury and cardiac surgery patients. (The latter two groups were excluded from the original MPM II derivation and validation sets). MPM II_0 score was calculated for each patient and the following data were collected: sex, referring specialty, APACHE II diagnostic weighting, admission or refusal of admission to ICU and hospital survival. MPM II_0 consists of 14 physiological and diagnostic variables and is the only severity scoring system available at ICU admission. Logistic regression analysis using a forward stepwise conditional method was performed using SPSS for Windows. Variables included as possible predictors of survival were sex, MPM II_0, APACHE II diagnostic weighting, ICU admission, and interactions between admission and MPM II_0, and admission and APACHE II weighting.

Results: Three hundred and eighty-three patients were studied of whom 229 were admitted. Low MPM II_0, low APACHE II diagnostic weighting and admission to ICU were found to be independent predictors of hospital survival with a hospital survival odds ratio for ICU admission/ refusal of 2.41 (95% CI: 1.48–3.93).

Discussion: This result demonstrates that admission to ICU is an independent predictor of survival when compared with available likely predictors. It is unlikely that the association between admission and survival is due to selective admission of those patients more likely to survive as the association was independent of severity of illness, type of illness and sex. Our results therefore strongly support a positive answer to the question 'Does admission to ICU improve outcome?'.

P250 Comparison of the APACHE II, MEES and GCS in patients with nontraumatic coma for prediction of mortality

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Crit Care 1999, **3 (suppl 1)**:P250

Introduction: Due to the numerous prehospital descriptive scoring system it is uncertain whether they are efficient in the description

of how serious illness are and furthermore whether they can have prognostic role in the estimation of the illness outcome (what is their validity in connection with the prognostic scoring system APACHE II).

Methods: In prehospital setting were collected from each patient postintervention values of the MEES and GCS. The APACHE II score were recorded on the day of admission to hospital. This study was undertaken over a 2 year period (January 1996 to October 1998) and included 286 consecutive patients hospitalized for nontraumatic coma. Patients less than 16 years old were not included. There were 168 men and 118 women. Their age varied from 16 to 87 years with a mean 51.8 ± 16.9. Sensitivity, specificity and correct prediction outcome measured by the χ^2-method in four severity scores. The Youden Index was also obtained. The best cutoff point in each scoring system was determined by the Youden index. The difference in Youden index was calculated by Z score. A P value <0.05 was chosen to reject the null hypothesis. For each score receiver operating characteristically curve (ROC) were obtained. The difference in ROC was calculated by Z score.

Results: For prediction of mortality, the best cutoff points are 19 for APACHE II; 18 for MEES and 5 for GCS. The Youden index has best cutoff point at 0.63 for APACHE II, 0.61 for MEES and 0.65 for GCS. Correct predictions outcome (%) was for APACHE II 79.9 ± 1.6; for MEES 78.3 ± 1.9 and for GCS 81.9 ± 1.5. The area under ROC is 0.86 ± 0.02 in the APACHE II; 0.85 ± 0.06 in the MEES and 0.88 ± 0.03 in the GCS. There was no statistical differences among APACHE II, MEES and GCS in terms of correct prediction outcome. Youden index and the area under ROC ($P < 0.05$).

Conclusion: APACHE II is not much better than prehospital descriptive scoring system (MEES and GCS). APACHE II and MEES may not replace the role of GCS in the prediction mortality in nontraumatic coma. For the assessment of mortality the GCS score provides the best indicator for these patients (simplicity, less time-consuming and effective information, especially in an emergency situation).

P251 Application of prognostic score to patients following cardiac arrest

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Crit Care 1999, **3 (suppl 1)**:P251

Introduction: The use of prognostic scores in continuous form may help in decision-making in the post-resuscitation phase following cardiac arrest.

Objective: To evaluate the clinical efficacy of a prognostic score [1] on intrahospital mortality of patients suffering extrahospital cardiac arrest.

Material and method: A 6 month prospective study carried out on 37 patients in the Emergency Unit of a 650 bed hospital (attending to a total of 74 000 patients per year). A score of 0–6 based on cardiac rhythm at time of arrest was applied (cardiac rhythm different to ventricular tachicardia without pulse or ventricular fibrillation = 3). Glasgow score at the time of admission (4 or 5 = 1 and 3 = 2) and type of cardiopulmonary resuscitation received up to arrival of Emergency Assistance (no first aid from qualified personnel at time of arrest = 1).

Results: Average age was 61.8 ± 14.9 years (29–84), with sex distribution of 59.4% male and 40.5% female.

Conclusion: 1 The application of this score may prove useful in clinical practice to evaluate the continuity of life-support. 2 Neurological assessment is the most valuable clinical variable for prognosis in the follow-up phase. 3 As in other studies, age is not a determining factor in intrahospital mortality following cardiac arrest. 4 Median arterial pressure shows a difference of some 20 points between the surviving and non surviving groups. 5 Mortality among males is significantly greater than females after receiving CPR. 6 The type of assistance received prior to arrival of health services is of significant value in the survival chain.

