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MEETING ABSTRACTS

P001

Medical versus surgical treatment in supratentorial intracerebral hemorrhage

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Critical Care 1997, **1(Suppl 1):**P001

Background and objectives: The optimal mode of treatment in spontaneous supratentorial intracerebral hemorrhage (SICH) is controversial. We assessed the value of hematoma evacuation in SICH in a case–control study.
Methods: One hundred and forty-five patients with SICH without tumor or vascular abnormalities. Indication for surgery were made upon admission in 11 and after clinical deterioration in 13 patients. Assessed were age, sex. Glasgow Coma Scale (GCS), pupillary reaction on admission, localisation, etiology and hematoma volume, presence of ventricular blood, and Glasgow Outcome Scale on discharge. From further analysis patients > 80 years or with hematoma volume < 10 ml were excluded. Statistical analysis included: (i) a multiple regression model to determine prognostic factors; (ii) comparison between medical and surgical patients; (iii) matching the 24 evacuated with 24 medical patients according to those parameters retained from the regression model and additionally to other suspected factors influencing outcome; (iv) comparison between both groups to confirm comparability; and (v) testing for different outcome between the groups.
Results: Prognostic factors were GCS, hematoma volume and location. All 24 evacuated patients could be matched to a medically treated patient regarding age, hematoma volume and location. GCS and pupillary reaction. Differences between both groups could not be detected. Outcome was not different between the medical and surgical group.
Conclusions: Hematoma evacuation does not improve outcome in supratentorial spontaneous hemorrhages. Since mainly deteriorating patients were evacuated, the only effect of hematoma evacuation may be to stop deterioration rather than to improve overall outcome.

P002

Is 'brain swelling' a clinical particular kind of severe brain injury?

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Critical Care 1997, **1(Suppl 1):**P002

Introduction: Brain swelling (BS) is a kind of response observed in 15%–20% of severe head injury. Its pathophysiology is not well known yet, and its diagnosis is exclusively scanographic in emergency.
Objectives: To determine a particular difference between BS and the other kinds of severe brain injuries in their epidemiological, clinical, biological signs and evolutive result.
Material and methods: In the past 5 years, among 400 severe brain injured patients (gun shot excluded) with a Glasgow Coma Score ≤ 8.88 (22%) showed scanographic BS: no mass lesion and ventricles, cortical sulcal, basal cisterns effacement.
All patients were treated according to EBIC guidelines and epidemiological, clinical, biological, evolutive parameters were compared to these of the 312 other patients with standard traumatic lesions (STL).
Results: Whereas severity is the same in the two groups (GCS-STL = 5.07 ± 1.76/GCS-BS = 5.05 ± 1.43), three parameters, age, coagulation and evolution are different.
Age: BS is more frequent among young patients (STL = 40.31 ± 20.42 years, BS = 25.92 ± 10.14 years; $P < 10^{-9}$). No patient > 50 years developed BS. Is the reason a higher brain compliance in young patients?
Coagulation: No biological sign is different in the two groups except coagulopathy (STL = 30/254, BS 16/58; $P = 0.02$). More generally, BS patients (haemorrhagic shock excluded) have an intravascular brain thromboplastin rush which seems to show that BS does not result from hyperhaemia only, but from mass commotion too (Table 1).
Evolution: After 6 months, BS patients seem to have a better Glasgow outcome scale in regards with baseline GCS (Table 2).

Table 1 (abstract P002)

	STL = 254	BS = 58	*P*
Platelet (10^9/l)	288 ± 105	145 ± 30	< 0.0001
Prothrombin T (%)	78 ± 14	63 ± 14	< 0.0001
Fibrinogen (g/l)	2 ± 0.6	1.74 ± 0.4	= 0.03

Table 2 (abstract P002)

	STL = 312	BS = 88	*P*
GOS 1–2	95	16	
GOS 3	73	12	< 0.001
GOS 4–5	144	60	

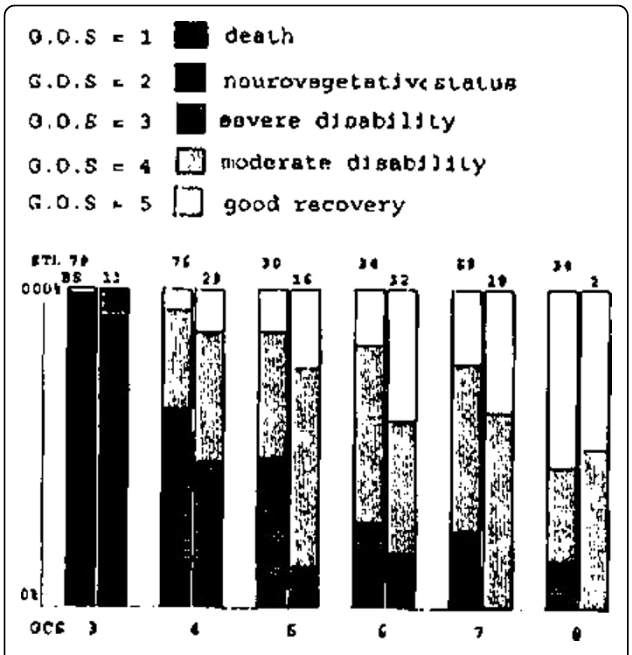

Figure (abstract P002) In BS-GCS = 4-5, death and severe disability are leaded by associated primary brain stem lesion or secondary uniform herniation. In BS-GCS = 6-8, about 95% will get a social activity.

P003

Brain temperature monitoring and modulation in patients with severe MCA infarction

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Critical Care 1997, **1(Suppl 1):**P003

Background and objectives: Brain temperature has been measured only occasionally in humans. After head trauma a temperature gradient in brain temperature compared to body temperature of up to 3°C higher in the brain has been reported. Elevated temperature is known to facilitate neuronal injury after ischemia. At present no information concerning changes in brain temperature after acute stroke is available.
Methods: In 15 patients who had suffered severe ischemic stroke in the MCA territory, intracerebral temperature was recorded using two different thermocouples, with intraventricular, epidural, and parenchymatous measurements. Body-core temperature (Foley catheter temperature) and jugular bulb temperature (n = 5) were recorded simultaneously. Measures for reducing brain temperature were compared.
Results: In all patients brain temperature exceeded body-core temperature by at least up to l°C (range 1.0–2.1°C). Temperature in the ventricles exceeded epidural temperature by up to 2.0°C. Brain temperature modulation was independent of single pharmacological (paracetamol, metamizol) treatments. Only systemic cooling was effective and sustained hypothermic (33–34°C) brain temperatures.
Conclusion: After MCA stroke, human intracerebral temperature is higher than central body-core temperature. There is also a temperature gradient within the brain, with the ventricles warmer than the surface. Mild hypothermia in the treatment of severe cerebral ischemia using cooling blankets is both easy to perform and effective in the therapy of severe hemispheric infarction.

P004

Study on brain protection of mild hypothermia in cardiopulmonary resuscitation

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Critical Care 1997, **1(Suppl 1):**P004

Cardiac arrest (CA) is often followed by postischemic-anoxic encephalopathy. A ventricular fibrillation CA model in dogs was used in this study to understand the effect of oxygen free radical (OFR) and lactate (LA) in the postischemic-anoxic encephalopathy, and to explore the effect and mechanism of mild hypothermia (32-36°C) induced immediately with reperfusion after cardiac arrest (resuscitation).
Results: (i) The SOD levels in blood and CSF after resuscitation were lower than those before CA (P < 0.01), the LPO and LA levels in blood and CSF were significantly higher than those before CA (P < 0.01). (ii) The SOD level in CSF in mild hypothermia group was higher than that in normothermia group (P < 0.05), the LPO level in CSF was significantly lower than that in normothermia (P < 0.01). But the LA level in CSF and the SOD, LPO and LA levels in blood were not significantly different between these two groups, (iii) The total brain histopathologic damage scores in mild hypothermia group were lower than those in normothermia group (P < 0.01).
Conclusions: (i) The OFR and LA have some important effect in postischemic-anoxic encephalopathy. (ii) Mild hypothermia induced immediately with reperfusion after CA may improve cerebral outcome. (iii) The mechanism of this beneficial effect may be to reduce the generation of OFR and to mitigate the lipid peroxidation induced by OFR.

P005

Effects of brain hypothermia for the patients with severe head injury and post-resuscitation encephalopathy

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Critical Care 1997, **1(Suppl 1):**P005

Cerebral and extracerebral effects of mild hypothermia (core temperature 34°C) and moderate hypothermia (32°C) were studied in four patients with severe head injury and two patients in post-resuscitation encephalopathy. According to our cooling criteria, three patients applied in moderate hypothermia, and three patients who were thought to be unable to receive moderate hypothermia applied mild hypothermia. Hypothermia was induced by cooling the patient's body surface with water-circulating blankets within a mean of 6 h. The cooling period was determined with intracranial pressure (ICP) and other monitoring parameters, and the range was 35 h to 9 days. The patients were rewarmed at the rate of 0.5°C per 5 h, and the temperature change was maintained within 2°C in a day.
Good recovery was observed in two out of three patients in the moderate hypothermia group, and two out of three patients in the mild hypothermia group. Two patients died from sepsis and disseminated intravascular coagulation. As to extracerebral effects, patients had more or less systemic complications, including hypotension, paralytic ileus, hypokalemia, and decrease in platelet count. The moderate hypothermia group was likely to have higher incidence and greater extent of complication.
The tendency toward better outcome may indicate that hypothermia for severe head injury and post-resuscitation encephalopathy is effective in recovering the brain damage. Further investigation for indication and method is required.

P006

Midlatency somatosensory evoked potentials and explicit memory functions during recovery from propofol/sufentanil anaesthesia

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Critical Care 1997, **1(Suppl 1):**P006

Adequate anaesthesia and avoiding awareness in patients is of major concern for anaesthesiologists during anaesthesia. In a prospective study midlatency somatosensory evoked potentials (SEP) were investigated in relation to explicit memory function during recovery from propofol/sufentanil anaesthesia.
After approval of the local Ethics Committee and written informed consent 20 patients (43 ± 12 years, 71 ± 14 kg, ASA I-II) were included in the study. Anaesthesia was induced with 0.5 µg/kg sufentanil, 2 mg/kg propofol and 0.1 mg/kg vecuronium. After endotracheal intubation and normo-ventilation with FiO_2 0.3 anaesthesia was maintained with 8 mg/kg/h propofol. SEPs were recorded at Erb, C6 and C4′ (N20, P25, N35, P45, N50) following electrical stimulation of the median nerve (3 Hz, intensity of twofold motor threshold, 200/average, bandwidth 0.02–2 kHz). SEP recordings were performed the day before surgery (AWAKE) and during recovery from anaesthesia, until patients were able to identify a shown object (RECOVERY). Monitoring included HR, MAP, $P_{et}CO_2$, SaO_2, arm and body temperature. The day after surgery patients were interviewed about their memory of the recovery period and classified into two groups: group 1, no memory; group 2, memory for recovery period. Statistics: Student *t*-test with $P < 0.05$ significant. Patients were able to identify a shown object 26 ± 7 min after the end of anaesthesia (RECOVERY). One day after anaesthesia nine patients did remember events during the recovery period (group 2), while 11 patients did not have any memory (group 1). At RECOVERY latencies P45 (45 ± 6 versus 51 ± 4 ms) and N50 (64 ± 12 versus 78 ± 9 ms) were significantly shorter in the patients of group 2 than in group 1 ($P < 0.05$). The earlier midlatency SEP components and amplitudes did not differ between the two groups. In conclusion reversal of anaesthesia induced SEP changes of latencies P45 and N50 may indicate recovery of explicit memory functions after anaesthesia.

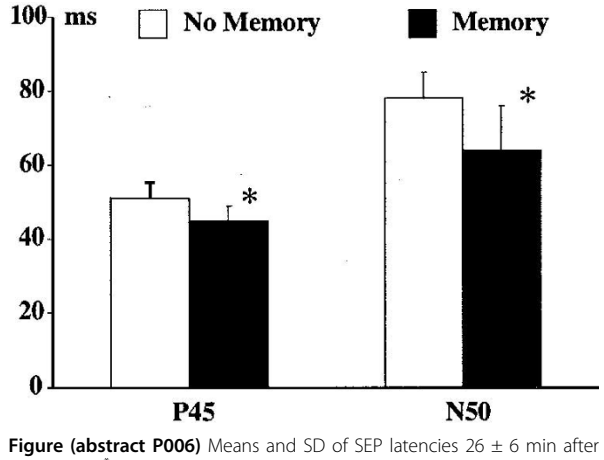

Figure (abstract P006) Means and SD of SEP latencies 26 ± 6 min after anaesthesia. *P < 0.05 between patients with (group 2) or without memory (group1) for recovery period after 24 h; n = 20 patients.

P007

Pulsed ICA Doppler blood flow as a step in brain death diagnosis

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Critical Care 1997, **1(Suppl 1):**P007

Introduction: Confirmation of brain death diagnosis, in addition to clinical examination, requires demonstration absent of cerebral blood flow with conventional cerebral angiography or magnetic resonance angiography. Transcranial Doppler is an alternate method to conventional cerebral angiography that is not invasive and does not require transport of the patient to the radiology department.
Objective: To evaluate the role of ICA Doppler as a step tool in brain death diagnosis.
Setting: A multidisciplinary ICU in our University Hospital.
Patients and methods: Twenty-four patients (mean age 23 ± 3, 15 male, 9 female) with diffuse cerebral edema on CT and had conventional anti-edema therapy were included in the study. In all patients at the time of the study GSC:3, spontaneous respiration (apnea test) and brain stem reflexes (including pupillary, corneal, oculocephalic, vestibulocephalic reflexes, tracheal gag) atropine test were absent.
Bilateral pulsed ICA Doppler blood flow measurements were done with Duplex (ATL ULTRAMARK 9/USA) and recorded. Extracranial blood flow velocity patterns of internal carotid arteries were bilaterally detected through the skin by a directional, 5–10 Hz pulsed-wave Doppler ultrasound.
ICA blood flow cessation was determined by the observation of early and small systolic spikes or reversal of blood flow in diastole.
Results: In I5 patients normal ICA blood flow, in three patients early small systolic spikes and in six patients reversal of blood flow in diastole was observed.
Conclusion: In diagnosis of brain death our experience confirms that extracranial ICA Doppler in bedside is a clinically useful technique to separate the patients for further investigation (carotid angiography or magnetic resonance angiography). For 15 (63.5%) patients we could decide that there is no need for this invasive confirmatory technique. If transcranial Doppler is not available this non-invasive and most routinely available ICA Doppler method can be a good step for diagnosis of cerebral blood flow cessation in clinical brain death.

P008

Relationship between brain tissue oxygen ($PbrO_2$) and cerebral perfusion pressure (CPP)

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Critical Care 1997, **1(Suppl 1):**P008

Introduction: Ischemia is the leading cause of secondary brain damage after severe head injury (SHI). Adequacy of cerebral oxygenation can be assessed by monitoring: cerebral perfusion pressure (CPP), the driving pressure of cerebral perfusion; oxygen saturation of jugular bulb (SjO_2), the ratio between global cerebral oxygen availability and consumption: partial pressure of brain tissue oxygen ($PbrO_2$), the driving pressure of oxygen diffusion to mitochondria at tissue level [1,2].
Methods: Our preliminary evaluation of $PbrO_2$ in 10 patients with SHI (GCS = 8), in which $PbrO_2$ was recorded for more than 7 days along with CPP, is reported. Intracranial pressure (ICP) was measured with an intraparenchymal fiberoptic transducer (Camino Laboratories), $PbrO_2$ was measured with a Cark-Type catheter (Catheter PO_2 Micro-Probe, CMP, Licox GMS, Kiel, Germany); CPP was obtained as difference between mean ABP and mean ICP.
All patients, when ICP increased over 20 mmHg, were treated according to a standard protocol: better sedation; moderate hyperventilation;

Table (abstract P008)

CPP classes	Mean	sd	95% mean	Confidence for the	CPP classes	Mean	sd	95% mean	Confidence for the
40-45	25.79	10.01	24.37	27.20	70-75	37.23	19.76	36.83	37.63
45-50	36.05	10.53	24.96	27.14	75-80	38.35	20.47	37.97	38.74
50-55	25.82	11.73	25.09	26.54	80-85	36.33	20.73	35.95	36.72
55-60	29.60	14.48	28.96	30.24	85-90	35.12	16.53	34.68	35.56
60-65	31.98	18.36	31.46	32.49	>90	28.13	12.58	27.86	28.40
65-70	33.35	19.99	32.91	33.79					

mannitol infusion; barbiturates. Two patients had severe and repeated increases in ICP and eventually underwent surgery for evacuation of hemorrhagic contusion.
Results: Data were collected every minute and analysed recoding CPP values in classes of 5 mmHg between 40 and 90 mmHg and one class for values over 90 mmHg. Using two way analysis of variance with CPP classes and patients as factors, a significant dependency of mean $PbrO_2$ from CPP can be demonstrated.
Conclusions: Although $PbrO_2$, is directly influenced by PaO_2, using appropriate statistical methods and a large number of data, significant low $PbrO_2$ values can be associated to a low cerebral perfusion pressure. Individual $PbrO_2$ values depends from single patient and from PaO_2. It is difficult to define precisely a $PbrO_2$ value that can be used as a target for treatment. With PaO_2 between 80 and 150 mmHg. $PbrO_2$ values between 25 and 40 are expected, but whatever value decreasing in spite of a constant PaO_2 can be regarded is an alarming sign of impinging on cerebral oxygenation

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P009

Usefulness of near-infrared spectroscopy for monitoring a cerebral tissue oxygen saturation during cardio-pulmonary resuscitation (CPR)

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Critical Care 1997, **1(Suppl 1):**P009

Introduction: Near-infrared spectroscopy has been verified to be a reliable monitoring method in detecting a regional cerebral tissue oxygen saturation (rSO_2) in the field of neurosurgery, cardiovascular surgery and neonatal ICU. Cerebral tissue oxygenation is promptly and continuously monitored during resuscitation, and moreover, we can compare the efficacy among the resuscitation techniques with this method.
Materials and methods: In the 40 cardio-pulmonary arrest (CPA) cases, rSO_2 was monitored during CPR with INVOS 3100A (SEMANTICS). A traditional external CPR was started in all cases and an open chest CPR was added in 10 cases. We also measured oxygen saturation of jugular vein (SjO_2) in 14 cases at regular intervals.
Results: Serial changes of rSO_2 were 27.6 ± 10.7% at arrival, 32.7 ± 12.2% during external CPR (n = 20), 36.2 ± 5.8* during open chest CPR (n = 10), and 61.3 ± 10.0% after return of spontaneous circulation (ROSC) (n = 10) (mean ± SD), and synchronous changes were observed according to cessation and re-starting of CPR (*P < 0.02 and **P < 0.03 versus at arrival). SjO_2 was measured in 8.6 ± 3.1 min after the arrival, and initial SjO_2 during external CPR was 16.3 ± 9.8%. In some cases, increased bicarbonate concentration was observed probably due to the reflux from the infusions through central venous catheter.
Conclusions: Near-infrared spectroscopy is rapid, noninvasive, and easily applied monitoring system during resuscitation for CPA patients, and our data demonstrated to be a reliable monitoring method in detecting a cerebral tissue oxygenation. On the other hand, SjO_2 is invasive, time-consuming method, and is not always accurate because of to-and-fro flow.

P010

Selectins in multiple injured patients with severe head trauma

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Critical Care 1997, **1(Suppl 1):**P010

High mortality rates days or weeks after multiple injury are often due to multiple organ dysfunction (MODS). Recent studies put a close view to the course of immunological mediators as the members of the selectin family to figure out their contribution to shock, sepsis and organ failure [1]. Brain contusion is supposed to cause cellular infiltrates and inflammation in brain tissue [2].
P-selectin (CD62P) is stored in endothelial cells (EC) Wiebel-Palade-bodies and in thrombocytes. It is rapidly released after cell activation. E-selectin (CD62E) is expressed on the cell surface of EC and shed from there after IL-1/TNF stimulation. L-selectin (CD62L) can be found on the surface of leukocytes. Cell activation leads to shed L-selectin by proteolytic processes [3].
We examined soluble E- and P-selectin and L-selectin on B-lymphocytes in multiple injured patients without or with moderate or with severe head injury. The classification of head injury was performed following the injury severity score (ISS) (0-2 pts, moderate; 3-5 pts, severe head injury).
sE-, P- and L-selectin were- measured in 51 multiple injured patients with samples taken on 10 time points (from the location of the accident = 0 h to the 6th post-traumatic day = 144 h) by using commercially available standardized enzyme-linked immunoassays (ELISA). CD62L levels on leukocyte subpopulations were detected using the monoclonal antibodies CD62L (LECAM-1), CD3 (T-cell), CD19 (B-cell), CD14 (monocyte) and a standard flow cytometer.

Table 1 (abstract P010)

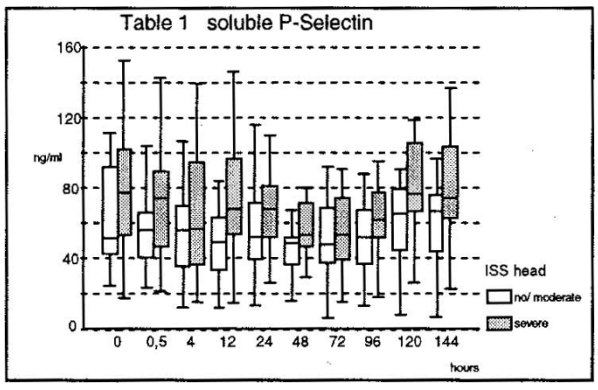

Table 2 (abstract P010)

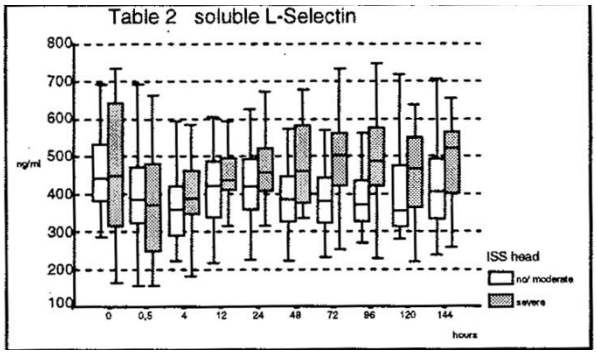

Table 3 (abstract P010)

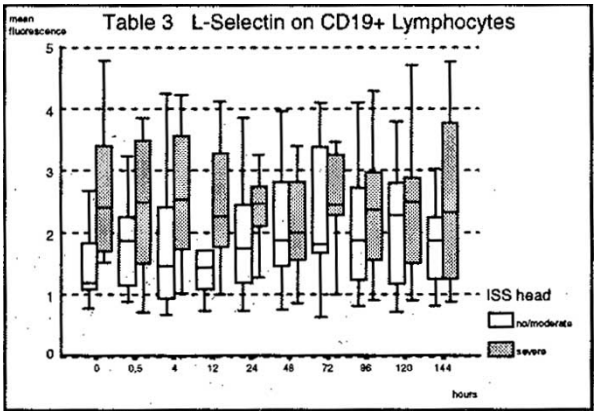

Table 1 demonstrates the very early increase of sP-selectin in patients with severe head injury ($P = 0.0001$) compared to those with moderate or no head injury.
Table 2 illustrates the later increase ($P = 0.0026$) of sL-selectin levels (72 h) in severe head injured individuals while L-selectin on CD19+ B-lymphocytes is expressed significantly stronger ($P = 0.0001$) in the very early post-traumatic phase (0-24 h) = Table 3.
The gravity of head trauma seems to influence the immunological response and subsequently the cell-cell interactions.

Acknowledgement: Supported by the BMVg, Grant InSan 1 0993-V-1296.

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P011

Tau in serum and CSF during cerebral injury

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Critical Care 1997, **1(Suppl 1):**P011

Introduction: Elevated levels of neuron-specific proteins, such as neuron-specific enolase (NSE) and/or neuromodulin in serum or cerebrospinal fluid (CSF) of brain trauma patients are of prognostic value for the patients' outcome. Recently tau, a neuron-specific microtubule-associated protein, has been found to be elevated in CSF of Alzheimer patients. This elevation is at least partially due to loss of neuronal cells. Until now tau has not been detected in serum. Therefore, we investigated whether tau in serum or CSF can be used as a marker for neuronal loss in patients with various forms of acute cerebral injury.

Materials and methods: Consecutive samples of CSF and serum of patients admitted to the intensive care unit with cerebrospinal drain were simultaneously drawn on a daily basis. Tau was determined by Innotest hTau antigen (Innogenetics, Gent, Belgium).

Results: Forty-four CSF and serum samples were evaluated from eight patients suffering craniocerebral trauma ($n = 4$, GCS < 8, 2 survivals), tumor surgery complicated with massive edema ($n = 1$, survived), subarachnoidal hemorrhage (SAH, $n = 1$, GCS < 6, survived) and intracerebral hemorrhage ($n = 1$, died). In CSF, tau was correlated ($r^2 = 0.406$, $P < 0.01$) with neuromodulin. In CSF, the lowest maximal tau values were found in the patient with SAH (628 pg/ml) well above the normal levels 150–200 pg/ml found in control patients. The other patients had very high tau concentrations (maximal values > 10,000 pg/ml). No correlation was found between tau and total protein concentrations or the serum/CSF albumin quotient. In this preliminary study we found no correlation with survival, severity of the disease or outcome. Tau was found to be increased in the serum in all trauma patients (182 to 1200 pg/ml), but not in the others.

Conclusion: Tau is increased in CSF after severe cerebral injury indicating the occurrence of recent neuronal damage. A further increase of tau in CSF after admission implies a secondary neuronal damage. Craniocerebral trauma, accompanied by damage to the blood-brain barrier, results in detection of tau in serum.

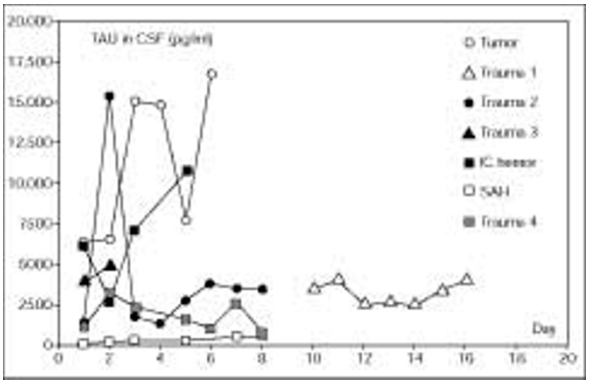

Figure (abstract P011)

P012

Early measurement of double negative (CD4-CD8) T-cells as a possible predictor for MODS after severe blunt trauma?

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Critical Care 1997, **1(Suppl 1):**P012

The exact pathogenesis of the multiple organ dysfunction syndrome (MODS) as the leading cause of late postinjury death is still unclear. We investigated 35 patients with an injury severity score (ISS) greater than 15 (range: 17 to 50, mean 30) and an age greater than 16) years (range: 16 to 89; mean: 38.1 years) during the first 6 days after severe blunt trauma. Patients who died within the first 24 h were excluded. The clinical state of the patients was - among various other clinical parameters and scores - examined by daily calculating of the multiple organ failure score according to Goris *et al*. To recognize immunological alterations in the early postinjury phase, we observed several subpopulations of lymphocytes (labelled with monoclonal antibodies and analysed by flow cytometry) at 10 times, starting at the site of accident.

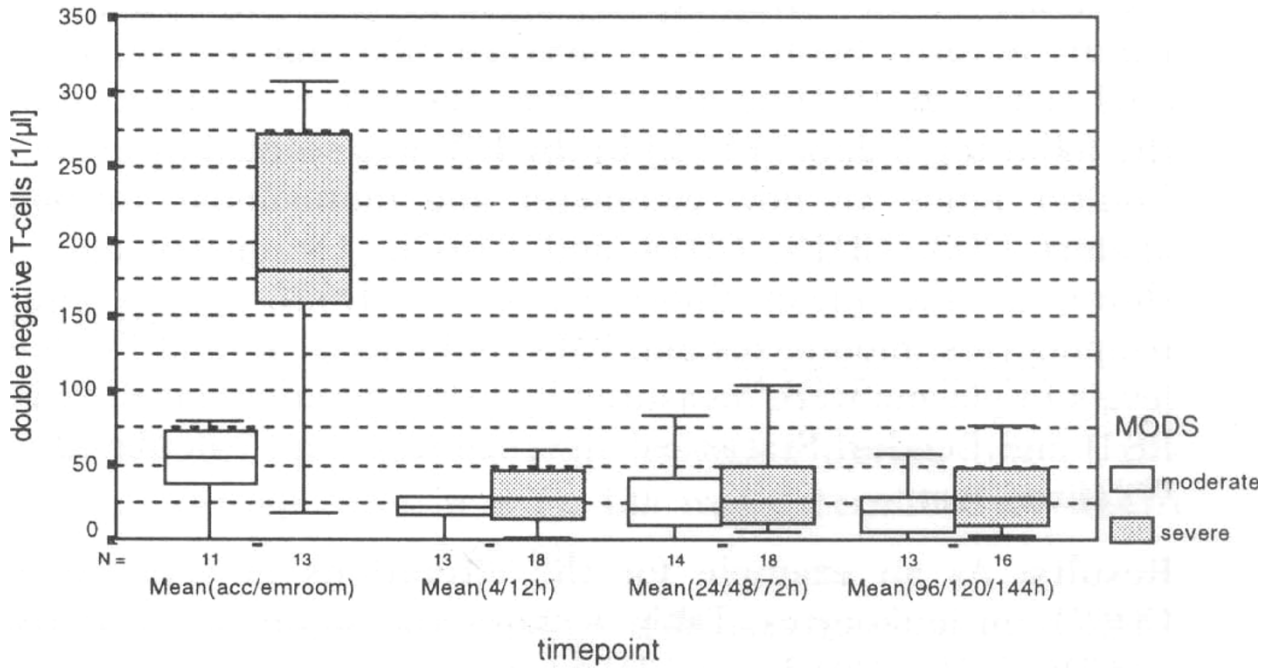

Figure (abstract P012) Numbers of double negative T-cells during the first 144 h after severe blunt trauma. Patients, who get a severe MODS (Goris-score = 5) during the first 6 days after injury, have initial (site of accident/emergency room) significant higher cell numbers as the other patients ($P < 0.0001$). Ten timepoints are summarized to four groups due to statistical reasons.

Two of the regarded cell-groups were T-lymphocytes ($CD3^+$) and one of their subpopulations, the double negative T-cells ($CD3^+$ $CD4^-CD8^-$). The vast majority of these cells are ?d-T-cells [1], a little cell population (1 to 9% of the T-cells) which expresses another T-cell receptor as the longer known aß-T-cells. To ascertain that the examined cells were really ?d-T-cells, we additionally labelled the cells of the last seven patients with ?d-antibodies, compared both groups and noticed that they were corresponding.

?d-T-cells are completely different from aß-T-cells, eg they do not show MHC-restriction. Although their exact function remains still (10 years after discovery) unknown, they have some characteristics which seem to be very interesting for our examination [2,3]: (i) Their prominent residence epithelial tissues, primary in the intestines, an area which is strongly involved into the early pathogenesis of MODS. (ii) They show a rapid mobilisation in the early response to infections. (iii) They have immunoregulating functions for the specific and non-specific immune system and they secrete many lymphokines.

Corresponding with these functional descriptions, we found significant differences (Wilcoxon two sample test for groups of cases: $P < 0.0001$) in the counts of double negative T-cells during the first two samples (site of accident and emergency room) (Fig). The patients with severe MODS (reaching a Goris-score of = 5 during the observation period) showed high cell counts whereas the other patients showed low cell counts (moderate: P_{25} = 38/µl, P_{50} = 56/µl, P_{75}, = 72/µ severe: P_{25} = 159/µl. P_{50} = 181/µl. P_{75} = 272/µl). To exclude the possibility that this effect would not be limited on ?d-T-cells, but would be characteristic for all T-cells or for all lymphocytes, we examined the ratio of ?d-T-cells to all T-cells and we saw a less clear, but significant and similar picture (moderate: P_{25} = 3.2%. P_{50} = 5.4%, P_{75} = 7.25%; severe: P_{25} = 7.75%, P_{50} = 9.55%, P_{75} = 14%). We further controlled the influence of other clinical parameters on the MODS (by using Fisher's Exact Test), but we found no statistical connection between any other clinical parameter and the multiple organ dysfunction.

Thus the MODS seems to be related with the number of ?d-T-lymphocytes in the first hour after severe blunt trauma.

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P013

Association of soluble and cell-linked selectins, multiple organ dysfunction and systemic inflammatory response syndrome

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Background: The soluble members of the selectin family (L-, E- and P-selectin) as well as the cell-linked L-selectin play a key role in leukocyte - endothelial-thrombocyte interaction as they are known to promote leukocyte rolling and tethering under flow conditions [1] .

Altered sL-, sP- and sE-selectin levels are made responsible for the development of different complications in intensive care medicine as ARDS [2], reperfusion injury [3] and other inflammatory disorders.

Objective: To determine if the plasma levels of L-, E-, and P-selectin and the expression of L-selectin on different leukocyte subpopulations in the very early post-traumatic phase and the first critical week on the ICU differ between patients with multiple organ dysfunction (MODS) or SIRS and those without, 51 polytraumatized patients were examined.

Methods: Blood withdrawn from 51 severely injured patients (Injury Severity Score 17-75, average 32.5; age 16-89, average 38.4 years) at 10 time points from the site of accident during the following 6 days (144 h) in the ICU was studied by using the Coulter Epics XL flow cytometer and monoclonal antibodies against CD3, CD19, CD14 and CD62L. Cytometry data are shown as the mean fluorescence of CD62L on B- and T-lymphocytes, monocytes and PMN. Soluble L-, E- and P-selectin levels in plasma were measured by using commercial ELISAs by R&D and Bender. Statistical significances were calculated with Wilcoxon test.

Results: As an example for the alterations in expression of CD62L on leukocytes, Table 1 shows the significant difference in CD62L (LECAM-1) on CD14+ peripheral mononuclear cells in patients who reached = 5 points in the daily Organ Dysfunction Score (Goris *et al*) during day 1 and 6 ($P = 0.0006$), similar to CD62L on CD19+ B-lymphocytes ($P = 0.0001$) and on CD3+ T-lymphocytes ($P = 0.0001$) (data not shown).