Reference

1. *Lancet* 1995, **346**:417-421.

		Survival						
Variables		Yes			No			
		No	%		No	%	Total no	*P**
Males		3	27		19	73	22	0.009
Score:	1–2	6	75		2	25	8	0.002
	3–4	5	26		14	74	19	
	5–6	0			10	100	10	
		No	Average	SD	No	Average	SD	*P***
MAP		11	84.4	19.9	20	65.5	30.1	0.07
Age		11	62.9	11.8	26	61.3	15.1	ns
Score		11	2,4	1.5	26	4.3	1.5	0.001

MAP, Median arterial pressure hospital admisssion. *Significant difference between groups, Chi Square. ***t* test.

P252 Outcome of children with near drowning requiring treatment in PICU

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A number of near drowned children needed admission to a PICU due to the severity of their condition. The aim of this review is to illustrate the epidemiology, the clinical features, the management and the outcome of near drowned children admitted to our PICU. For this purpose, we reviewed the charts of near drowned children admitted to our unit during the last 11 years. The study population consisted of 11 children (7 boys and 4 girls) aged 2.5–12.5 years (mean age 7.2 years, SD4,1, SE1.3). At the same period a five-fold number of near drowned children were hospitalized in pediatric wards. The submersion site, among our patients, was sea in 6 cases, a swimming pool in 3, a pond in 2 cases. Ten children were transferred from district hospitals where they had initially received advanced life support. 6/10 children were transferred intubated. 4/10 children were in cardiac arrest after the accident, 3/4 had been given basic life support at the accident site and subsequently 2 of them were intubated on their arrival at the nearest district hospital. 1/4 was intubated in the nearest hospital where he was transferred with brain death without having received appropriate basic life support for about 30 min. 2/3 children who initially were apnoeic and comatose, required intubation. The remaining 4 children had respiratory distress and irregular respiration but only one needed intubation. 8/11 patients have clinical and roentgenographic features of pulmonary oedema. The intubated children remained on mechanical ventilation from 12–36 h. Convulsions occurred in 3 children. In 1/11 patients there were signs of high intracranial pressure with good response to mannitol administration. 10/11 patients survived and discharged from hospital after 3–6 days of hospitalization overall. The patient who was admitted with brain death, never recovered. All survived children had no neurological sequalae on their follow up 2–5 years later. Our results emphasize that even the most severe cases of near drowning have a favorable outcome, provided that the victims are given basic life support at the accident site.

P253 Prognosis related to organ dysfunction in intensive care unit

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Crit Care 1999, **3 (suppl 1)**:P253

Objective: To develop a model for assessing severity of organ dysfunction (OD) among patients on the first 24 h of Intensive Care Unit (ICU) stay, using a score to determine the probability of ICU mortality.

Design: Prospective cohort study.

Setting: General medical and surgical ICU in a tertiary teaching hospital in City of São Paulo, Brazil.

Patients: Three hundred and seventy-eight consecutive, unselected patients over the period from March to October of 1996: developmental sample. Three hundred patients over the period from February to June of 1997: validation sample.

Outcome measure: Patients vital status at ICU discharge. None intervention was considered.

Statistical analysis: APACHE II score was calculated for all patients. A Lowess Regression model, using the variables that demonstrated $P \leq 0.10$ in the univariate analysis was made to identify the level of severity of each variable. The variables were then entered into a multiple logistic regression analysis resulting in a probability of ICU mortality equation. The Goodness-of-fit test was used to evaluate model calibration; discrimination was evaluated using area under the receiver operating characteristic curve (ROC), in the developmental and validation samples.

Main results: OD was considered in five systems: neurologic, pulmonary, renal, cardiovascular and hematologic, plus the presence of chronic disease. The points were assigned from 1 to 4 according to the levels of severity (Table). The results showed good calibration ($P = 0.96$; $C = 2.33$; $dF = 8$ and $P = 0.90$; $C = 3.01$; $dF = 10$) respectively in the developmental and validation samples, and good discrimination (ROC curve of 0.81 and 0.82, respectively).

Conclusion: Cardiovascular dysfunction was the most severe organ dysfunction, followed by pulmonary, renal and neurologic dysfunction. Hematologic dysfunction and the presence of chronic disease were less severe. This model can be used as end point in epidemiologic studies of organ dysfunction in our ICU when the points are summed according to the horizontal lines (severity within an organ system), or as a predictor of death when the points are summed vertically, once the β is the same for all variables.

	0	1	2	3	4
GLASGOW Coma Scale	15–14	13–9		≤8	
Mean blood pressure (MBP) Heart rate (HR)	MBP >70 and HR <140	MBP <70 and HR ≤120	HR ≥140 or MBP <70 and HR >120		MBP <50
(A–a) DO_2	<200	200–349	350–549	≥550	
Creatinine (ARF)	até 1.4	1.5–1.9	2.0–3.4	≥3.5	
Hematocrit	≥30	<30	≤20		
Chronic disease	não		sim		

ARF, Acute renal failure

P254 Characteristics of patients with sepsis and multiple organ failure in the UK

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Crit Care 1999, **3 (suppl 1)**:P254

Introduction: This study examined the characteristics and ICU outcome of patients admitted with severe sepsis and compared them with patients who develop severe sepsis after admission to the ICU.

Method: The Riyadh Intensive Care Program (RIP) database 1989–1996 contains 28 094 complete demographic data, daily APACHE II and TISS scores from 21 UK ICUs. 2790 patients retrospectively satisfied the criteria of severe sepsis and multiple organ failure.

Results: See Table.

Conclusion: The timing of development of severe sepsis and multiple organ failure appears to be an important factor for outcome with a significantly higher mortality among those admitted with sepsis. The admission APACHE II score and the score on the day of development of sepsis were lower among those who developed sepsis. This may be attributable to these patients already being in the ICU environment and thus receiving closer monitoring and more timely intervention. This finding may be of importance in the design of future trials to evaluate new treatment modalities.

All severe sepsis and multiple organ failure patients

	Total	Survivors	Non-survivors	*P*
n (%)	2790	1162 (41.6%)	1628 (58.4%)	
Mean age (SD)	60.2 (16.7)	58.5 (17.7)	61.5 (15.9)	<0.001
Admission Apache II (SD)	21.5 (7.6)	19.1(7.1)	23.2 (7.5)	<0.001
Apache II on 1st day of sepsis (SD)	22.6 (7.5)	19.7 (6.9)	24.7 (7.2)	<0.001
No organ failures (SD)	2.3 (0.6)	2.2 (0.5)	2.4 (0.7)	<0.001

Differences between those admitted with and those that developed sepsis

	Admitted with	Developed	*P*
n (%)	782 (28%)	2008 (72%)	
Mortality (%)	491 (62.8%)	1137 (56.6)	0.003
Mean age (SD)	59 (17.3)	60.7 (16.5)	0.01
Admission Apache II (SD)	25.8 (7.2)	19.8 (7.0)	<0.001
Day of sepsis Apache II(SD)	25.8 (7.2)	21.4 (7.2)	<0.001
No organ failure (SD)	2.5 (0.7)	2.3 (0.7)	<0.001

P255 Important factors for the modelling and design of clinical trials for severe sepsis and multiple organ failure

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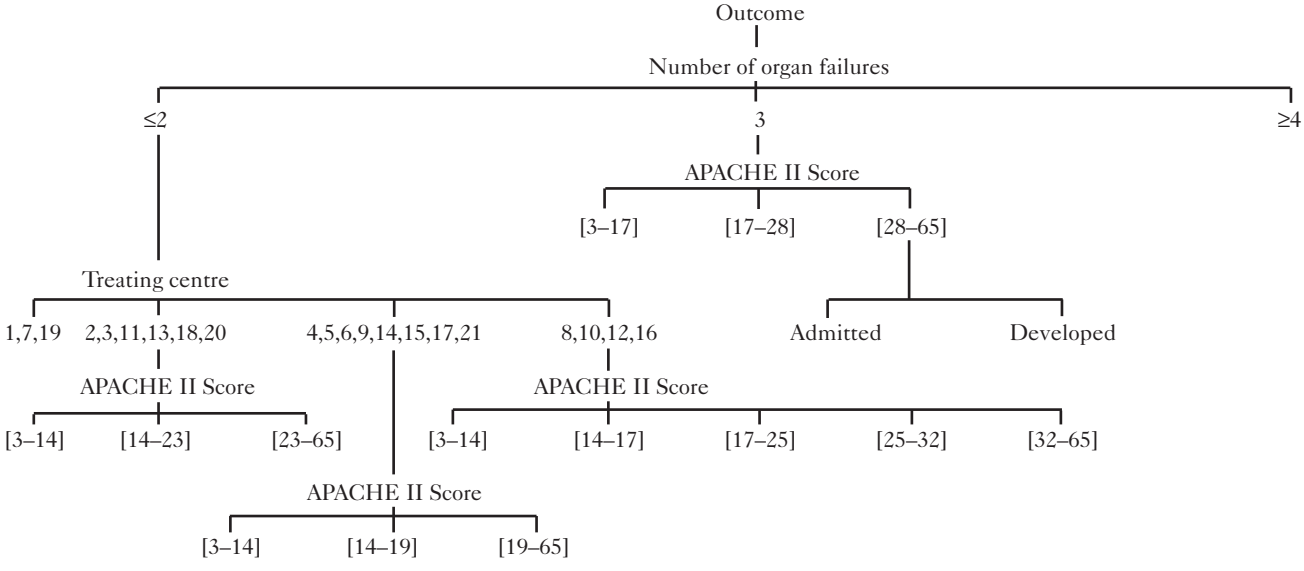
Crit Care 1999, **3 (suppl 1)**:P255

Introduction: No large, well-controlled, trial has been able to demonstrate a statistically significant and reproducible benefit of experimental treatment in severe sepsis and multiple organ failure. This study was done to determine the factors that have to be controlled for in future design of clinical trials in sepsis.