Table 1 (abstract P013)

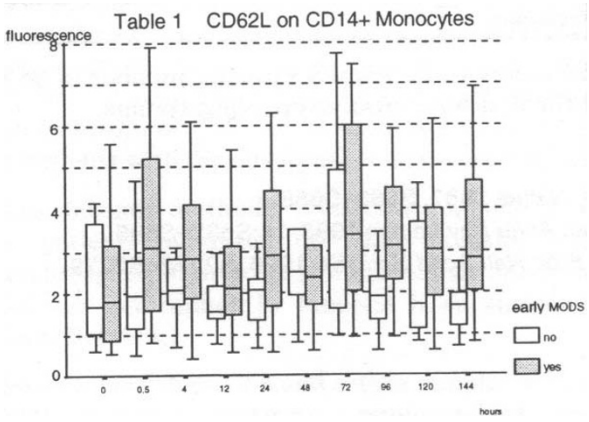

Table 2 (abstract P013)

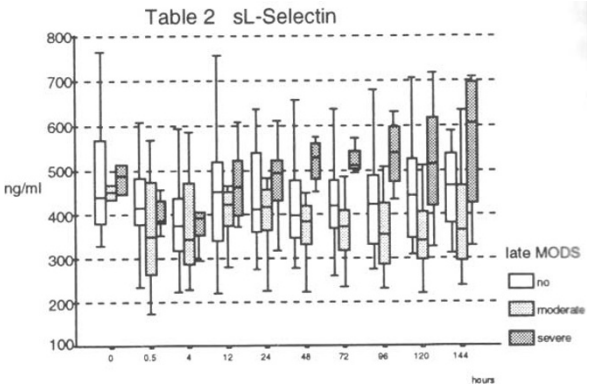

Table 3 (abstract P013)

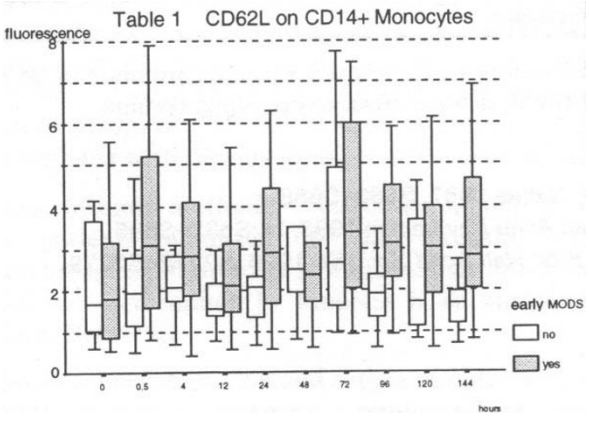

Table 2 illustrates the increase of sL-selectin plasma levels starting 48 h after trauma and growing to day six in patients who will develop severe MODS (ie = 5 points in the ODF score) after the 6th post-traumatic day, compared to those with moderate (1-4 points) and without organ dysfunction ($P = 0.0001$).

Table 3 shows the high increase of soluble E-selectin beginning 24 h after trauma and remaining on elevated level in patients who will develop severe MODS (ie = 5 points in the ODF score) after the 6th post-traumatic day, compared to those with moderate (1-4 points) and without organ dysfunction ($P = 0.0018$).

Discussion: While the early cellular response on multiple trauma shows differences in the amount of expressed CD62L on leukocytes parallel to the clinical situation concerning organ dysfunction, the sE- and sL-selectin levels are increased in patients with a later onset of MODS. Any prospective value of selectin levels for early clinical intervention should be the subject of further investigations.

Acknowledgement: Supported by BMVg Grant InSan 1 0993-V-1296.

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P014

Correlation of cytokine levels with clinical markers of organ hypoperfusion in sepsis syndrome patients (INTERSEPT trial)

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The consequences of severe sepsis syndrome and septic shock include inadequate perfusion of organs and eventually organ failure. Organ hypoperfusion results in anaerobic glucose metabolism, metabolic acidosis and a predominant eatabolic state. The baseline levels of cytokines such as TNF and IL6 correlate with the number of organ hypoperfusions and with well known clinical laboratory markers for these metabolic changes.

Five hundred and fifty-three patients (pts) with sepsis syndrome were treated with a 30 min infusion of 3 or 15 mg/kg of a murine monoclonal antibody to human TNF or placebo. Plasma levels of 504 pts prior to infusion (baseline) and 1 h after infusion were analysed for TNF (ELISA) and 1L6 (B9[1] bioassay). At baseline there was a significant correlation between cytokine levels, particularly IL6, and the number of organ hypoperfusions (TNF: 55.0 pg/ml for I organ hypoperfusion to 100.0 pg/ml for 5 organ hypoperfusions, $P = 0.0002$; IL6: 1.69 ng/ml for I organ hypoperfusion to 25.02 ng/ml for 5 organ hypoperfusions, $P < 0.0001$). Likewise, the number of organs failing (range from 0 to 5) prior to infusion was significantly correlated with either cytokine (TNF: $P = 0.0072$; IL6: $P = 0.0032$: Kruskal-Wallis). The baseline levels of TNF and/or IL6 were also significantly correlated with arterial blood pH (TNF: $r = -0.0709$. $P = 0.1715$: IL6: $r = -0.1966$, $P < 0.0001$), plasma lactate (TNF: $r = 0.3861$, $P < 0.0001$; IL6: $r = 0.3984$, $P < 0.0001$), total serum protein/albumin (TNF: $r = -0.1073$. $P = 0.0544$; IL6: $r = -0.1642$, $P = 0.0031$) or urea (TNF: $r = 0.2517$, $P < 0.0001$; IL6: $r = 0.0561$, $P = 0.2815$), as well as with laboratory markers for renal failure and DIC such as serum creatinine (TNF: $r = 0.3716$, $P < 0.0001$: IL6: $r = 0.1903$. $P = 0.0002$), partial thromboplastin time (PTT) (TNF: $r = 0.2042$. $P = 0.0001$; IL6: $r = 0.2940$, $P < 0.0001$) and platelet count (TNF: $r = -0.2777$, $P < 0.0001$: IL6: $r = -0.2190$, $P < 0.0001$).

P015

Leukemia inhibitory factor during sepsis in adults and neonates

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Introduction: Leukemia inhibitory factor (LIF), a glycosylated single chain polypeptide, induces differentiation in and suppression of leukemia cell lines. It switches signalling of autonomic nerves from adrenergic to

cholinergic mode. stimulates the acute phase response and has profound effects on fat metabolism, calcium homeostasis and participates in hematopoiesis. Depending on priming or its concentration. LIF influences neutrophil chemotaxis and activation. This pleiotrophic cytokine is secreted by different nucleated cells after stimulation with LPS or other cytokines. LIF participates in the pathophysiology of several diseases and the protein is found to be increased in urine during urinary tract infection. The aim of this preliminary study was to evaluate the presence of LIF in urine and serum in an ICU population.

Materials and methods: Blood and urine was drawn from patients responding to the sepsis criteria with detected site of infection (group SEPS, *n* = 17). Pro-operative patients without signs of infection and negative microbiologic assays served as control (group CONT, *n* = 37). Weekly, serial urine samples were drawn from neonates which had no evidence of infection (group NCONT, *n* = 23) or with infection during one of the samplings (group NINF, *n* = 7). LIF was determined by ELISA with detection limit of 10 pg/ml.

Results: In group CONT urinary LIF was low (mean ± SEM: 17.5 ± 5 pg/ml) and serum LIF was only detectable in five patients (< 23 pg/ml). Compared to group CONT, urinary LIF in group SEPS was significantly higher (105 ± 50 pg/ml). Serum LIF was significantly more detected in group SEPS (*n* = 6, range up to 274 pg/ml). No correlation was found between urinary and serum LIF concentrations; No detectable LIF was found in urine of group NCONT. Two patients of group NINF (5 samples) with MRSE sepsis had increased urinary LIF.

Discussion: Serum or urinary LIF levels may increase during sepsis, but LIF cannot be used as diagnostic marker for the diagnosis of urinary tract infection or sepsis. The wide range of LIF concentrations in urine or serum indicate the magnitude of regulatoy factors of LIF secretion.

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P016

Endotoxemia, immunocompetence and the responsiveness of neutrophils in critically ill patients

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Introduction: Lipopolysaccharide (endotoxin) is a potent inducer of a complex pattern of pre-inflammatory and anti-inflammatory cytokines that generate a predictable pathophysiologic response in animal and healthy human subjects. However, measuring endotoxin in the blood or serum of critically ill patients has been problematic.

We have recently developed an assay for endotoxin in whole blood which is rapid and reliable. Using chemiluminescent technology. primed patient neutrophils mixed with an anti-endotoxin antibody are analysed for respiratory burst activity corresponding to neutrophil recognition of complexes of endotoxin and anti-endotoxin antibody. The chemiluminescent assay provides reliable quantitation of whole blood endotoxin and provides a method of measurement of the in vivo state of activation (cl-max) and immunocompetence (responsiveness) of circulating neutrophils.

Purpose: To validate the utility of the chemiluminescent assay tor simultaneous measurement of endotoxemia, and neutrophil activation and responsiveness in a cohort of critically ill patients.

Methods: Using the chemiluminescent assay, we measured endotoxin levels in whole blood samples from 64 consecutive patients who met the SCCM/ACCP Consensus Conference criteria tor sepsis and 20 non-septic patients in our 36 bed Medical-Surgical ICU. Each patient sample was analysed in duplicate. Anti-endotoxin antibody was added to the first sample to aid in the measurement of endotoxin, then the second sample is challenged with a maximum stimulatory dose of endotoxin (800pg/ml) to allow endotoxin quantitation and measure the state of neutrophil activation is assessed by the maximal chemiluminescent response. The cl-max is proportional to the number of neutrophils and degree of activation. The responsiveness is a measure of the normalized level of activation of neutrophils by a maximal antigen-antibody challenge (LPS-anti-LPS immune complex).

Table (abstract P016)

Category	*n*	LPS (pg/ml)	Cl-max (counts/min)	Responsiveness
Control	30	–	1.2 (± 0.8)	47.0 (± 15)
Non-sepsis	20	226.0 (± 345)	7.1 (± 5.6)*	43.5 (± 17)
Sepsis	64	404.2 (± 353.8)†	12.0 (± 11.8)*‡	29.0 (± 24)*‡

*P = 0.0001 versus control, ‡P = 0.001 versus non-sepsis, †P = 0.05.

Results: Compared to healthy controls, non-septic patients have a significantly higher cl-max (1.2 ± 0.8 versus 7.1 ± 5.6. *P* = 0.0001) but similar responsiveness (47.0 ± 14.6 versus 43.5 ± 16.7, *P* = 0.95). Septic patients were significantly different from controls with regard to el-max and responsiveness but also to critically ill, non-septic patients (see Table). Mean endotoxin levels were significantly different between non-septic and septic patients. Results follow (± SD).

Conclusions: The chemiluminescence assay can identify a group of patients who have significant endotoxemia. Furthermore, the assay contributes information on the state of activation (cl-max) and potential responsiveness of circulating neutrophils. The assay provides a reliable and rapid method to assess neutrophil activation and opsonin dependent immunocompetence and may serve as a clinical tool for selecting patients who may benefit from anti-endotoxin strategies.

P017

Lactoferrin effects on immune response in critically ill

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We have studied in vitro the effect of lactoferrin on the proliferative response of peripheral blood mononuclear cells and their ability to produce IL-6 and TNF-alpha in three groups of patients - septic survivors, septic non-survivors and patients after multiple organ injury. Lactoferrin is an iron-binding glycoprotein with a wide spectrum of biological activities (*Ann Rev Nutr* 1995, **15**:93). It may contribute to the protection against pathogens and their metabolites by enhancing phagocytosis, cell adherence, and controlling release of pro-inflammatory cytokines such as IL-1, IL-6 and TNF-alpha.

Material: We investigated 53 adult patients (40 men and 13 women, aged 15-73 years) meeting the ACCP/SCCM criteria of sepsis or sepsis shock (*Crit Care Med* 1992, **20**:864) who were treated in our intensive therapy unit for peritonitis, pancreatitis. ARDS, or major trauma. The mean APACHE II score on admission was 21.85 and 18.5 in septic and post-traumatic patients, respectively. The patients were divided into three groups: multiple trauma (T, *n* = 10), septic survivors (SS, *n* = 14), septic non-survivors (SN, *n* = 19). The control group consisted of 13 healthy volunteers.

Methods: The proliferative response of PBMC in vitro was tested using 3-day culture with mitogens (PHA, LPS). The cell proliferation was measured using MTT colorimetric method. The activity of TNF-alpha and IL-6 was measured with bioassary using indicator cell lines WEHI-164.13. and 7TDI. respectively.

Results: Lactoferrin significantly inhibited PHA-induced proliferation in three groups of patients during the whole monitoring period (*P* < 0.05). Lactoferrin alone appeared to be a very good inducer of IL-6. The effect of lactoferrin on LPS-induced IL-6 production by leukocytes was also stimulatory. The influence of lactoferrin on IL-6 production was very significant especially in the group of septic survivor patients. Lactoferrin appeared to be a very good inducer of TNF-alpha, however, its action varied considerably among particular groups of patients. In trauma patients lactoferrin exhibited a moderate up-regulatory activity. Most significant stimulatory effects of lactoferrin were seen in septic survivor group, which resulted in a permanently high TNF-alpha production during the whole monitoring period. Quite different response pattern was observed in the group of septic non-survivor patients; their cells ability to produce TNF-alpha was low and the effect of lactoferrin was not so significant as in the survivor group.

Conclusions: (i) Lactoferrin seems to exert a beneficial action on the immune response. It slightly decreases the PHA-induced lymphocyte proliferation, (ii) Lactoferrin is a good inducer of IL-6 and TNF-alpha production. It cannot, however, break through lymphocyte anergy, as measured in LPS-induced cytokine secretion test.

P018

Plasma nuclear matrix protein (NMP) levels in patients with multiple organ failure

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Functional failure of an organ is caused by functional failure of its constituting cells. NMP is released upon cell death including apoptosis, the number of dying cells can be quantified by measuring the plasma NMP level. In the present study, plasma NMP levels were analysed by using an ELISA kit in 52 patients with multiple organ failure (MOF). The patients were classified into two groups: 34 patients with sepsis-associated MOF (group B). NMP is not detectable in normal subjects. The plasma NMP levels was 770 ± 932 U/ml in group A. which was higher than 478 ± 776 U/ml, the plasma NMP level group B- However, there was no significant difference between the two values. There was a significant correlation between the NMP levels and the number of organ dysfunction. Our result suggests that plasma NMP level increases in such conditions as MOF, irrespective of the presence or absence of infections, and indicates cell damage.

P019

Negative and reversible feedback inhibition of the endothelial nitric oxide (NO) synthesis by interleukin-1β (IL-1β)-induced generation of nitric oxide

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Introduction: The synthesis of NO in endothelial cells plays a major role in the control of vascular homeostasis in part due to its ability to inhibit vascular tone and activation of platelets. Inflammatory mediators such as IL-1β impair the NO-mediated endothelium-dependent relaxations in isolated blood vessels. Since IL-1β is a potent inducer of the inducible NO synthase (iNOS), the role of the induced synthesis of NO and the inhibitory effect of IL-1β was examined.
Materials and methods: Vascular reactivity studies were performed with rabbit carotid arteries with endothelium using organ chambers and the release of biologically active NO was assessed under bioassay conditions.
Results: The concentration-dependent relaxations to acetylcholine, substance P and to the calcium ionophore A23187 were inhibited in IL-1β (100 U/ml for 7 h)-treated compared to control carotid arteries while those to sodium nitroprusside were not affected. No inhibitory effect was obtained in carotid arteries which had been exposed to IL-1β (100 U/ml) for only 15 min or to IL-1β (100 U/ml for 7 h) in the presence of either cycloheximide (20 μg/ml, an inhibitor of the protein synthesis), N-α-tosyl-L-lysine chloromethyl ketone (100 μM, an inhibitor of iNOS expression) or S-methylisothiourea sulfate (l0 μM, a preferential inhibitor of iNOS activity). Perfusates from IL-1β (100 U/ml for 7 h)-treated carotid arteries relaxed detector blood vessels without endothelium to a smaller extent than those from control arteries. Similar relaxations to acetylcholine were obtained in control carotid arteries and in IL-1β (100 U/ml for 7 h followed by a 17 h incubation in medium without the cytokine, a condition which is not associated with an induced synthesis of No)-treated arteries.
Summary and conclusions: These findings indicate that the IL-1β-mediated inhibitory effect on the endothelium-dependent relaxations is due to an inhibition of the calcium-dependent NO synthase activity in endothelial cells by the induced synthesis of NO. Such an inhibitory mechanism may help to explain the blunted endothelium-dependent vasodilatory capacity of arteries subjected to an inflammatory response such as in sepsis and in atherosclerosis. Since the effect of IL-1β is reversible. it may represent a mechanism which prevents an excessive production of NO in the blood vessel wall at sites of injury.

P020

Pteridines and cytokines induce apoptotic cell death in alveolar epithelial cells

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Introduction: The pteridines neopterin and 7.8-dihydroneopterin influence the cellular oxidant-antioxidant balance as well as the expression of the inducible nitric oxide synthase (iNOS) gene. Since apoptotic cell death can he initiated by reactive oxygen intermediates and nitric oxide (NO) we studied whether both pterdines induce apoptotic cell death in vitro.
Materials and methods: As cell culture model we selected the rat alveolar epithelial cell line L2. Confluent L2 cells were incubated for 24 h with neopterin (1 μM-1000 μM). 7.8-dihydroneopterin (1 μM-1000 μM), the cytomix (interferon-γ IFN-γ, 100 U/ml plus tumor necrosis factor-α, TNF-α 500 U/ml) as well as the combination of the pteridines and the cytomix. Apoptosis was estimated by FACS analysis. iNOS gene expression was investigated after 9 h incubations by an RT-PCR. Synthesis of the stable NO-metabolites nitrite and nitrate was determined in the cell-free supernatants incubated for 24 h by a modified Griess reaction.
Results: Neopterin as well as 7.8-dihydroncopterin induced a significant increase of percentual apoptotic cells. Maximal apoptosis was found with 100 γM neopterin (mean ± SEM = 22.7 ± 2.5%; n = 6) and 100 μM 7.8-dihydroneopterin (mean ± SEM = 21.9 ± 2.5%: n = 6). respectively. Co-incubation of both pteridines with the cytomix lead to a significant higher apoptosis than the cytomix alone. In contrast to the cytomix. no iNOS gene expression and no NO release could be detected after incubation with neopterin as well as 7,8-dihydroneopterin.
Conclusion: We conclude that neopterin and 7,8-dihydroneopterin are per se inducers of apoptosis. They enhance apoptotic cell death by IFN-γ and TNF-α. In contrast to these cytokines apoptotic cell death due to the pteridines is not mediated by nitric oxide. The pronounced apoptosis by the pteridines may be of importance in inflammatory pulmonary diseases associated with an activation of the cellular immune system.