Method: 2790 patients from the RIP database satisfied the criteria of severe sepsis and multiple organ failure. Logistic regression



analysis was carried out to determine the factors that influenced ICU outcome. The CHAID model of an expert system AnswerTree (SPSS, UK) was also used to derive decision rules that govern the outcome of these patients.

Results: Of the eight independent variables entered into the logistic regression analysis four in order of importance were selected: APACHE II score on the day of development of sepsis, treating centre, number of organ failures, age. The area under ROC was 0.75. The level and branches of the decision rules by the expert system is shown in the Figure on the previous page. The difference in outcome for all the nodes is $P < 0.0001$

Conclusion: As the area under the curve of the ROC = 0.75, one is unlikely to use logistical regression analysis to risk stratify patients for future trials of severe sepsis; however, expert systems can delineate statistical significance and patterns which influence outcome in a complex trial population.

P256 Does SOFA and TISS scores correlate in long term ICU patients?

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Crit Care 1999, **3 (suppl 1)**:P256

Introduction: SOFA score is a useful tool for monitoring of organ function in ICU patients [1]. TISS score is used for measuring of workload in intensive care [2]. We studied if there is any link between SOFA and TISS scores in long term ICU patients (i.e. patients staying in the ICU >3 days).

Materials and methods: Daily SOFA and TISS scores of ICU patients admitted between July and November 1998 who stayed in the ICU >3 days were retrieved from data collection system. An experienced ICU doctor has collected SOFA scores into this system daily. Pooled scores for the whole group, for ICU survivals (S) and nonsurvivals (NS) separately and the scores on the first day of ICU stay were analysed.

Results: Sixty-two patients (i.e. 42% out of total admissions; age 60.0 ± 14.7 years) fulfilled the inclusion criteria and stayed in the ICU for the mean of 11.9 ± 10.8 days). ICU mortality was 30.6% (19 patients). Significant correlation was found for pooled SOFA and TISS scores ($r^2 = 0.52$, $P < 0.0001$) and it was more pronounced in survivals (S) than in nonsurvivals (NS) ($r^2 = 0.52$, $P < 0.0001$ and $r^2 = 0.19$, $P < 0.0001$, respectively). Significant link between the two scores was already present on the first day of ICU stay ($r^2 = 0.54$, $P < 0.0001$).

Conclusion: In long term ICU patients a significant correlation is present between organ failures (scored by SOFA) and workload (measured by TISS). This link is already present on the day of admission and later on is more pronounced in survivals possibly because in NS the care is more often witheld or withdrawn.

References

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2. Dickie H *et al.*: **Relationship between TISS and ICU cost.** *Intensive Care Med* 1998, **24**:1009-1017.

P257 Daily SOFA scoring for ICU patients?

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Crit Care 1999, **3 (suppl 1)**:P257

Introduction: SOFA might be a useful tool for monitoring of organ function in ICU patients [1]. We evaluated optimal frequency of SOFA acquisition in long term ICU patients (i.e. patients staying in the ICU >3 days).

Materials and methods: Daily SOFA scores of ICU patients admitted between July and November 1998 who stayed in the ICU >3 days were retrieved from the data collection system. An experienced ICU doctor has collected SOFA scores into this system daily. Original daily SOFA score flow charts and adapted (simplified) SOFA score flow charts (SOFA on days 1, 4, 7, 10, 14, 21, 24, 28 etc.; i.e. values of unlisted days expressed as trends between data collection days) were compared for individuals and the whole group of patients. Data are presented as means ± SD; $P < 0.05$ was considered significant.

Results: Sixty-two patients (i.e. 42% out of total admissions; age 60.0 ± 14.7 years) fulfilled the inclusion criteria and stayed in the ICU for the mean of 11.9 ± 10.8 days. ICU mortality was 30.6% (19 patients). Original and adapted data did show equal values for the whole group of patients (MANOVA group by time effect 0.98 at Day 4, 62 patients and 1.00 at Day 7, 36 patients). Out of total 736 ICU days, in 374 there was theoretical possibility of data difference (adapted SOFA scores). Significant difference (defined as ΔSOFA >2) between original and adapted values was found in 64 cases (17.1%) In 30 cases adapted values were higher then original ones.

Conclusion: SOFA score collected 2–3 times a week describes sufficiently characteristics of long term ICU patients. Significant individual data might be lost when SOFA score is not collected on daily basis.

References

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P258 Evaluation of the SOFA (Sepsis-related Organ Failure Assessment) Score in 303 consecutive patients of a medical intensive care unit

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Objectives: The SOFA (sepsis-related organ failure assessment) score describes quantitatively the degree of organ dysfunction. Although primarily not designed to predict outcome any assessment of morbidity must be related to mortality to some degree. We therefore investigated whether an increasing SOFA score is associated with a higher hospital mortality in patients (pts) of a medical intensive care unit (ICU).

Methods: All consecutive pts who stayed >24 h in ICU were included in this prospective study between 11/97 and 2/98. SOFA score and SAPS II were determined after 24 h. Discrimination power of the scores for survivors (S) and non-survivors (NS) [hospital mortality] was assessed by the area under the Receiver Operating Characteristic (AUROC) curve.

Results: 303 pts (216 male [71.3%], 62 ± 12 years, length of ICU stay 3.7 ± 4.7 days, SOFA 2.5 ± 2.9, SAPS II 26 ± 12.6) were studied. Hospital mortality was 14.5%. SOFA score for NS was significantly higher than for S (5.9 ± 3.7 vs. 1.9 ± 2.3, $P < 0.05$). The AUROC was 0.82 ± 0.04 for the SOFA score and 0.77 ± 0.04 for SAPS II.

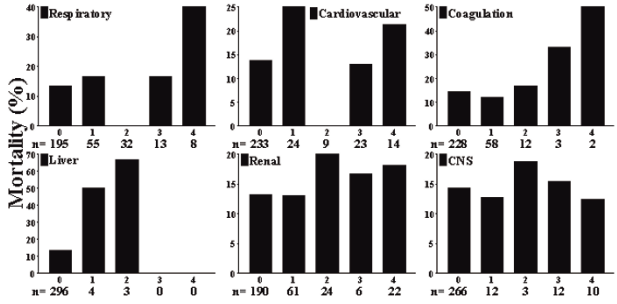

Figure. Mortality (%) versus SOFA score.

Conclusion: SOFA score discriminates well between S and NS 24 h after admission. Respiration, liver and coagulation showed an increasing mortality rate with a higher SOFA score for each organ. Although the SOFA score was primarily designed for use in septic patients it may be also applied for pts of a medical intensive care unit.

P259 Statistical modeling of prognostic indices

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Introduction: Severity scoring models can provide accurate outcome prediction but their performance is very influenced by variations in patient case-mix. Therefore, none of the usual scoring systems (APACHE II, SAPS II and MPM 24) fitted to this ICU: they had good discriminatory power but poor calibration. Logistic regression analysis of their variables was performed to identify the most predictive association to ICU mortality.

Methods: Data of 823 consecutive patients (pts) admitted to the ICU were prospectively collected. Pts who stayed less than 24 h at the ICU or were burn or had less than 16 years old were excluded. For pts with several admissions, only the first ICU admission was considered. The remaining 709 pts were divided in two groups: 418 (59%) pts constituted the development set and 291 (41%) pts became the validation set. After calculating the scoring indices, their variables and respective weights were separately analysed. Variables with P value <0.05 at univariate analysis were included as independent variables at logistic regression and vital status at ICU discharge was considered as dependent variable.

Results: There were 67% male and 33% female pts; median age was 46 years old, postoperative care took up 330 (46.7%) cases, of which 275 (83%) were emergency surgery. Trauma was the admission cause for 200 (28%) pts. ICU mortality rate was 25.1% and

	Variables	Points assigned as	β	*P*	OR
	Age	SII	0.0266	0.000	1.1187
Neurologic	Glasgow coma scale	AII	0.3325	0.000	1.3945
Cardiovascular	Heart rate	AII	0.3802	0.017	1.4627
	Vasoactive drugs	M24	0.7928	0.019	2.2095
Respiratory	Oxygenation	AII	0.2997	0.005	1.3494
Infectious	Temperature	AII	0.4433	0.022	1.5579
	WBC count	SII	0.2571	0.014	1.3120
	Infection present	M24	0.7692	0.013	2.1582
Urinary	Serum creatinine	AII	0.1852	0.003	1.2034
	Urine output	SII	0.1310	0.041	1.1400

APACHE II, AII; SAPS II, SII; MPM 24, M24, OR, odds ratio

hospital mortality 33.7%. APACHE II was 16.7 ± 8.4 and SAPS II was 33.5 ± 16.5. Through statistical modeling, an hibrid model was generated, with variables and points from the three indices. With this model, the prediction obtained was: development set with discrimination ROC = 0.89 and calibration goodness-of-fit C = 1.68 and validation set with ROC = 0.84 and goodness-of-fit C = 7.72.

Conclusion: Hemodynamic instability, infection, impaired renal function, respiratory failure and coma were the best predictors of death. Early identification of patients at major risk may allow treatment with more resources and interventions, in order to improve survival. Furthermore, this study shows that suitable statistical management may be useful to customize and enhance the prognostic accuracy of the currently available scoring systems.