P021

The effects of gaseous nitric oxide on platelets and leukocytes in membrane oxygenators

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Nitric oxide (NO), known as a potent endogenous platelet anti-adhesive, anti-aggregating, and disaggregating radical, was shown to reduce platelet trapping in microporous membrane oxygenators [1]. In an additional study we investigated the effects of gaseous NO on platelet and leukocyte activation markers during extracorporeal circulation. Two parallel separated extracorporeal circuits (n = 6) were filled with heparinized (1 IE/ml) fresh drawn blood from one healthy volunteer. The gas inlets of both oxygenators (M8 Jostra/Germany) received dry gas (21% oxygen, 5% carbon dioxide, 84% nitrogen); gaseous NO (20 ppm) was added to the gas inlet of one of the oxygenators, whereas the other one was used for control. Blood samples obtained from a venous reservoir and from the blood donor were investigated by flow cytometry for the following markers: leukocytes-CD11a, CD11b, HLA-DR, CD62L (L-selectin), and CD14. Platelets-P-selectin (CD62P), CD42b (GPIb), CD41a (GPIIbIIIa), and activated conformationally changed GP-IIbIIIa. Additional,

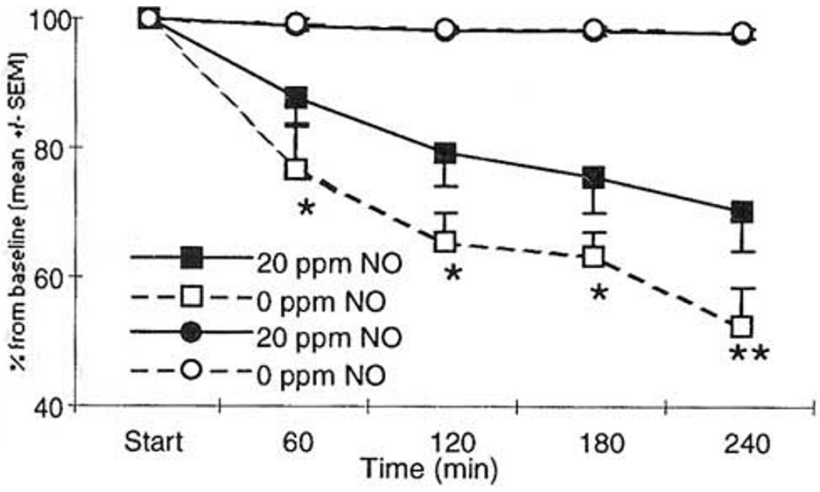

Figure 1 (abstract P021) Platelet (squares) and hemoglobin (circles) values in percent from baseline (start). $^{*}P < 0.05$, $^{**}P < 0.01$, paired *t*-test.

platelets were stimulated with ADP (10 μM), epinephrine (10 μM), or both (each 5 μM) to investigate platelet reactivity. Further analysis included: coagulation parameters (fibrinogen, ATIII, heparin-time, prothrombin-time, fibrin monomers); platelet counts (in quadruplet); blood gas analysis; and leukocyte differential count. The main results are: (i) NO significantly attenuated platelet trapping within the membrane oxygenator (Fig 1); (ii) In both oxygenators only small amounts (1-2%) of circulating activated (P-selectin or activated GPIIbIIIa) platelets were detectable over time; (iii) platelet reactivity to stimulating agents decreased during circulation, indicating platelet damage; (iv) NO seemed to preserve platelet reactivity to some degree which was pronounced with duration of circulation (Fig 2); (v) there was no significant difference in loss of leukocytes, ie trapping of PMN and monocytes (lymphocytes remained stable) between the two oxygenators; (vi) leukocyte adhesion molecule expression was significantly altered during circulation, however, no differences were found between NO and control: HLA-DR and CD14 increased on monocytes, CDIIa increased on lymphocytes, CDIIb increased on monocytes and PMN, and L-selectin was reduced on monocytes and PMN, whereas L-selectin expression on lymphocytes increased over time; (vii) no significant differences were found lor coagulation parameters or blood gas analysis.

Conclusion: Gaseous NO attenuated platelet trapping within the used membrane oxygenators. NO had no effects on leukocyte trapping or altered adhesion molecule expression on circulating leukocytes. NO preserved platelet reagibility to stimulating agents under these special conditions which stands in contrast to its known inhibitory effects on platelet activation marker expression [2]. Further studies should demostrate whether application of gaseous NO to membrance oxygenators might be advantageous during extracorporeal lung assist.

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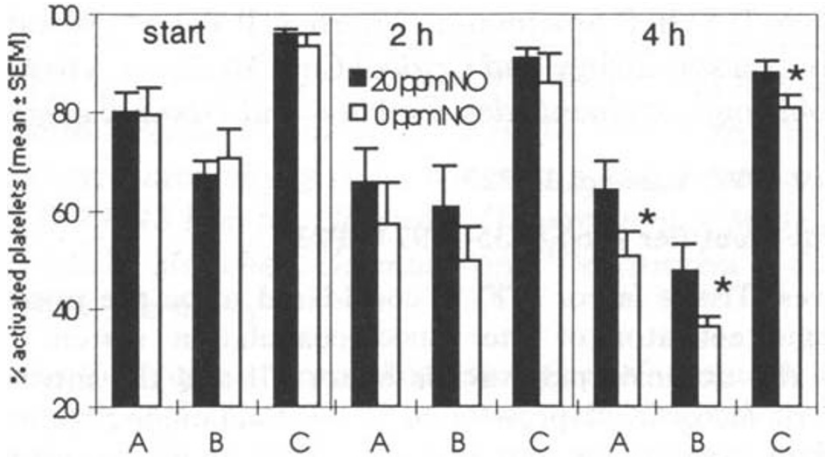

Figure 2 (abstract P021) Activated GPIIb-IIIa on platelets stimulated with 10 μM ADP (A), 10 μM epinephrine (EPI) (B), or 5 μM ADP + 5 μM EPI (C) at different timepoints. Note the time-dependent loss of reactivity to stimulating agents in both membrane systems, however, gaseous NO preserved reagibility, demonstrating the protective effect of NO on platelets ($^{*}P < 0.05$, paired *t*-test).

P022

Pathogenesis of organ damage during sepsis. In vitro influence of lipopolysaccharides and cytokines on the microtubular system

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Lipopolysaccharides (endotoxins) from Gram-negative bacteria and septic mediators like interleukins or TNF-α are known to be involved in the pathogenesis of septic shock and multi-organ failure. Whether this is due to tissue hypoxia by alterations of the microcirculatory blood flow or by direct cytotoxic effects is controversial.

Microtubules are long, non-branching hollow-cylindric proteinaceous organelles found in almost all eukaryotic cells. Their wall consists of protofilaments (mostly 13), composed of longitudinally associated ab-tubulin dimers. Microtubules are involved in the maintenance of cell shape, translocation of cytoplasmic organelles, and secretory and signal transfer processes.

In the present work, we have studied the effect of different lipopolysaccharides (*Klebsiella pneumoniae*, *E coli, Pseudomonas aeruginosa* and *Salmonella minnesota*) and cytokines (IL-1β, IL-6, IL-10 and TNF-α) on polymerization of microtubulc protein and on structure of preformed microtubules in vitro. There was a time-, pH- and concentration-dependent inhibition of microtubule formation with respect to lipopolysaccharides, but not to cytokines. The strongest effects were observed with lipopolysaccharides from *Pseudomonas aeruginosa* (at pH 7.0, 37°C, 50 µg/ml LPS, 20 min, about 55% inhibition; $n = 3$) and *Salmonella minnesota* (at pH 7.0, 37°C, 50 µg/ml, 20 min, about 62% inhibition, $n = 3$). Incubation with lipopolysaccharides leads to a marked breakdown of preformed microtubules. Electron microscopy showed that incubation of preformed microtubules with LPS leads to disrupted microtubule structures, too. The inhibiting influence of LPS on polymerization of microtubule protein could be compensated by addition of purified MAP-2 and tau. By electrophoretic analysis it was shown that LPS prevents MAP-1, MAP-2 and tau from interaction with tubulin.

The results indicate that the microtubule cytoskeleton and above all microtubule associated proteins could be a major target of direct cellular effects of lipopolysaccharides, but not of cytokines.

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P023

Peroxynitrite reduces endotoxin-induced tissue factor expression in human peripheral blood monocytes

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Objectives: Tissue factor (TF) is considered to be the primary physiologic activator of the blood coagulation system. TF initiates the extrinsic pathway via factor VII and the intrinsic pathway via factor IX. Expression of TF by blood monocytes is an established trigger for intravascular coagulation in several pathologic conditions such as cancer, sepsis and inflammation, since activated macrophages, endothelial cells and type II epithelial cells synthesize nitric oxide (NO), superoxide anion (O_2) and other free radicals under such conditions, we examined their influence on endotoxin-induced TF expression in human peripheral blood monocytes.

Methods: Human peripheral blood monocytes were isolated by Ficoll-gradient centrifugation and incubated with LPS (0–10 µg/ml) for 4 h at 37°C (incubator). SIN1 (0–2000 µl) — an NO and O_2 releasing compound —, NOC18 (0–2000 µM) - a pure NO donor —, superoxide dismutase (SOD) (0–500 IE/ml), hypoxanthine (1 mM) with xanthine oxidase (0–1 U/ml) — an O^-_2 liberating system — and peroxynitrite (0–2000 µM) — a reaction product of NO with O^-_2 were added under different conditions. TF was assayed by flow cytometry using a monoclonal antibody against TF, by a one stage clotting assay and by PCR.

Results: SIN1, peroxynitrite and the combination of NOC18, hypoxanthine and xanthine oxidase reduce the LPS-induced TF expression in a dose and time dependent manner, NOC18 or hyroxanthine/xanthine oxidase alone had no effect, SOD reversed the SIN1 mediated TF production having a weak decreasing effect on its own. Low doses of SIN1 resulted in a slight increase in TF expression.

Conclusion: These data implicate that free radicals influence the TF expression of peripheral human blood monocytes and, that the balance of NO and O^-_2 plays a crucial role for that regulation.

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P024

Induction of endotoxin (ET) tolerance by atoxic endotoxin - a new prophylactic concept to the septic syndrome

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Repeated, small doses of ET induces resistance to subsequent larger doses of ET in both animals and men. This preconditioning, termed ET tolerance is a well-controlled active response that is orchestrated to prevent excessive inflammation. The ET of distantly related Gram-negative bacterial species like the sulfur-containing or the sulfur-free purple bacteria appear to have low endotoxicity or to be completely non-toxic but maintain many of the beneficial immunomodulatory activities.

The present experiment was designed to test the response to the non-toxic ET of *Rhodopseudomonas sphaeroides* to protect the animals after 5 days of immunization against a continuous ET challenge-dose of 250 ng/kg BW/h over a 12 h observation period. Results are summarized in the Table below.

Clinical signs of endotoxemia could be observed in both groups within the first hour of the experiment. However, in contrast to the tolerant animals which appeared cardiorespiratorily stable for most of the observation period, the control animals sustained serious reductions in MAP, CO and arterial PaO_2 (see Table). While only one animal survived in the control group only one animal died in the tolerant group during the observation period.

Table (abstract P024)

Time after ET	Group	0	2	4	6	8	10	12
MAP (mmHg)	C	88	73	63	61	56	-	-
	T	79	70	73	68	71	80	78
HR (/min)	C	72	101	136	172	151	-	-
	T	69	75	82	85	104	103	96
CO (l/min)	C	3.3	3.0	2.8	2.3	1.9	-	-
	T	3.2	3.6	2.7	2.3	2.4	2.5	2.7
SVO_2 (mmHg)	C	47.2	39.4	42.1	43.0	48.3	-	-
	T	42.1	46.1	39.9	33.2	38.0	37.6	39.5

Survival time was enhanced significantly ($P < 0.01$) in the tolerant group (T) in comparison to the controls (C) from 490 to 670 min.

The encouraging results of this study emphasize the potential role of atoxic ET as a therapeutic agent. As a new prophylactic approach ET tolerance as such seems interesting — as prophylaxis in high-risk patients it may prevent septic complications. The tolerance state however is relative and never complete — it can be overcome by raising the ET challenge dose or adding other negative stimuli like second or subsequent hit.

P025

Cellular mechanisms of acute septic cardiomyopathy: cardiodepressive profiles of endotoxin, tumor necrosis factor α and interleukin-1 in the cardiomyocyte

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Aim of study: Cardiodepression in sepsis and septic shock is mainly attributed to endotoxin-induced release of tumor necrosis factor α (TNFα) and interleukin 1 (IL-1) into the circulation It is supposed that the negative inotropic action of these cytokines in the heart is mediated by induction of inducible nitric oxide synthase (iNOS). When applied in vivo, endotoxin and TNFα indeed mimic the cardiovascular pattern of sepsis. Elevated levels of TNFα and IL-1 are measured in sepsis. The purpose of this study was to compare the cardiodepressive profiles of endotoxin. TNFα and IL-1 on the cardiomyocyte level and determine whether or not their effects are mediated by nitric oxide (NO).
Methods: Spontaneously beating neonatal rat cardiomyocytes were cultured in the presence of endotoxin (1–10 µg/ml), IL–1 (20–100 U/ml) or TNFα (10–1000 U/ml) for 24-72 h. Spontaneous beating as well as electrically triggered contractions (yielding values of pulsation amplitude) were monitored and recorded by means of a photo-optical device. Nitrite in the cell culture supernatant as a measure of NO production was determined by the Grieβ reaction. iNOS in cardiomyocytes was measured by reverse transcriptase polymerase chain reaction (RT-PCR). Cell-associated IL-1-activity was determined by a bioassay.
Results: Both endotoxin and TNF and IL-1 block β-adrenergic response in isolated cardiomyocytes after a 24 h culture-period. In neither case, morphological signs of cytotoxicity were observed, as determined by phase contrast microscopy. iNOS is induced by IL-1 (100 U/ml, 24 h) and endotoxin (1 µg/ml, 24 h); both signals are suppressed by simultaneous administration of dexamethasone (0.1 µM). Nitrite content of the supernatant is enhanced by IL-1 (42.0 ± 5.8 nmol/mg protein: control: 29.9 ± 3.0; $P < 0.05$) and endotoxin (≥ 1 µg/ml) (both suppressible by dexamethasone, 0.1 µM). IL-1 (100 U /ml) does not significantly increase basal contractile frequency in cardiomyocytes. TNFα in high concentration (1000 U/ml, 6 h/24 h) only very weakly induces iNOS (RT-PCR) in RCM, the signal is suppressed by simultaneous application of dexamethasone (0.1 µM). In the presence of the pathophysiologically relevant TNFα concentration of 10 U/ml, mRNA for iNOS in minimal amounts is evidenced after 6 h of culture, but no longer after 24 h. NO production was not enhanced by TNFα (10 U/ml, 24 h) (absence and presence of dexamethasone). After stimulation with endotoxin (10 µg/ml, 24 h) cell-associated IL-1 activity is enhanced in rat cardiomyocytes.
Conclusions: Endotoxin has a direct effect on rat cardiomyocytes in vitro, as evidenced by contractile disturbance. iNOS induction and increase in cell-associated IL-1-activity. Although both endotoxin and IL-1 and TNFα block β-adrenergic response in cardiomyocytes, only endotoxin and IL-1 lead to an increased NO production in these cells, whereas TNFα-cardiodepression seems to be independent of NO.

P026

Disturbance of energy metabolism in acute septic cardiomyopathy: decreased activities of the complexes I and II of the mitochondrial respiratory chain and phosphofructokinase

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Acute septic cardiomyopathy accounts for about 10% of fatalities in sepsis and septic shock. Currently, therapy of septic cardiomyopathy is merely symptomatic. Causal therapeutic approaches could help reduce mortality. In the skeletal muscle of septic patients elevated oxygen partial pressures have been detected indicating a diminished oxygen consumption of mitochondria in sepsis. There is evidence that tumor necrosis factor α and interleukin 1 disturb mitochondrial function of cardiomyocytes in vitro. It was therefore assumed that mitochondrial function in septic cardiomyopathy may be disturbed. Ten key enzymes of energy metabolism were determined in vitro in myocardial tissue (removed post mortem) of septic and non-septic (sham) baboons under systemic anaesthesia, a standardised and hemodynamically well-characterised model of *E coli* sepsis. Measurements were performed spectrophotometrically and enzyme activities referred to non-collagen protein (NCP) (mU/g NCP, mean ± SEM). A newly developed principal component analysis of data was used to detect impaired enzyme pattern in myocardial specimen. Two sepsis protocols were compared: single challenge and multiple challenge (less *E coli).* A 50% reduction of the activity of complex II of the respiratory chain was found after single challenge (3.6 ± 0.6) in comparison to the multiple challenge group (7.3 ± 2.1, $P < 0.05$). The other enzymes were less affected. The activities of the complexes I and II and phosphofructokinase were significantly lowered after single challenge in the heart in lethal septic shock (I), in comparison to non-lethal septic shock (II) and to the sham animals *$P < 0.05$).
The effects on cytochrome-c-oxidase, succinate dehydrogenase and complex III were essentially smaller, and citrate synthase was nearly unaffected. Similar changes were observed after multiple challenge protocol too.
Conclusion: Septic cardiomyopathy is characterized by a prognostically relevant pattern of diminished enzyme activities, pointing at disturbances of mitochondrial function.

P027

The effect of hemorrhagic shock on IL-10

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IL-10 is an anti-inflammatory cytokine. Its blood concentration is said to rise in response to various invasive stimuli together with inflammatory cytokines. Studies on the effects of hemorrhagic shock on cytokine production are few, and they refer mainly to inflammatory cytokines. In

Table (abstract P026)

	Sham	Group I	Group II
Complex I	4.3 ± 1.7 ($n = 2$)	0.7 ± 0.2 ($n = 7$)*	2.8 ± 0.4 ($n = 19$)*
Complex II	6.3 ± 1.8 ($n = 2$)	0.9 ± 0.5 ($n = 7$)*	2.8 ± 0.4 ($n = 19$)*
Phosphofructokinase	244 ± 22 ($n = 2$)	56 ± 24 ($n = 4$)*	2.8 ± 0.4 ($n = 17$)*

this study, IL-10 was measured in patients with hemorrhagic shock. Its transition over time and its relation to inflammatory cytokines was investigated. The subjects were four patients in hemorrhagic shock due to non-trauma and 17 patients in hemorrhagic shock due to trauma. Their average age was 40.1 years. The APACHE-II score for the trauma subjects was 18.6 and 25.8 for non-trauma, with an average of 20.0 for all subjects. The average ISS of the trauma subjects was 26.1. A positive correlation was found between IL-10 and IL-6 ($r = 0.777$). IL-6 is generally regarded as reflecting the severity of a patient's condition, and as a consequence of our findings, IL-10 should also be useful as a marker of patient severity. Changes in cytokine levels were assessed in relation to the cause of hemorrhage. IL-6 and IL-10 levels were high in hemorrhagic shock due to trauma but did not rise remarkably in shock due to non-trauma, indicating that tissue injury is an important factor in causing high cytokine levels.

P028

The relationship between adult respiratory distress syndrome (ARDS) stage and severity of intra-abdominal sepsis (or intoxication parameters) in early postoperative period

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Objectives: To find the relationship between severity of intra-abdominal sepsis, intoxication level and intensity of respiratory failure in peritonitis patients.
Design: Prospective clinical-diagnostic study of peritonitis patients on the lst-14th day after surgery.
Subjects: We examined 82 patients (300 observations) from 14 to 81 years-old with different abdominal aetiology.
Methods: To monitor the lung respiratory function we evaluated respiration, peak of CO_2 pressure at the end of inhalation, ventilation/perfusion relation, O_2 and CO_2 pressure in arterial capillary blood. The clinical information system for permanent monitoring of circulation was used to register the heart rate, stroke and cardiac indexes, system arterial resistance index, systolic and diastolic arterial pressure, central venous pressure and also impedance between breast and neck electrodes during central reography. We determined middle molecules (MM) and serum urine nitrogen (SUN) levels by spectrophotometry. To estimate patient's severity score the integral prognostic index (PI) was calculated using parameters mentioned above, laboratory and some clinical data (*Surgery* 1993, **10**:16–19). PI value fluctuated between 0 and 1, where 0–0.1 predicted lethal outcome and 0.9–1, survival, 0.1–0.9 range was subdivided into some intermediate statuses. We made a conclusion about ARDS stage employing decisive rules of diagnostic algorithm that were found using values of external ventilation parameters, blood gas pressure and central reography data (*Intensive Care Med* 1996, **22**:410). Correlation analysis was used for statistical data processing.
Results: According to the data obtained we found that the aetiology of peritonitis and type of intra-abdominal exudate had no sufficient influence on ARDS developing. ARDS stage and the extension of peritonitis were weakly ($r = -0.17$) but reliably ($P < 0.02$) correlated: ARDS developed frequently in patients with generalized peritonitis. ARDS stages III and IV were never found in diffused peritonitis. Severe ARDS stages were observed in later period after surgery. The possibility of lethal outcome (MOR) progressively increased as respiratory failure was deepening. The investigation of relationship between PI and ARDS stage showed weak but sufficient correlation. Some intoxication parameters were also correlated with ARDS stage (see table).
Conclusion: Statistically reliable relationships between ARDS stage and some parameters reflecting peritonitis severity and its outcome confirm that this syndrome influences significantly the status of these patients. However, values of correlation coefficients indicate that ARDS is important but not sole syndrome injury which makes its contribution to peritonitis pathogenesis. On the other hand, ARDS developing (which is a component of intra-abdominal sepsis pathogenesis) is caused not only by stress effect of initial lung microcirculation alteration but also by adequacy of organism reaction, ie compensatory possibility of the given homeostatic system.

Table (abstract P028)

	MOR	PI	MM	SUN
ARDS stage	$r = 0.34$	$r = -0.43$	$r = 0.29$	$r = 0.50$
	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$	$P < 0.0001$

P029

SIRS in ICU: a different approach in sepsis assessment: clinical predictivity, severity scores, costs

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The systemic inflammatory response syndrome (SIRS), based on the changes of four physiological features like temperature, white cells, heart rate and ventilation, can be observed after a wide variety of insults.
Because sepsis is the systemic response to infection and it is the most common cause of death and of multiple organ failure (MOF) in ICU, we have tried to use SIRS as a predictive tool against the risk of sepsis, severe sepsis and septic shock.
Many authors chose two of the four criteria of SIRS to verify this hypothesis, but results were misleading: a significant predictive power of SIRS against sepsis was not found.
Although SIRS is not disease specific, we performed a retrospective study on 384 unselected patients admitted consecutively to our ICU from 1 January 1993 to 31 May 1995, connecting epidemiological data to our research.
We found that three-four criteria of SIRS (group SIRS 1) are significantly better than the two criteria pattern (group SIRS 2) as predictive power.
This result was confirmed by the significant difference of APACHE III and SAPS II scores (87 and 55 respectively versus 78 and 48), by the longer length of stay of survivors (24 days versus 12) and by bigger costs (78 million versus 38 million Italian lire) in the group SIRS 1.
We concluded that by adding one or two SIRS criteria to those normally used, the predictive liability of SIRS against risk of sepsis is significantly enhanced.

P030

Multi-organ-failure (MOF) with and without sepsis: differences in incidence and pattern of detected arrhythmias

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Background and objectives: Aim of the present study was to prospectively examine if there is a difference in spectrum of arrhythmias

Table (abstract P030)

	Group 1 ($n = 25$)	Group 2 ($n = 15$)	Group 2 ($n = 7$)
Elebute score	17.8 ± 6.0	7.1 ± 2.8*	0.4 ± 0.5*
APACHE II score	32.4 ± 6.8	26.1 ± 7.3*	10.7 ± 13.7*
TNF-α (pg/ml)	88 ± 72†	31 ± 27‡	29 ± 16
s-SVES/24 h**	1 736 ± 3717	1966 ± 4982	744 ± 1451
SVT/24 h	37.7 ± 107.2	279 ± 906	86.7 ± 175
s-VES/24 h**	652 ± 1672	790 ± 2394	1143 ± 2357
v-Couplet/24 h	49 ± 485	90.6 ± 308	81.7 ± 194
VT/24 h	184 ± 709	9.5 ± 28.3	41.6 ± 105

*$P < 0.05$, data are presented as mean ± SD> There was no correlation between SVES/VES and iv therapy with norepinehrine, epinephrine, dopamine and dobutamine, respectively. †$n = 12$, ‡$n = 13$, §$n = 6$, **s = single (SVES/VES).

occurring in patients with Elebute and Stoner score (≥ 12, group 1) - quantified sepsis in relation to MOF patients without sepsis (group 2). Group 3: ICU patients without severe MOF and without sepsis.
Methods: 24 h Holter-monitoring, APACHE-II and sepsis-scoring; plasma levels of cytokines.
Results: See table.
Conclusions: In our pilot study, no significant higher incidence of ventricular arrhythmias has been seen in MOF patients with and without sepsis.

P031

A study of medical in-patients reveals a high number with organ failure

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Objective: To investigate the number of patients on the general medical wards who fulfill the current UK National Health Service Executive (NHSE) criteria for admission to a high dependency unit (HDU) [1].
Design, subjects and methods: On one day, a detailed survey of 174 patients already admitted to nine medical wards was performed. Demographical data, the function of six organs as assessed by the Sepsis-related Organ Failure Assessment (SOFA) score plus the level of interventions using the Therapeutic Intervention Scoring System (TISS) was recorded.
Results: See table.
Conclusions: This study suggests that 16% of patients on general medical wards fulfilled the UK NHSE guidelines for admission to High Dependency Care [1]. Currently there are no recommendations regarding the size of these units and these data suggest that the resource implications would be considerable. However the benefits for patients of this higher level of care has yet to be scientifically established but many institutions already recommend it to reduce morbidity and mortality [2].

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P032

Evaluation of an interdisciplinary minimal dataset for intensive care documentation

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Critical Care 1997, **1(Suppl 1):**P032

Objectives: The Austrian working group for the Standardization of a Documentation System for Intensive Care (ASDI) has defined a minimal dataset (MDS) for a national, interdisciplinary documentation standard for intensive care. Goal of the study was to evaluate the concordance between the contents of the defined dataset and actual needs.

Table (abstract P031)

Median (ranges)	No organ failure (n = 147)	At least 1 failing organ (n = 27)
Age years	61 (19-95)	68 (21-90)
Male : female %	58 :42	52 : 48
For active treatment %	89	85
SOFA score*	0 (0-1)	4 (2-14)
TISS points*	4 (0 - 27)	9 (1-53)
Hospital stay* days	10 (2-337)	24 (5-149)
Hospital mortality %	3	7

*P < 0.01.

Design: Thirteen ICUs participated in a trial, using the provided program for documentation of all admitted patients during a period of 4 weeks. In addition, a questionnaire, including a printout of the dataset, was distributed to the unit coordinators to evaluate documentation needs.
Results: Three hundred and seventy-six patients were documented in 1591 patient days. Valid SAPS II scores were found in 29% of discharged patients [39.1 ± 15.5 points (mean ± SD)]. Seven out of 122 MDS parameters (5.7%) were found superfluous. Several items, necessary for cost calculation and performance analysis were found to be missing. Moreover, documentation effort exceeded preset limits (10 min per patient and day) in 38% of the cases.
Conclusions: The contents of the ASDI dataset fitted existing needs closely. However, the questionnaires uncovered the need for structural changes to reduce documentation effort to the default limits. Moreover, the low number of valid SAPS II scores indicates that several ICUs have not enough resources to evaluate all data items for all patients on a daily base. The MDS was revised according to these results. It now represents a broad-based consensus, which seems to be qualified as a foundation for the national documentation system.

P033

The cardiopulmonary bypass supported high-risk PTCA (CPB-PTCA): a useful model for the study of CPB-dependent systemic inflammatory response syndrome (SIRS)?

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The mechanisms underlying myocardial depression following open heart surgery with extracorporeal circulation is still a matter of debate. One important trigger mechanism responsible for myocardial depression seems to be related to the release of cytokines during the systemic inflammatory response. Aim of the present study was to investigate whether CPB supported PTCA might be a useful model for the differentiation of surgery-dependent and CPB-SIRS-induced myocardial depression.
Methods: PTCA supported angioplasty with CPB; transesophageal echocardiography; wall motion score (WMS); plasma levels of cytokines

Table (abstract P033)

	I	II	III	IV	n
MAP	93.3 ± 24.7	59.3 ± 6.2	60.3 ± 7.5	71.0 ± 16.0	5
HR	89.3 ± 30.5	81.5 ± 3.5	82.0 ± 14.4	105.3 ± 23.5	4
CVP	12.8 ± 2.9	12.3 ± 1.0	15.0 ± 6.1	17.0 ± 6.8	5
cSVR	771.3 ± 312.8	691.8 ± 172.4	748.3 ± 167.7	635.3 ± 975.9	5
Total flow*	3.0 ± 0.9	2.9 ± 0.7	2.4 ± 1.0	2.0 ± 0.7	4
WMS	1.9 ± 0.4	2.3 ± 0.5	2.1 ± 0.2	2.2 ± 0.3	3

APACHE II-score on day 1 and after PTCA: 11.4 ± 2.1 versus 14.9 ± 6.4 (n = 7)

Table (abstract P033)

	At the start	After 5 h	n
TNF-α	8.3 ± 6.2 pg/ml	20.1 ± 19.0 pg/ml	4
TNF R p55	2.0 ± 0.4 ng/ml	3.1 ± 0.3 ng/ml	4
TNF R p75	2.5 ± 1.3 ng/ml	5.1 ± 1.6 ng/ml	4
IL-6	10.6 ± 4.4 pg/ml	98.5 ± 54 pg/ml	4
Endotoxin	0.5 ± 0.2 EU/ml	0.3 ± 0.1 EU/ml	2

*Total flow = cardiac index and CPB-flow mean ± SD.

and parameters as shown in the table. Seven patients, mean age 61.3 years, ejection fraction, 17–64%: five patients with three-vessel-CAD; two patients with two-vessel-CAD: four patients with CABG. (I) Before CPB: (II) beginning CPB: (III) immediately before PTCA; (IV) end CPB.
Results: See table.
Summary: CPB-PTCA helps to discriminate between surgery-induced and CBP-dependent systemic inflammatory response syndrome.

P034

A new type of glycoconjugate vaccine containing *Klebsiella* fimbriae type 1 and 3 as carrier proteins

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Opportunistic pathogens continue to be a major cause of infections among hospitalized patients. The vaccination as a primary defence strategy and the development of new vaccines of broad specificity offer an important tool to use against bacterial infections. Our study concentrates on a glycoconjugate vaccine based on covalently attached bacterial antigen to *Klebsiella* fimbriae type 1 and 3.
Fimbriae mediate the attachment of many pathogenic bacteria to host cells. The mannose-specific fimbriae of type 1 are expressed in many enterobacterial species. The mannose-resistant type 3 of fimbriae are produced by majority strains of *Klebsiella* [1]. These surface antigens may serve as carrier proteins and also as a common antigen for vaccine of broad specificity. For the studies of stimulation of immune mediators it is necessary to have the fimbrial preparations free of endotoxin. In order to isolate pure fimbriae, simple methods have been adopted, especially considering the contamination with lipopolysaccharide. The procedure involves homogenization, ammonium sulfate precipitation, gel filtration in the presence of 6 M urea and hydrophobic chromatography on phenyl-sepharose. The purity was checked in SDS-PAGE, with silver staining specific for proteins and lipopolysaccharides as well as in mass spectrometry with MALDI-TOF technique, which allowed also to determine the precise molecular mass of fimbrial monomers. We have also undertaken the studv on stimulation of cytokine induction by fimbriae. The type 3 of *Klebsiella* fimbriae are moderate inductors of IL-6 and interferon, whereas type 1 is even less potent inductor. Both types of fimbriae are almost inactive regarding the stimulation of TNF when tested in human whole blood assay. These results prompt us for studies on practical use of fimbriae, especially type 1, as carriers for conjugate vaccine. Therefore we conjugated fimbrial protein with a core oligosaccharide fraction obtained from *Escherichia coli* K-12 lipopolysaccharide, which has been found to contain an epitope common for several enterobacterial species [2]. The conjugate was immunogenie in rabbit model regarding to the oligosaccharide hapten and fimbrial carrier, respectively.
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P035

Investigation of an outbreak of multiresistant *Enterobacter aerogenes* infection in an intensive care unit

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In February 1996 we have experienced an outbreak with a multiresistant *E aerogenes* strain in a 12-bed intensive care unit (ICU) separated in two rooms. Over a 3-day period, four patients were found to be colonized at multiple sites (endotracheal aspirate, urine) by *E aerogenes*. The medical and nursing charts were reviewed in order to define the sequence of events which led to colonization in these patients. It was found that one patient probably acted as the index-case since he was retrospectively found to be already colonized with *E aerogenes* in another ward before his admission to the ICU. The three other patients were housed in boxes immediately adjacent to the one of the index case but no strict isolation precautions were taken for these patients since the index case had not been reported as being colonized with a multiresistant organism. All four patients had previously received broad-spectrum antibiotics and three of them were intubated and mechanically ventilated. Colonization ultimately progressed to infection in three of the four patients [one pneumonia, two urinary tract infections (UTI)]. Three patients were treated with cefepime as single drug therapy (2 × 1–2 g iv/day); two of them died (one due to underlying disease, the other because of uncontrolled infection) whereas one was cured clinically. Bacteriological failure was observed in two patients and eradication failure was associated with the development of resistance to cefepime during treatment in one of them. All *E aerogenes* strains isolated in the four patients had the same identification characteristics and displayed a similar in vitro antimicrobial resistance profile (the strains were sensitive only to gentamicin, amikacin, imepenem and to cefepime). Molecular epidemiological typing studies using random amplification of polymorphic DNA (RAPD) with two different 10-mer oligonucleotide primers yielded indistinguishable patterns for the four outbreak strains while these were clearly different from five non-outbreak associated strains which were included as controls.
Nosocomial outbreaks due to multiresistant *E aerogenes* is an emerging concern in ICU. Infections caused by this organism are often not detected at an early stage and are both difficult to control and to treat. In the present case, antibiotic treatment with cefepime did not prove very effective for controlling the outbreak which terminated only following the reinforcement of handwashing and isolation contact precautions. RAPD fingerprinting proved useful in this outbreak for discriminating the outbreak strains from epidemiologically unrelated strains. Further clinical trials are needed to optimize the therapy of multiresistant *E aerogenes* infection.