P260 The determination of the duration of the nursing activities in the intensive care unit and the therapeutic intervention scoring sysem (TISS)

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The purpose of this study was to calculate nurse/patient radio by using TISS-28, and to assess time allocation to nursing activities in the intensive care unit. In this study the TISS scores of 416 patients were calculated in the intensive care unit 10 weeks long using the TISS-28 form. In order to determine the duration of the nursing care activities due to nursing care categories the work sampling method was used. A sampling matrix for 10 weeks was created and the nursing care activities were observed 7 days a week for two day shifts (08.00–16.00). The data collection instruments were, the 'TISS-28' and 'Work sampling form for intensive care unit nursing activities'. The TISS-28 point for ICU was 40.41 for day shift. One TISS-28 point equals 11.88 min of the 480 min in each shift. Related literature shows that nursing care activity for one day makes 40–50 TISS score. The percentage of nursing time spent on nursing activities in the ICU was calculated by using work sampling. Results indicated that 44.25 % of nurses time was spent in activities in TISS-28; 12.87% in activities not in TISS-28; 25.8% in indirect patient care, 6.21% in organnizational activites, 10.64% in personnel activities and 0.15% in other activities. It is shown that category one represents TISS-28 and that the increase in TISS score results in the increase in nursing care activity duration. These result show that the TISS-28 can be useful to determine the patient/nurse ratio in intensive care units.

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P261 Fast-track intensive care procedure after cardiac surgery in the 9th decade

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Objective: Outcome with fast track intensive care medicine after cardiac surgery in patients older than 80 years.

Methods: Between 7/96 and 7/97, 86 cardiac operations (3.7%) have been performed in patients older than 80 years out of an overall number of 2349 cardiac operations. Preoperative NYHA Status was III in 36.1% and IV in 46.5% of the old patients. LVEF was 49%, LVEDP 16 mmHg. Additional desaeses were: diab. mell. 23.3%, renal insufficiency 11.6%, cerebral stroke 10.5% and myocardial infarction 37.2%. Performed cardiac operations have been: CABG (61.6%), AVR (23.3%), CABG and AVR (12.8%), MVR (1.2%), CABG and MVR (1.2%) and REDO operations (4.6%). Mean time on ECC was 84 min and overall operation time was 169 min (mean). Anesthesia was conducted as balanced anesthesia with early extubation as a main aim.

Results: Patients were extubated 6 h (median) after surgery, shortest duration of ventilation was 30 min. Mean stay on ICU was 2.6 days and mean time of hospitalisation was 9.4 days. 30-day-mortality was 3.4% in the old patients and 2.2% in the overall population.

Conclusion: Fast-track procedure after cardiac surgery in the octanarian is feasible with even better results and without any additional risk than conventional intensive care procedure.

P262 Prognosis and functional capacity a year after a myocardial infarction on elderly 80-year-old patients

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Objective: To evaluate prognosis and functional capacity a year after a myocardial infarction (MI) in elderly 80-year-old patients.

To analyse differences between sex, localization and developed or no Q wave.

Design: Retrospective analysis.

Patients: All patients of ≥80 years admitted between 1.1.94 and 31.10.97 with a myocardial infarction.

Evaluation of evolution curve: The study was done through telephonic interview. We analysed mortality at the reception (REC), 1, 3, 6, 9 and 12 months (M). Was used a daily activity scale (DAS) with five factors (walking, dressing, bathing, cleaning and eating) with a punctuation from 0 to 2 every activity (0 = total dependence, 1 = partial dependence and 2 = independence), with a range 0 to 10.

Statistical analysis: The statistical significance of the variables was tested by Fisher's test of *t* Student test. Values less than 0.05 were considered statistically significant.

Results: We included 112 patients, 54 (48.21%) male and 58 female. The localization of the myocardial infarction was anterior (Anter) in 71 cases (63.39%) and inferior (Infer) in 41, and 87 patients (77.67%) developed Q wave. At the reception 41 (36.60%) patients dead and 16 patients dead at the following 12 months (accumulated mortality at year = 50.89%). Q wave and anterior myocardial infarction had more mortality, with $P < 0.001$ and $P < 0.05$ respectively. At year, the survivors had a mean DAS 8.72 ± 1.89. It was higher in non-Q wave ($P < 0.05$) and males ($P < 0.05$).

The evolution is shown in the Table.

Conclusion: Though the mortality between elderly 80 years old patients with myocardial infarction is high, they have an acceptable functional capacity (more in males and non-Q-wave myocardial infarction).

	Patients with MI	Exitus REC	Exitus 1° M	Exitus 3° M	Exitus 6° M	Exitus 9° M	Exitus 12° M	DAS at year
Total	112	41	47	49	51	56	57	8.72 ± 1.89
With Q	87	39	45	47	48	52	52	8.33 ± 1.88
Non-Q	25	2	2	2	3	4	5	9.36 ± 1.72
Anter.	71	30	34	36	37	39	40	8.57 ± 2.03
Infer.	41	11	13	13	14	17	17	9.01 ± 1.54
Female	58	24	26	26	28	31	31	8.13 ± 2.09
Male	54	17	21	23	23	25	26	9.35 ± 1.39

P263 Very old patients (older than 85 years) at a medical ICU: indications, interventions, outcome

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Crit Care 1999, **3 (suppl 1)**:P263

Objective: The part of elderly people in the population has been increasing during the last decades. In 1995, 16% of the Middle-European population have been older than 65 years, up to the year 2010 there should be an increase up to 22%. German investigations have shown, that a 1/3 of the population older than 65 years are suffering from 3–4 chronic diseases, 98% of the population older than 80 years from one chronic disease.

Through those facts the number of old patients admitted to ICUs is increasing. Aim of following paper was to objective the treatment and outcome of very old patients (over 85 years) at a medical ICU of a general hospital over an 18-month period (1997-01-01 to 1998-06-30).

Results and outcome: 899 patients had been admitted to the ICU during the study period, 48 (5.3%) older than 85 years. At admission the APACHE II-score ranked between 19 and 32. Indications had been mainly cardial (27), metabolic (8), gastrointestinal (6), outside CPR (5) and acute respiratory failure (2). 11 patients had been mechanical ventilated (1–8 days, mean 2.7 days), 6 patients received a cardiac pacemaker, 5 underwent endoscopical interventions, 4 thrombolysis (AMI, 100 mg Alteplase 'front loaded'), 2 patients PTCA/IABP and one female patient ACBG.

Duration of stay had been 3.8 days (overall 3.9 days), mortality 27.7% (overall 14.8%).

Conclusion: Comorbidity and mortality had been higher in patients older than 85 years compared to all patients. 6 month after the ICU stay 24 patients (68.5%) were still alive. With good quality of life. Despite higher mortality very old patients benefit from ICU stay and interventions.

P264 Quality control with autopsy on a medical intensive care unit

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Postmortem examination is considered as the golden standard for the evaluation of clinical diagnosis. However due to several reasons (costs, permission of family members), few medical

centers continue to perform autopsy as a means of quality control. From 1995 to 1996, we performed an autopsy study in a medical intensive care unit of a university hospital: 93% of the 140 deceased patients in our medical ICU underwent an autopsy, 100 consecutive patient files were studied.

The clinical diagnosis were made by internists, specialized in intensive medicine; the diagnosis on autopsy were made by a pathologist. According to the criteria of Goldman[1], the clinical and autopsy findings were categorized into major and minor diagnoses. A missed diagnosis on clinical grounds was classified as a class I error (if detected before death, this would probably have caused a therapeutic change with possible altered outcome) or as a class II error (if known before death, this diagnosis would not have led to a change in therapy).

In 16% of the patients, a class I missed diagnosis was detected (cardiac tamponade, myocardial infarction, fungal pneumonia); in 9%, a class II missed diagnosis was detected (most frequently tumors). Sometimes the diagnosis was missed due to a combination of severe, acute problems (e.g. development of cardiac tamponade after insertion of a venous catheter during hemorraghic shock), or due to a lack of sensitive and specific investigational methods (fungal pneumonia is frequently suspected in immunocompromised patients, but is often difficult to confirm), or due to logistic transportation problems in the hemodynamically unstable patient (e.g. retroperitoneal hemorrhage is not always detectable on bedside echography; for diagnosis, CAT-scan is needed).

Conclusion: Even in the era of increasing diagnostic possibilities, due to improved medical technologies in the ICU, postmortem examination still remains useful in detecting unexpected diagnoses, missed in the premortem clinical evaluation. Our observations suggested the need for constant alertness and an aggressive investigational planning in patients with unexplained shock or pulmonary infiltrates.

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P265 Quality of life before and after medical intensive care

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Introduction: We prospectively analysed changes in the quality of life (QOL) in patients before and 6 months after admission to a medical intensive care unit (ICU).

Patients and methods: All patients admitted to the ICU were eligible for inclusion. Patients <18 years and those who died or were discharged within 24 h of admission were excluded, QOL measures were collected during interview during the first 24 h of ICU stay and 6 months after admission using a questionnaire especially designed for ICU patients developed by the Spanish Group for Epidemiological Analysis of Critical Care Patients [1]. Baseline QOL referred to the 2 months prior to admission and were compared with measures at 6 months using Wilcoxon matched-pairs test, $P < 0.05$ was considered statistically significant.

Results: During the first 12 months of the study period 326 patients met the study criteria; mean age was 58 ± 17 (± SD) years, median 60, range 19–95 years, 55% were male. Mean ICU length of stay was 10.4 ± 15.1 days, range 2–127 days. Mean APACHE II score was 23 ± 10, range 0–51. Mean TISS score after 24 h was 33 ± 14, range 0–69. Mortality rates were: ICU 24%, hospital 6%, 9% within the following 6 months after hospital discharge. Up to now 147 patients completed the questionnaire after 6 months, six patients (1.8%) were lost to follow-up. Relative to baseline a significant worsening was noted in the subscale of normal daily activities ($P = 0.013$). No significant changes were seen in total QOL score ($P = 0.25$) an the subscales of physiologic basic activities ($P = 0.06$) and emotional state ($P = 0.09$). No correlation existed between APACHE II scores and QOL ($r = 033$).