P036

ICU comparative survey of bacteremia in a teaching hospital

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Many studies have established that nosocomial infection rates are more important in intensive care units (ICU). The objective of the study was to evaluate frequency and severity of imported and acquired nosocomial bacteremia in the different ICU of a teaching hospital in relation to bacteremia occurring in the entire hospital.
Methods: The prospective study was carried out from 1 November 1995 to 30 April 1996 in a 1837 bed teaching hospital including 121 ICU beds. Bloodstream infection (BSI) criteria were defined according to CDC criteria. All data were collected by a medical and nursing team from positive blood cultures isolated in the microbiology department, and the recruitment used an evaluation schedule. All infection data was validated by an external investigator and analyses were performed on EPI INFO.
Results: Of patients with nosocomial bacteremia, 28.9% (69/239) needed a stay in ICU. The ICU represent 6.6% of the total beds, 10.9% of the admissions, and 6.5% of the hospital days. Nosocomial BSI complicated 1.68 per 100 admissions to the ICU during the study period with an incidence density of 3.61 per 1000 days of care. There were no significant differences in patient characteristics, except for their origin: transferring of another hospital increased the risk for patients admitted in ICU [Relative risk (RR) × 2.6, $P < 0.001$].
Clinically, hypothermia occurred nearly only in ICU (RR × 17, $P < 0.001$), but neutropenia ≤ 1500 was less present (3% versus 14%, $P < 0.05$).
Only respiratory tract infection multiplied by 5 ($P < 0.0l$) the risk of BSI in ICU patients comparatively to patients of other units. There was no

significant difference for the other sources: intravascular devices, surgical wound, gastrointestinal tract and skin infections. On the contrary, genitourinary sources of BSI were more frequent outside ICU (with a protective effect in ICU: RR = 0.53. $P < 0.01$).
The patient was more frequently already treated with antibiotics in ICU when BSI occurred (49.3% versus 34.7%, $P < 0.01$).
The average length of stay in hospital increased by 8 days for patients needing a stay in ICU. The mortality rate also increased and was multipled by 3 ($P < 0.01$). The mortality was not bound with the underlying disease (Mac Cabe, surgical patients, ASA). SAPS II above 40 the day of the bacteremia was a predictive value of early mortality.
Conclusion: BSI prevention policy must take place in a total nosocomial infection control and must not be restricted to sole ICU.
Acknowledgement: This work was supported by the Scientific Committee of Option-Hôpital, with a grant of Roussel-Uclaf Company.

P037

Positive cultures of central venous catheter (CVC) in intensive care unit (ICU) patients: results from a prospective survey

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A 1-year prospective survey was conducted to determine the incidence rate of positive catheter culture (PCC) in ICU patients.
Methods: All consecutive CVC including dialysis catheters were studied. All dialysis catheters were single lumen CVC. The sites of CVC insertion, and the number of lumen of non-dialysis CVC were at the discretion of the attending physician. After CVC removal a quantitative culture of the CVC distal tip was performed. A 10^3 cfu/ml CVC quantitative culture threshold defined PCC. The risk factors studied for PCC were type of CVC, site of insertion, number of lumen, duration of catheterization, fever, and inflammatory local signs at the time of CVC removal.
The introducers for pulmonary artery catheters were studied separately.
Results: During that time 420 CVC were placed in 173 patients. Among them, 153 were dialysis catheters. The sites of insertion were internal jugular vein (n = 250), femoral vein (n = 120), subclavian vein (n = 34), and axillary vein (n = 16). Twenty-nine CVC were tunneled included the 16 CVC axillary sites. The number of single lumen, double lumen, and triple lumen CVC were 170, 191, and 59, respectively. The median duration of catheterization was 5 days. The incidence rate of PCC was 13.7%. It corresponded to 2.2 PCC/100 CVC-day. The type of CVC, the site of insertion, the number of CVC lumen, and fever at the time of CVC removal are not associated with PCC ($P = 0.15$, $P = 0.35$, $P = 0.73$, and $P = 0.57$, respectively). The risk factors for PCC were duration of catheterization > 5 days ($P = 0.017$), and the presence of local inflammatory signs ($P < 0.001$). Erythema was the only inflammatory sign associated with PCC in 12/13 cases, and a CVC site infection defined as presence of pus occurred in one case. The PCC yielded coagulase negative staphylococci (n = 26), *Enterobacter* spp (n = 11), *Staphylococcus aureus* (n = 8), *Pseudomonas aeruginosa* (n = 7), and others (n = 9). Bacteremia related to CVC with PCC occurred in five cases (1.19%), none of them were Gram-negative bacteria.
Twenty-two introducers were placed for a median duration of 4 days. The sites of insertion were internal jugular vein (n = 15), subclavian vein (n = 7). None of the introducers were associated to local inflammatory signs. Only one introducer culture yielded ≥ 10^3 cfu/ml (coagulase negative *Staphylococcus*).
Conclusion: In this study *Enterobacter* spp emerged as the second PCC etiologic agent. However, none of the *Enterobacter* spp were causative agents of CVC-related bacteremia. Physicians should be aware of PCC risk in cases of local erythema, and consider removing CVC.

P038

Meropenem versus imipenem/cilastatin in the treatment of serious bacterial infections in ICU: an open randomised multicentre study

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In an open randomised multicentre trial the efficacy (clinical and bacteriological) and safety of empirical monotherapy with meropenem (MEM: 1 g every 8 h, iv) have been compared with imipenem/cilastatin (IMI: 1 g every 8 h, iv) in patients with serious bacterial infections at one or more of the following sites: systemic, intra-abdominal and lower respiratory tract infections.
A total of 212 patients (107 MEM, 105 IMI) entered the study of whom 199 (100 MEM, 99 IMI) were evaluable for clinical response and 180 (92 MEM, 88 IMI) for bacteriological response.
In the clinically evaluable population, 85 (85.0%) of the 100 MEM patients and 84 (84.8%) of the 99 IMI patients had a single site of infection whereas the remainder had two or more sites of infection. Infections of the lower respiratory tract and peritoneal cavity predominated accounting for 133 (62.7%) and 58 (27.4%) cases respectively. sepsis/ bacteraemia/ FUO accounted for 21 (9.9%) cases.
Patients were clinically evaluated as satisfactory (completely cured or improved) or unsatisfactory (unchanged or worse).
In an intention-to-treat analysis overall, satisfactory response rates were 84.0% (84 of 100 patients) in the MEM group and 76.8% (76 of 99 patients) in the IMI group. The difference (MEM-IMI) is 7.23%, the 95% CI is -3.76% to 18.22% and the corresponding P-value is 0.199. The satisfactory bacteriological responses were 72.8% (67 of 92 patients) in the MEM group and 69.3% (61 of 88 patients) in the IM1 group. The difference (MEM-IMI) is 3.51%, the 95% CI is -9.74 to 16.75 and the corresponding P-value is 0.604. The causative organisms were mainly *Escherichia coli* (n = 45) and *Pseudomonas aeruginosa* (n = 28). The clinically satisfactory response rates for the specific sites were 79.4% (MEM) and 75.0% (IMI) for the lower respiratory tract infections, 96.0% (MEM) and 83.9% (IMI) for the intra-abdominal infections and 85.7% (MEM) and 66.7% (IMI) for the systemic infections.
Both drugs were well tolerated with adverse events considered to be related to the study drug reported for four (3.7%) of 107 patients in the MEM group and for three (2.9%) of 105 patients in the IMI group. No drug-related nausea and vomiting were reported in either group but one drug-related seizure was reported in the IMI group.
In conclusion MEM is clinically and bacteriologically at least as effective as IMI for the treatment of serious bacterial infections in ICU patients and is well tolerated.

P039

Ecological and economic impact of ceftazidime and probabilist antibiotherapy limitation strategy in ventilator-associated pneumonia

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Aims of the study: In our intensive care unit, the ventilator-associated pneumonia coefficient and density of incidence were respectively 21 for

Table (abstract P039)

%	*Ps aeruginosa*	*Ps cepacia*	*Acinetobacter baumanii*	KES	*Staph aureus*
G1					
Incidence	19	16.7	6	14.3	19
CTZ-S	61	85	0	90	-
AMK-S	55	0	40	83	-
CPX-S	50	0	0	83	-
OXA-S	-	-	-	-	30
G2					
Incidence	13	11.5	3	23	-
CTZ-S	85	100	33	94	-
AMK-S	80	0	33	94	-
CPX-S	40	0	0	88	-
OXA-S	-	-	-	-	63

Ps, Pseudomonas; KES, *Klebsiella-Enterobacter-Serratia; Staph, Staphyloccocus;* CTZ-S, ceftazidime-sensitive; AMK-S, amikacin-sensitive; CPX-S, ciprofloxacin-sensitive; OXA-S, oxacillin-sensitive.

100 ventilated-patients, and 20 for 1000 days of ventilation. In 1995, we had observed an increase of ceftazidime-resistant *Pseudomonas aeruginosa* frequency. We, therefore, compared the ecology and the cost of antibiotherapy between the first 1995 semester and the first 1996 semester, after we prescribed less of ceftazidime, and we limited the probabilist treatment in only at risk patients.
Patients and methods: For suspicion of ventilator-associated pneumonia in patients presenting the criteria of Andrews we realized 75 bronchiolo-alveolar lavages in the first 1995 semester (GI) and 70 in the first 1996 semester (G2). The diagnosis of this pneumonia was positive when bacteriologic quantitative cultures were > 10^4 cfu/ml.
Results: See table.
Between the two periods the total cost of antibiotherapy and the cost of beta-lactamins respectively decreased to 15 and 25%.
Conclusion: Our strategy was favourable for ecology and economy in our intensive care unit. These results must be confirmed during the 2 complete years.

P040

Administration of amphotericin B in lipid emulsion decreases nephrotoxicity: a controlled study in critically ill patients

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Objective: To evaluate the differences in administered in a lipid emulsion compared to amphotericin B (AmpoB) in dextrose 5%, for the treatment of *Candida albicans* infection.
Sixty consecutive critically ill patients with confirmed or suspected *Candida* infection received AmphoB (1 mg/kg/24 h) administered randomly in either dextrose 5% (group A) or in lipid emulsion (20% Intralipid®) (group B).
Measurements and main results: Clinical tolerance (fever, chills, hemodynamics), liver function tests, electrolytes and coagulation profile were evaluated. Patients receiving AmphoB in lipid emulsion experienced a lower incidence of drug-associated fever (61.4% versus 5.8%, $P < 0.003$), rigors (54% versus 8.5%, $P < 0.004$), hypotension (17% versus 0%) and nephrotoxicity. Significant thrombocytopenia (264,500 ± 71,460/mm^3 to 163,570 ± 34,450/mm^3, $P < 0.01$), not associated with active bleeding, occurred with AmphoB-lipid emulsion but not with the dextrose regimen.
Conclusions: Treatment with AmphoB-lipid emulsion of critically ill patients with *Candida* infection seems to be safer and as effective as the conventional mode of administration.

P041

Valuation of bacteriological quantitative cultures obtained by broncho-alveolar lavages in ventilator-associated pneumonia

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Aims of the study: Quantitative cultures obtained by protected specimen brush (PSB) with at least one microorganism > 10^3 cfu/ml were the reference for ventilator-associated pneumonia diagnosis. This prospective study compared the bacteriological results of broncho-alveolar lavages (BAL) to PSB.
Patients and methods: In 100 cases of late ventilator-associated pneumonia (13 ± 4 days of ventilation), we realized PSB then BAL. Seventy-five specimens were realized on antibiotherapy era and 25 without antibiotherapy treatment. We calculated the sensitivity (SEN), specificity (SPE), the positive and negative predictive value (PPV, NPV), and the efficiency (EFF).
Results: See table.
Conclusion: Quantitative cultures obtained by BAL was an alternative for ventilator-associated nosocomial pneumonia, particularly if the antibiotherapy was stopped before BAL performed.

Table 1 (abstract P041)

n	BAL+PSB+	BAL+PSB-	BAL-PSB+	BAL-PSB-
Total = 100	29	29	3	39
With ATB	18	25	3	29
Without ATB	11	4	0	10

Table 2 (abstract P041)

n	SEN %	SPE %	PPV %	NPV %	EFF %
Total =100	90.6	57.3	50	92.8	68
With ATB	85.7	53.7	41.9	90.6	62.7
Without ATB	100	71.4	73.3	100	84

P042

Risk factors for mortality in mechanically ventilated patients with nosocomial pneumonia

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Background: Patients who develop pneumonia while receiving mechanical ventilation appear to have a two- to tenfold increased risk of mortality compared to patients without pneumonia.
Objective: The aim of this study was to identify possible risk indicators for pneumonia leading to death in critically ill patients.
Methods: Several potential risk factors for mortality in ventilated patients with nosocomial pneumonia were evaluated using multivariate statistical techniques.
Results: Eighty-two (26%) episodes of nosocomial pneumonia were detected in 314 consecutive patients admitted to an 18-bed general intensive care unit from January to December 1995. The mortality of patients with nosocomial pneumonia was higher when compared with fatality rates of patients without pneumonia (34% versus 17.2%, $P < 0.01$). Multivariate analysis selected three prognostic factors significantly associated with higher risk of death: the presence of septic shock (OR 18.93, 95% CI, $P < 0.01$); ARDS (OR 30.64, 95% CI, $P < 0.01$); and APACHE II score at the time pneumonia was diagnosed (OR 1.27). Of note is that many other factors were significantly associated with mortality but were not an independent predictors of mortality.
Conclusion: In the present study, the presence of shock and ARDS were the strongest predictors for mortality in ventilated patients with nosocomial pneumonia.

P043

Nosocomial pneumonia and bacteraemia in the Belgian intensive care units (ICU) network: epidemiology and risk factors

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Introduction: Surveillance of nosocomial infections (NI) with feedback of own results to healthcare personnel has repeatedly been shown to be an efficacious measure, that can significantly contribute to the prevention of these infections. Moreover, multicentric surveillance can give an added value to local results by offering aggregate results as a basis tor comparison. However, one of the prerequisites for meaningful comparisons to be made is that the results be comparable in terms of case mix, intrinsic patient risk and exposure to high-risk devices and treatments.
Objectives: The aim of this study was to measure the incidence of nosocomial pneumonia (PN) and blood stream infection (BSI) in Belgian ICUs and to evaluate the influence of the different risk factors included in the surveillance on these NIs.

Table (abstract P043)

Risk factors for pneumonia	OR	Risk factors for bacteraemia	OR
SAPS II score ≥ 20 and < 30	2.3	SAPS II score ≥ 30 and < 50	5.1
SAPS II score ≥ 30 and < 50	4.4	SAPS II score ≥ 50	8.4
SAPS II score ≥ 50	11.7	Infection at entry (any site)	1.3
Prior thoracic surgery	3.5		
Unscheduled surgical admission	1.6		

Materials and methods: In January 1996, a new voluntary nationwide surveillance system was initiated jointly by the Belgian Intensive Care Society (SIZ) and the Institute of Hygiene and Epidemiology (IHE). Between January and June, 8475 patients from 64 different ICU units were observed during a total of 77 ICU-trimesters. Data included patient characteristics at entry (including type of admission. SAPS II score and underlying disease), day-by-day exposure to high-risk devices and treatments (including ventilation and central lines), and vital status at discharge.
PN and BSI were definitions based upon HELICS criteria. For each episode diagnostic criteria were registered in detail, including microbiological evidence. Multivariate logistic regression was used to determine the significant risk factors (RF) and their associated odds ratios (OR).
Results: In total, 547 PN and 200 BSI were observed (incidence: 6.5% and 2.4%; first episodes only). Median SAPS II score was 28 (PN: 42, BSI: 41.5); median length of stay was 4 days (PN: 14, BSI: 15) and global death rate was 9.8% (PN: 30.5%, BSI: 35.5%). Significant RF at admission ($P < 0.01$) and their OR are given in the table.
During stay, crude IN risk is evidently linked to duration of stay, PN risk to number of ventilation days, BSI risk to central catheter days and incurrent pneumonia. However, the complex nature of the confounding by duration of stay, (early) mortality or discharge requires more complex models than this first approach by logistic regression.
A logistic model was also used to predict mortality risk for the whole group and for the PN and BSI subgroups.
Conclusions: Our results are in accordance with those currently found in the literature. Even if the risk factors are not exactly the same, they represented the two classical risk poles: severity of illness and the exogenous exposition to specific devices. More research is needed to see how risk assessment can be simplified, whilst keeping its value for risk adjustment with the aim of comparing performance between individual units.

P044

A nosocomial infection surveillance network in Belgian ICUs: methodology and feedback

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Introduction: The risk for nosocomial infections (NI) in ICUs is five to 10 times higher than in other hospital care units, causing extra morbidity, mortality and costs. Previous studies have shown a significant decrease in NI after the set up of effective surveillance programs. If this surveillance is performed in a multicentric setting, the results from the aggregate database can offer an added value to the local results. The most important element is the production of meaningful feedback reports, allowing each ICU to evaluate its own situation as compared with the aggregate results of the whole studied group.
Objectives: The aim was to provide each ICU with its own incidence of nosocomial pneumonia (PN) and blood stream infection (BSI), and their mortality rate after controlling for the relevant risk factors. These include severity of illness (SAPS II) and exposure to specific devices and risks. Additionally, the feedback reports should also provide the results of the same analyses performed on the national database, obtained by pooling the data of all participating units.
Materials and methods: In December 1995, all Belgian ICUs were invited to join a voluntary prospective NI surveillance network, using a common protocol, which was largely based on the consensus obtained in the HELICS project. Participation was for 3-month periods, starting as of January 1996. During the first two trimesters of 1996, in total 64 different ICUs (from 28% of the Belgian acute care hospitals) have joined the network.
Data included: (i) Patient characteristics at admission: administrative data, type of admission. SAPS II score, prior surgery or antibiotics, impaired immunity, trauma, and infection at entry, (ii) During ICU stay, exposure to ventilation, central catheters and a number of other devices and treatments were recorded on a daily basis, (iii) If a PN or BSI occurred, diagnostic criteria were registered in detail, including microbiological evidence. Finally, (iv) vital status at discharge was registered.
Results: From January to June 1996, over a total of 77 ICU-trimesters. 8475 patients were observed. The same set of feedback tables was produced for each individual ICU and hospital (by trimester and for both trimesters, if applicable). Besides the mortality and the incidence of PN and BSI by major risk categories, each ICU could also compare its own case mix, length of stay and level of utilization of relevant devices (ventilation. central catheters, antibiotics, feeding practices, etc) with the corresponding figures in the national database.
The fact that some hospitals presented high infection rates after control for the relevant risk factors, without any increase in length of stay nor in death rate, poses challenges to the interpretation of the results.
Before high infection rates can he attributed to deficiencies in the process of care, one must carefully control for differences in case mix, risk factors and length of stay, and make sure that the validity of the results is sufficient and homogeneous.
Even so, the availability of standardised surveillance results should be of great help in any ICU willing to critically evaluate and improve its own performance.