Conclusion: Six months after ICU treatment patients had a significant decrease in the level of their daily activities. Basic physiologic activities and emotional status are not significantly altered. 90% of the long-term survivors were living at home and all previously occupied patients were able to return to their previous profession.

Reference

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P266 Withdrawal of intensive care in the patient's home

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Death should be managed as vigorously as life saving. Historically intensive therapy is withdrawn in the intensive care unit, but we would like to present four cases where intensive care treatment was withdrawn at home. The staff of the Intensive Care Unit at Middlemore Hospital have taken four patients home, on ventilatory and inotropic support, and withdrawn care when the patient was settled in their home, surrounded by family. This is felt to aid in the grieving process, and in many cases is culturally desirable. The cases thus far are subarachnoid haemorrhage, massive intracerbral bleed and intractable septic shock. From our experience we recommend that certain selection criteria are observed. There is a need for the patient and family to live locally, support is required from the local general practitioner and district nursing service, and a clear explanation of the whole process must be understood by all family members prior to leaving the intensive care unit. A palliation plan must be commenced prior to leaving the intensive care unit.

We see this as a practical option in selected intensive care patients.

P267 Results of an ethical questionnaire distributed to members of the Australian and New Zealand Intensive Care Society

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Three hundred and sixty-seven (67%) of questionnaires on ethical issues distributed to members of the Australian and New Zealand Intensive Care Society were returned and included for analysis. The questionnaire was similar to a questionnaire that had been distributed to members of the European Society of Intensive Care Medicine, but adapted and augmented for local use, and provides a useful comparison of how issues are considered in Australasia. Intensive Care beds are a limited resource, and availability restricts admissions. Nonetheless, 76% of respondents admitted patients with a poor prognosis for survival. There was high (82%) concordance of what was felt should be done and what was done in clinical scenarios. Respondents considered that they provided high information to patients, including in the event of iatrogenic complication. In terms of end-of-life decisions, 35% of respondents wrote that they would involve the family in discussions (not an option available for selection): this appeared to be a pragmatic approach to dealing with relatives. Withdrawal of treatment was considered to be different to withholding treatment by 43% of respondents. 34% of respondents would change a do-not-resuscitate order that had been previously instituted. 15% of respondents considered that an Ethics Consultant would assist in their practice, with 95% supporting the inclusion of ethics teaching during medical training.

P268 Withholding and withdrawing life support: national French prospective study

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Introduction: Controversies still exists regarding indications of WH and WD, ethical similarity or difference between WH and WD, the way to withhold or to withdraw treatments and what should be the family implications in these decisions

Aim of the study: To evaluate the reality of withholding and withdrawing life support (WH and WD), the type of withheld and withdrawn treatments and the conditions leading to decisions to WH or WD.

Material and methods: 113 French ICU participated to the study. The following data were collected for all the admitted ICU patients during a 2-month study period: age, sex, SAPS II, main diagnostic, previous chronic disease. In patients for whom WH or WD were indicated, additional data were recorded. The reasons to withheld or withdraw treatments and the type of WH or WD life support treatments were recorded.

Results: Treatments were withheld or withdrawn in 807 out 7309 (11%). WH and WD were indicated in 336 patients (4.6%) and 471 patients (6.4%) respectively. ICU patients undergoing WH or WD were older and had higher SAPS 2 than the remaining patients. Decisions of withhold or withdraw were more frequent in patients with previous chronic diseases or cardiac arrest before admission in ICU. Futility and the poor expected quality of life were the most frequently cited reason for WH or WD. Decision to not ventilate the patient was the most frequently reported withheld treatment ($n = 214$; 15%). Vasopressors were either not started or limited in their dosage in 196 patients (14%). The most frequently withdrawn life support treatment were vasopressors (19%). Extrarenal epuration was discontinued in 67 patients (7%). Lowering FiO_2 to 21% was indicated in 155 patients (14.5%), discontinued ventilation was ordered in 101 patients (9.4%) and extubation was performed only in 34 patients (3.1%). Withdrawal of hydration was rarely performed ($n = 16$; 1.5%). 1176 out of the 7309 (16.1%) included patients died. 628 out 1176 died (53%) after support was withheld or withdrawn. Most of the time WH or WD was decided by the medical team. A unique M.D. was involved in the decision in 37 (12%) of cases. Paramedic (nurses) opinions was taken in account for the decision in 482 (59.7%). Family was involved in the process in less than 50%.

Comments: The reality and the frequency of WH and WD life support treatments have been demonstrated in this large study involving an important number of French ICU.