P045

Nosocomial infection prevention practices in Belgian intensive care units

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Background: In January 1996, a multicentric surveillance of nosocomial infections in Belgian Intensive Care Units (ICUs) was initiated, proposing to all ICUs of the country a voluntary quarterly registration (pneumonia and bacteraemia acquired in the ICU). Besides this continuous registration, a questionnaire survey was conducted, investigating prevailing practices for the prevention of bacteraemia and pneumonia. Results are compared to the European EURONIS A study of 1990.
Objectives: To describe prevailing preventive practices in use among the ICUs participating in the national surveillance programme (90 units from 72 hospitals).
Method and population: In January 1996, a two-page questionnaire was mailed to all 90 participating units; 62 responded (68.9%). Mean size of the units was 8.7 beds. Response rate was higher among university hospitals (53.8% of all Belgian university hospitals).
Results: On average 2.2 nurse full time equivalents per ICU bed were available, slightly more than the Belgian figure in the 1990 Euronis survey (1.9 FTE/bed).
Nosocomial pneumonia. For aspiration of ventilated patients, 71.2% of the units use sterile gloves: 37.3 use non-sterile gloves. In 61.4% of the units, the respiratory circuit is only changed between even patient. This figure was 42% in 1990. Use of humidification equipment varies widely; heat and moisture exchanger (50%) are the most commonly used. A filter on the expiration tube is used systematically in 61.4% of the units.
Nosocomial bacteraemia. At insertion of a central venous catheter 97% of the respondents systematically use sterile gloves and 89.8% perform handwashing with an antiseptic. Masks, caps and aprons are used less frequently and in various combinations. For skin disinfection 81.3% of the units use alcoholic solutions, versus 15.2% using aqueous solutions. Once

the catheter is in place, dressings are changed daily in 37.3% and every other day in 42.4%. Catheter replacement was generally only performed at symptoms of infection: 64.4% (versus 69% in 1990). In the other units, replacement was systematic every week (20.3%), or more (11.9%).
Conclusions: During the last 5 years, preventive practices in Belgian ICUs have converged towards existing guidelines, but a greater variability in practices is observed where no consensus recommendations are available. The relatively low numbers of health care personnel remains a structural risk factor.

P046

Effects of endotoxin elimination therapy using polymyxin B immobilized fiber in patients with septic shock after surgical operation

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Introduction: Polymyxin B immobilized fiber (PMX-20R: Toray Industries, Inc) has been developed in Japan for direct removal of endotoxin. Hanasawa *et al* [1] reported the use of a PMX-20R column for treating endotoxemia in animal and clinical studies. Polymyxin B was chemically fixed onto polystyrene fiber to remove endotoxin by direct hemoperfusion. We used PMX-20R to treat septic shock patients who had developed complicated multiple organ failure.
Purpose: To assess the changes in hemodynamics and cytokine levels (IL-6, TNF) during hemoperfusion with PMX-20R in treating nine septic shock patients (2 females, 7 males, mean age: 60 years old) after surgical operation.
Methods: A double-lmuen catheter was inserted into the patient's femoral vein, and direct hemoperfusion was performed using a blood pump to remove endotoxins. The blood access for hemoperfusion consisted of a venous-to-venous system. Extracorporeal circulation was performed for 120 min wilh blood flow of 80-120 ml/min.
Results: Six (67%) of nine septic shock patients who had developed complicated multiple organ failure after surgical operation survived after using PMX-20R. The mean APACHE-2 score of the patients was 27 ± 9. During hemoperfusion, the patient's vital signs were stable. Mean arterial blood pressure in fair prognosis patients increased significantly compared with control values, while slight decreases occurred in leukocyte and platelet counts after 30 min of this treatment. The values of toxicolar and endospecy (Limulus colorimetric assay) greatly declined in fair prognosis patients. IL-6 and TNF levels in fair prognosis patients had declined at 24 h post PMX. On the other hand, the values in poor prognosis did not decline.
Conclusions: Hemoperfusion with PMX-20R may be a useful therapeutic strategy in patients with septic shock. This treatment should be considered for use in patients with suspected Gram-negative rod infections after receiving surgical operation.
Reference

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P047

Variations of atrial natriuretic peptide, cortisol and endothelin during different body positions

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Objective: Elevated cortisol in critically ill patients has traditionally been assumed to be an expression of prolonged stress, mediated by an increased activity of the hypothalamic-pituitary-adrenal axis. Recent studies have questioned this assumption by pointing out that septic and traumatized patients may have elevated plasma cortisol (C) while ACTH is suppressed [1]. Since endothelin (E) and atrial natriuretic peptide (ANP) have been reported to be elevated in these groups of patients too, it was suggested they might influence plasmatic cortisol levels and ACTH in different ways: while E was supposed to increase plasma cortisol by a permissive effect on the adrenal action of ACTH, ANP was reported to mediate a central suppression of ACTH; the latter being insufficient to counterbalance the peripheral increase of cortisol mediated by E.
Since hormonal investigations in critically ill patients are influenced by the disease itself and the therapeutic methods applied, we chose to test the interactions between C, E and ANP in healthy adults during different body positions as a simple method of modifying central volume load and thereby the concentration of ANP.
Methods and statistical analysis: After approval by the institutional ethical authorities and informed written consent we investigated nine healthy, non-smoking males in a randomized fashion on different days [supine position (P1) first and sitting position afterwards (P2), sitting position only (P3)]. After a resting time of 20 to 30 min within each observation period we took blood samples for the measurement of the plasma concentrations of C, ANP and E.
Statistical analysis was performed with Wileoxon's test for paired observations and Spearman's signed rank correlation test. Significance level was set to $P = 0.05$.
Results: C and ANP were significantly increased comparing the supine with the sitting position (*C*, $P < 0.04$ for P1 versus P2; $P < 0.05$ for P1 versus P3; ANP, $P < 0.03$ for P1 versus P3). E did not change significantly throughout the study.
We found a significant correlation between C and ANP in the supine position ($r = 0.8$, $P < 0.03$), which could not be demonstrated in the sitting position. We found no correlation between C and E and between ANP and E, respectively.
Conclusions: We found a positive correlation between ANP and C in the supine position and no correlation in the sitting position in healthy volunteers.
It has been suggested that the increase in ANP in critically ill patients would suppress ACTH, while a higher concentration of E would augment the adrenal's responsiveness to ACTH, leading to an increase of C. If this was true also for healthy subjects, one might expect a decrease of cortisol when ANP increases and E remains unchanged.
Our findings are in contrast to this assumption. Therefore we conclude that, at least in our study population, the suggested interaction between ANP and cortisol cannot be reproduced by altering posture and central volume load.
Reference

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Table (abstract P047)

	Supine (P1)	Sitting after supine (P2)	Sitting only (P3)
Cortisol (nmol/l)	308.8 ± 77.5	232.7 ± 128.8	242.2 ± 60.8
ANP (pg/ml)	28.16 ± 8.78	22.92 ± 10.9	17.26 ± 7.28
Endothelin (pg/ml)	20.5 ± 3.9	20.4 ± 3.3	17.2 ± 3.1

P048

Fluctuations of inspiratory concentration of nitric oxide (NO) during mechanical ventilation

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Critical Care 1997, **1(Suppl 1):**P048

Objectives: To test inspiratory NO concentrations along the inspiratory limb of the respiratory circuit during mechanical ventilation with different inhaled NO concentrations.
Methods: A Servo 300 NO-A prototype (Siemens-Servotek, Solna, Sweden) was used for controlled mechanical ventilation of an artificial test lung with a filling volume of 1 l at an FiO_2 of 1.0. Different NO concentrations of 0.1, 1, 10 and 100 ppm (NOin) were applied. In the Servo 300 NO-A a digital controlled valve is used allowing the exact

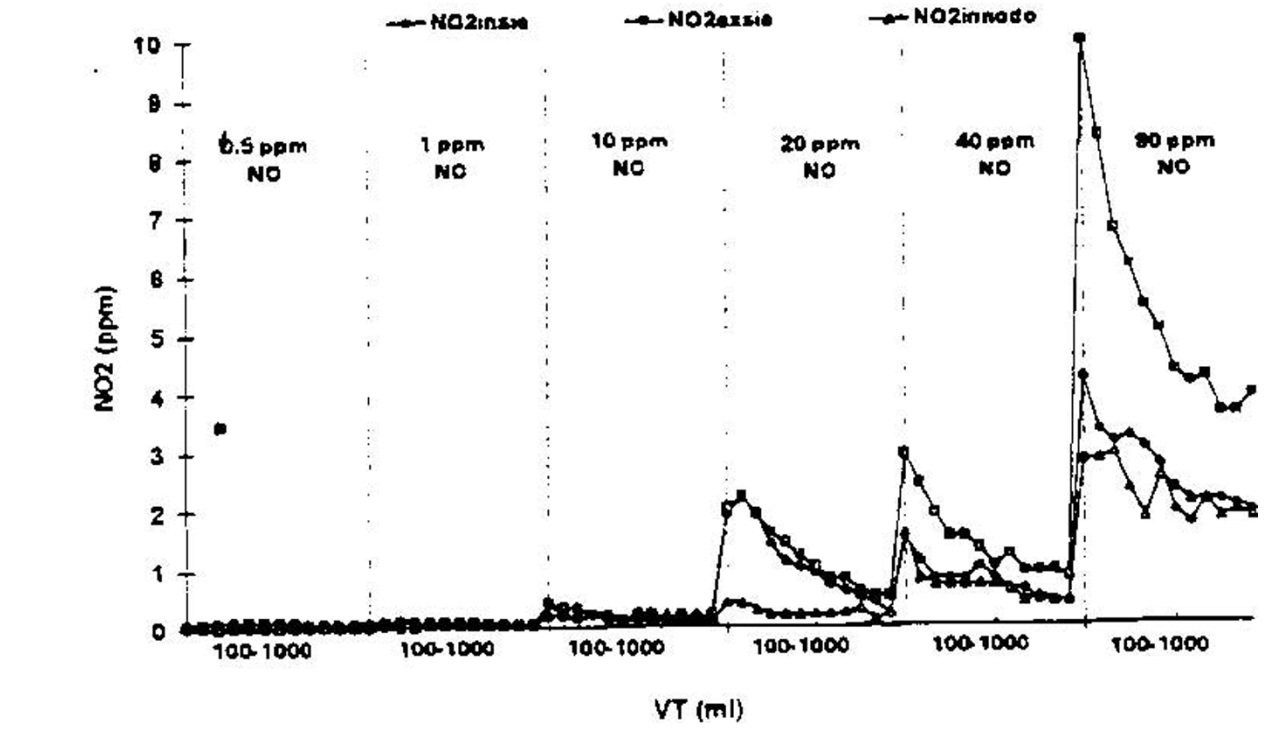

Figure (abstract P048)

flow-proportional admixture of NO into the inspiratory gas stream. NO is delivered from an NO tank with a fixed concentration dissolved in N_2. NO was measured by chemiluminescence (CLD 700 AL, Eco Physics, Duernten, Switzerland) at four different positions (Pos 1–4) along the inspiratory limb of standard respiratory tubing including an active heating system (Concha Therm III with Aerodyne humidification column. Kendall, Neustadt, Germany). Pos 1: immediately behind the respirator's inspiratory outlet: Pos 2: immediately behind the heating column: Pos 3: in the middle between the heating column and the y-piece: Pos 4: immediately before the y-piece.

Results: The results for the NO measurements at the different positions are shown in the figure (left hand side) for the different inhaled NO concentrations. Values are shown as a percentage of NOin. NO_2 concentrations in ppm are shown in the figure (right hand side) for the different NOin.

Conclusions: These data suggest that NO concentrations are fluctuating also when NO inhalation is accomplished with a device to administer NO flow proportional only during inspiration by means of a digital controlled valve. Interestingly, at the beginning of the inspiratory circuit NO concentrations are highest and decrease immediately behind the active heating system. This phenomenon is also obvious for NO_2 when the inspiratory NO concentrations are ≥ 10 ppm, so that a relevant oxidation to NO_2 takes place. The more distal along the inspiratory limb NO_2 is measured, the more it inereases again, probably due to further oxidation from NO and O_2. It might well be that the sharp decline in NO and NO_2 is due to a reaction of those compounds with the water in the active heating system. For the clinical use, this phenomenon should he cautiously observed during the inhalation of NO and the point for monitoring the inspiratory gas mixture should be as distal as possible along the inspiratory limb.

Acknowledgement: This study was in part supported by DFG: Fa139/4-l.

P049

Nitrogen dioxide (NO_2) production for different doses of inhaled nitric oxide (NO) during mechanical ventilation with different tidal volumes using two prototypes for the administration of NO

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Critical Care 1997, **1(Suppl 1):**P049

Objectives: To test the amount of NO_2 production during mechanical ventilation with different concentrations of inhaled NO (0.5-90 ppm) and different tidal volumes (V_T 100–1000 ml) using two prototypes for NO inhalation during mechanical ventilation.

Methods: The Servo 300 NO-A prototype (Siemens-Servotek, Solna, Sweden) and the NO-domo prototype combined with an Evita 1 ventilator (Dräger AG, Lübeck, Germany) were tested for controlled mechanical ventilation at an FiO_2 of 1.0 with different tidal volumes (V_T 100, 150, 200, 250, 300, 400, 500,... 1000 ml) using an artificial test lung with a filling volume of 3 1. Different NO concentrations of 0.5, 1,10, 20, 40 and 90 ppm (NOin) were applied. In the Servo prototype, NO is mixed into the inspiratory gas stream inside the ventilator and electrochemical electrodes for NO/NO_2 are mounted in a mixing chamber behind the expiratory valve of the respirator. The NO-domo prototype admixes NO into the inspiratory gas stream immediately behind the respirator's inspiratory outlet and the electrochemical measurement is mounted 30 cm distal from that point in the inspiratory limb. NO_2 concentrations were measured by chemiluminescence in the inspiratory limb of the respiratory tubing immediately before the y-piece (NO_2 insie for the Servo, NO_2 innodo for the NO-domo). Furthermore, for the Servo 300 NO-A an additional chemiluminescence measurement was mounted in the expiratory mixing chamber at the same point where the electrochemical electrodes measure (NO_2 exsie).

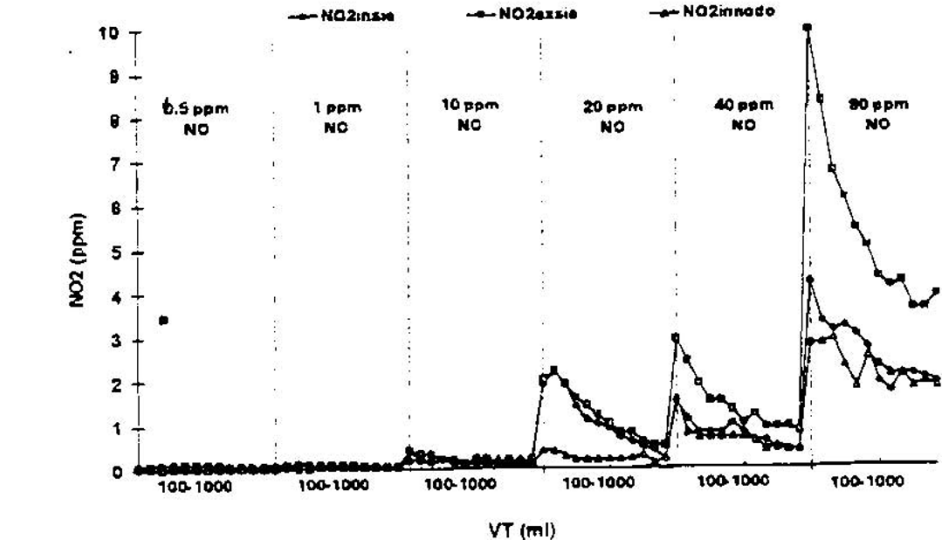

Figure (abstract P049)

Results: The NO_2 values for the different measurements are shown in the figure for the different NO concentrations. Each data point for a given NO concentration reflects a stepwise increasing V_T from 100-1000 ml.
Conclusions: From the presented data we conclude that as long as inhaled NO concentrations < 10 ppm are used, the NO_2 production is below the toxic range even for small tidal volumes. For NO concentrations ≥ 10 ppm the NO_2 production is higher when NO is admixed into the inspiratory gas inside the ventilator (Servo 100 NO-A) compared to mixing NO into the inspiratory limb of the respiratory tubing (NO-domo). One to lower flow rates and therefore increased contact time of NO and O_2, the NO_2 is higher for smaller tidal volumes. For the same reason the expiratory NO_2 measurement results in a clearly higher NO_2 level compared to the inspired concentrations and is therefore strongly misleading. NO concentrations > 20 ppm result in potentially toxic inspiratory NO_2 concentrations and should therefore be carefully monitored.

P050

Effects of inhaled nitric oxide during permissive hypercapnia in acute respiratory failure in piglets

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Objective: To evaluate gas exchange and pulmonary hemodynamic data during permissive hypercapnia (PHC) and inhaled nitric oxide (NO) in acute respiratory failure.

Design: Prospective, randomized, controlled study.
Setting: University research laboratory.
Subjects: Twelve 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 a femoral artery catheter, and an ultrasonic flow probe on the pulmonary artery and the ascending aorta. Acute respiratory failure was induced by the infusion of oleic acid (0.1 ml/kg) and repeated lung lavages with 0.9% NaCl (20 ml/kg). The protocol consisted of three randomly assigned periods with different $PaCO_2$ levels (NC = $PaCO_2$ 40 torr, PHC-60 = $PaCO_2$ 60 torr, PHC-80 = $PaCO_2$ 80 torr). Tidal volume was reduced to induce hypercapnia, pH was not corrected. At each $PaCO_2$ period the animals were ventilated with and without inhaled NO.
Measurements and results: Continuous monitoring included ECG, CVP, MPAP, MAP, SaO_2 and SvO_2 measurements. In addition, the blood flow in the pulmonary artery and aorta was measured continuously. Data are given as mean ± SEM. For statistical comparison ANOVA for repeated measures was used.
Conclusions: The pressure but not the flow in the pulmonary artery increased rapidly during acute permissive hypercapnia. Inhaled NO significantly reduced the pulmonary hypertension induced by acute permissive hypercapnia but did not influence the flow through the pulmonary artery. Inhaled NO significantly improved oxygenation in this model of ARF both during normocapnia and permissive hypercapnia.

Table (abstract P050)

	NC	NC	HC-60	HC-60	HC-80	HC-80
iNO (ppm)	0	10	0	10	0	10
MAP (mmHg)	79 ± 2.9	81 ± 2.4	72 ± 2.5	78.3 ± 4.3	74.2 ± 3.0	74.1 ± 3.0
MPAP (mmHg)	28.3 ± 1.8	25.8 ± 1.2	32.6 ± 1.8	26.7 ± 1.2*	35.1 ± 1.9	28.5 ± 1.9*
Flow-Pa (l/min)	1.91 ± 0.2	1.99 ± 0.2	1.73 ± 0.1	1.77 ± 0.1	1.89 ± 0.2	1.9 ± 0.2
PVR (dyn s/cm^5)	684 ± 85	582 ± 99	928 ± 157	642 ± 69	956 ± 142	685 ± 124
PaO_2/FiO_2 (torr)	82 ± 4.2	143 ± 26*	100 ± 7.8	151 ± 19*	96.8 ± 12	154 ± 25*
pH	7.34 ± 0.01	7.37 ± 0.01	7.21 ± 0.02	7.22 ± 0.02	7.12 ± 0.02	7.12 ± 0.02

*P < 0.05 NO 0 ppm versus NO 10 ppm, NC = one normocapnia, HC = hypercapnia.

P051

The pulmonary and haematological toxicity of inhaled aerosolised prostacyclin

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Inhaled aerosolised prostacyclin (IAP) has gained prominence as a selective pulmonary vasodilator (SPV), which may be used for the treatment of pulmonary hypertension and severe hypoxaemia, as may occur in conditions such as ARDS [1,2]. Prostacyclin (Epoprostenol™, GlaxoWellcome, Boronia, Victoria, Australia) is diluted in an alkaline (pH 10.5) buffer prior to nebulisation. The current study was devised to determine the toxic effects on respiratory mucosa of the alkaline buffer as well as any antiplatelet effect of high dose IAP.

Methods: Five piglets weighing 10–20 kg were anaesthetized with halothane in oxygen-enriched air (FiO_2-0.4) and pentobarbitone (8 mg/kg/h) and exposed to one of three aerosolised treatments via a jet nebuliser (MMD = 5.44 μm) as follows. Two piglets acted as controls – one received nebulised normal saline and one received no inhaled therapy, was killed and the lungs immediately harvested. Two piglets received nebulised glycine diluent and two piglets received IAP at a dose of 200 ng/kg/min. All the nebulised therapies were delivered at the same volume as would be required to deliver 200 ng/kg/min of IAP. This therapy was continued for 6–8 h.

Monitoring included invasive BP, rectal temperature and HR. Hourly thromboelastograph (TEG) measurements were carried out to determine any reduction in the maximum amplitude (MA), as a marker of platelet inhibition. At the end of the study period the lungs were harvested and sectioned. Multiple sections were examined histologically for the presence of polymorphonuclear leucocytes as evidence of acute inflammation. A ventilation scan using nebulised radiolabelled DTPA dissolved in the glycine diluent was carried out on one additional piglet to ensure widespread deposition of the nebulised therapy in the lungs of the study piglets.

Results: All piglets receiving either glycine diluent or IAP (prostacyclin in glycine diluent) showed evidence of acute inflammation, which was worse in the trachea and major bronchi than in the lower airways and lung parenchyma. Also, the changes were more marked on the luminal surface of the airways. The two piglets receiving IAP showed evidence of platelet inhibition as determined by a reduction in MA from baseline. The nuclear medicine ventilation scan confirmed widespread and distal deposition of the aerosol droplets.

Conclusion: Prolonged exposure (6–8 h) to nebulised glycine diluent in which IAP is delivered is associated with mild inflammation of the respiratory mucosa in the piglet. Also, high dose IAP results in the systemic absorption of prostacyclin with a resultant antiplatelet aggregation effect as determined by TEG. These findings differ somewhat from a previous animal model where no evidence of pulmonary inflammation could be found after response to IAP [3]. The current study employed higher doses of IAP (200 ng/kg/min) and the testing for inflammation was more specific, which may account for the difference in findings.

References

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P052

Permissive hypercapnia in infants and children with acute respiratory distress syndrome

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Objective: There is increasing evidence that the use of large tidal volumes (Vt) and high peak inspiratory pressures (PIP) during mechanical ventilation (MV) results in severe pulmonary damage. The aim is to present our experience with pressure controlled ventilation (PCV) and permissive hypercapnia (PHC) in paediatric patients with acute respiratory distress syndrome (ARDS).

Design: Prospective case report series.

Setting: A 12 bed multidisciplinary paediatric ICU in a University hospital.

Patients: From October 1993 to October 1996 paediatric patients (8 males, 2 females) with a mean age of 2.6 ± 1.4 years and a mean body weight of 12.5 ± 4.3 kg suffering from severe ARDS were included into this study. Before starting controlled hypoventilation six patients had signs of pulmonary barotrauma.

Methods: All patients were intubated, sedated and paralysed. The goal of mechanical ventilation was to limit PIP to 40 cmH_2O and expiratory tidal volume (Vtexp) < 10 ml/kg while titrating PEEP and I : E ratio; FiO_2 was reduced to 60–70%; acceptable SaO_2 values were at 85%.

Results: Mean duration of MV was 18.7 ± 5.3 days. During controlled mechanical hypoventilation PIP and Vtexp decreased from 41 ± 0.7 to 32 ± 1 cmH_2O ($P < 0.01$), and from 11.6 ± 0.3 to 8.3 ± 0.4 ml/kg ($P < 0.01$), whereas arterial PCO_2 increased from 44 ± 2.2 to 74.4 ± 4.5 mmHg ($P < 0.01$). Pulmonary barotrauma resolved rapidly in five patients during controlled hypoventilation. However, two patients subsequently needed extracorporeal lung support because of progredient hypoxemia. All but one patient survived.

Conclusion: PHC offers an attractive alternative to conventional MV in paediatric patients with ARDS resulting in improved pulmonary recovery and decreased mortality.

P053

Continuous insufflation of high flows of humidified gas in healthy sheep results in localized damage to tracheal epithelium

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Transtracheal administration of oxygen to patients with COFD can effectively reduce chronic hypoxemia, dyspnea and length of hospitalization. Usually the flows of insufflated gas are low, 0.5 1/min up to 3 1/min [1,2]. Insufflation of gas at higher flows (up to 8 1/min) has been demonstrated to reduce the amount of dead space and minute ventilation, while improving arterial PCO_2 [3,4]. We assessed the injury to the trachea and lungs of healthy sheep following 48 h of continuous insufflation with humidified gas at high flows.

Methods: We percutaneously positioned a minitracheotomy cannula (4 mm id Portex-Mini Trach II Seldinger, Kent, UK) through the cricothyroid membrane in eight healthy sheep (mean body weight, 29.6 kg). Through the cannula we inserted a Teflon catheter (8 Fr) with a silicon distal tip provided with 12 1-mm holes for gas diffusion. The catheter tip was placed at the carina. Adequate humidification is needed for flow rates over 4 1/min, as the flow is bypassing the upper airways [5]. We delivered the gas at 100% relative humidity close to body temperature. The femoral artery and the right jugular vein were percutaneously cannulated for continuous monitoring of systemic and central venous pressure and for blood sampling.

Sheep were divided into three groups: two sheep received 5 1/min of room air; three received 10 1/min of room air; and three controls did not receive any gas flow. Following 48 h of gas insufflation, sheep were anesthetized and killed with an injection of sodium pentobarbital and KC1. For histologic examination, samples of the trachea were taken from: (i) immediately distal to the minitracheotomy cannula; (ii) middle of the trachea; (iii) level of the tip of the catheter; (iv) level of the right upper lobe bronchus, and (v) level of the left upper lobe of the lung. Each sample included four tracheal rings, and was fixed in 10% formalin. Tissue blocks were dehydrated and embedded in paraffin. Sections (5 µm thick) were stained with hematoxylin-eosin, Mova, pentachrome and periodic acid-Schiff (PAS) methods. Sections from each of the five areas were evaluated by a pathologist for the following microscopic changes: (i) tracheal epithelial injury; (ii) inflammatory reaction; (iii) edema; (iv) vascular congestion, and (v) hemorrhage. These changes were graded as 0 = absent, 1 = mild, 2 = moderate, and 3 = severe.

Results: *Group 10 l/min:* in all sheep we found severe epithelial damage at level 3 of the trachea; severe inflammation, edema, hemorrhage and infiltration of neutrophils were observed in the submucosa. In two sheep,

mild epithelial damage and mild submucosal edema were also seen at level 4. There was no damage at other levels. *Group 5 l/min:* in both sheep, mild damage was observed at level 3, particularly in the epithelial layer. *Control group:* no damage was found in any area of the trachea. The lung appeared normal in all three groups. The gas exchange and the hemodynamic parameters remained within normal range throughout the study.

Conclusion: From these results, we conclude that continuous tracheal insufflation for 48 h of humidified room air at 10 1/min causes epithelial and submucosal damage localized to the area of trachea directly adjacent to the tip of the catheter. In the same area, at a low gas flow of 5 1/min, only mild damage was observed. Preliminary results from a new tip made of microporous material seem to exclude that the damage is flow-dependent, suggesting that better diffusion and partitioning of the flow of gas could prevent most of this injury.

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P054

ARDS: dramatic rises in arterial PO_2 with the 'open lung' approach

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In a pilot study the 'open lung' concept was applied 22 times in 13 patients of a university medical intensive care unit with ARDS (lung injury score 3.7 ± 0.7) due to sepsis of various origin (APACHE II score 27.4 ± 6.3). Starting with the actual respirator adjustment, peak inspiratory pressure was increased by 10 cmH_2O every 3 min up to a mean pressure of 61 ± 9 cmH_2O, depending on the hemodynamic state and blood gas results of the patient. PEEP was increased to 15 to 25 cmH_2O. After achieving maximal elevation of arterial PaO_2, the peak pressure was then lowered to 30, maximal 40, cmH_2O and PEEP adjusted just above the alveolar occlusion pressure which guaranteed a tidal volume of about 6 ml/kg body weight. Under this regimen, FiO_2 could be significantly lowered from 0.9 to 0.55 with marked rise in oxygenation index from 100 ± 36 to 177 ± 63 mmHg in responders (15 maneuvers in 11 patients). Plain chest X-ray and CT scan showed marked reduction of signs of pulmonary infiltration in a very short time.

The 'open lung' approach, though short-lived, might provoke pneumothorax and mediastinal emphysema. However, it enables rapid recruitment of previously atelectatic alveoli, thus resulting in better oxygenation on the one hand, and help avoid oxygen toxicity and protracted volu- and barotrauma on the other hand which are the usual sequel of prolonged ventilation using conventional mode in ARDS. Depending on our experience, the advantages of the concept are far more obvious than its possible risks. Continuous blood gas monitoring systems may help shorten the period of high inspiratory peak pressure. Multicentre studies are required to validate long-term results and possible complications.

P055

Weaning from mechanical ventilation in COPD patients: interest to measure, in post-extubation, the airway occlusion pressure (P0.1), in order to indicate non-invasive pressure support ventilation (NIPSV) to prevent relapse

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Critical Care 1997, **1(Suppl 1):**P055

Aims of the study: Methods of NIPSV are being proposed more and more for acute exacerbations of COPD (Brochard: *N Engl J Med* 1995, **333**:817-822) and also for respiratory insufficiency observed after extubation (Meduri: *Chest* 1996, **109**:179-193). Objective of our prospective study: to compare parameters measured just before extubation, then in post-extubation, between COPD patients who have benefitted from NIPSV (group I) to those who did not necessitate NIPSV (group II) after weaning with pressure support (PS) ventilation.

Patients and methods: Twenty-eight COPD patients completed the study. In group I (n = 10), patients had suspected ventilatory muscle fatigue after weaning from mechanical ventilation. They presented, in 72 h post-extubation, a markup of $PaCO_2$ of at least 20% as compared to the value measured post-extubation, and a respiratory rate > 25/min. Eighteen patients entered in group II.

We measured (Ventilator = EVITA 2 - Dräger®) P0.1, respiratory rate (RR), RR/V_T, PaO_2, $PaCO_2$, (i) before extubation, with PS = 6 $crnH_2O$, then (ii) in postextubation, during a session of facial mask ventilation of 30 min, with PS = 4 cmH_2O. We compared the two groups of patients using Mann-Whitney U test for quantitative variables.

Results: See table.

Conclusion: P0.1 measured in postextubation seems to be a valuable index to indicate promptly NIPSV in order to prevent relapse after weaning from mechanical ventilation, in COPD patients.

P056

Endoscopic diagnosis of laryngeal injury following endotracheal intubation

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Secondary changes in the laryngeal mucosa due to endotracheal intubation are inevitable. Degree of these pathological changes depend on some factors such as duration of intubation, size of tube, general status of patient, presence of infection. To prevent any irreversible sequelae of intubation, it is important to diagnose these changes as soon as early [1,2]. Purpose of these studies was evaluation of laryngeal injury in a group of patients who had intubations for more than 4 days in ICU.

Fourteen patients (4 female, 10 male) suffering from respiratory insufficiency or neurological disorder were included in the study. All patients were orally intubated by polyvinyl-cuffed, low-pressure, high volume endotracheal tubes (sizes 7.5–8.0 mm) and ventilated. Nasogastric tube placed all of them. Endoscopic examinations were made by fiber or rigid laryngeal endoscope (0°–30° angled telescope) in 6 cases when the endotracheal tube was

Table (abstract P055)

	PS = 6 cm H_2O before extubation					PS = 4 cm H_2O postextubation					
	RR	RR/V_T	$PaCO_2$	PaO_2	P0.1	RR	RR/V_T	$PaCO_2$	PaO_2	P0.1	
Group I (n = 10)	26 ± 5	75 ± 28	6.9 ± 0.8	9.8 ± 1.2	2.5 ± 0.7	27 ± 4	71 ± 19	7.8 ± 0.8	9.5 ± 1.3	4.2 ± 0.9	
Group II (n = 18)	24 ± 5	64 ± 24	6.5 ± 1.0	9.6 ± 2.1	2.4 ± 0.9	23 ± 5	60 ± 21	7.2 ± 0.9	9.7 ± 1.6	1.8 ± 0.8	
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	$P < 0.01$

PaO_2 - $PaCO_2$: kPa; P0.1 : cmH_2O.

replaced by a tracheotomy cannula, and in 8 cases after immediate extubation or decannulation. Photographic documentation of each one was collected and laryngeal injuries were evaluated.
Total duration of intubation was 10.6 ± 1.4 (4–24) days. Endoscopic signs of injuries of laryngeal mucosa due to intubation were edema (28%), granuloma (14%), ulceration (42%) and fibrosis (7%). All of the ulceration was seen in posterior commissura and interarytenoid areas. Edema was determined on arytenoids, aryepiglottic fold and membranous part of the vocal cords. Granuloma were detected on anterior part of the vocal cords and finally fibrosis was seen in posterior subglottic area.
As a conclusion of this preliminary study, incidence of the injury of laryngeal mucosa due to intubation was very high (64%). The most frequent pathologic finding was ulceration. Endoscopic examination is the best way to diagnose these lesions.

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P057

Ventilatory assistance during translaryngeal percutaneous tracheostomy

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Translaryngeal percutaneous tracheostomy (TLT) is a new technique to perform percutaneous tracheostomy.
The main advantage advocated in respect with other methods is the lower incidence of infection of the stoma and the safety of the procedure. The main disadvantage of TLT is the loss of ventilatory support during the manoeuvre of the extraction of the cannula. This can result in severe hypoxia mainly in patients with adult respiratory failure (ARF). To maintain an adequate level of blood oxygenation several methods have been proposed (high frequency ventilation, apneic oxygenation. etc). We describe our experience of TLT in ARF patients providing ventilatory support with a small size (4 mm ID) 40 cm long endotracheal tube.
Patient population: Six patients with ARF of different etiologies had been studied. PaO_2/FiO_2 144.4 ± 60 (88.7–250.7), mean PEEP 10.4 ± 4.8 (5–16) cmH_2O, mean age 53.5 ± 17 (23–74), intubation time 8.5 ± 4.8 (315) days.
Technique: For the procedure the patients were sedated and paralysed, and ventilated with a Siemens Servo 900 C in volume controlled ventilation (VCV). By means of end expiratory and inspiratory occlusions, external PEEP (PEEP ext), intrinsic PEEP (PEEP i), total PEEP (PEEP tot) and plateau pressure P Plat) were measured.
Following tracheal puncture and guidewire extraction, that a performed under direct tracheoscope guidance, the small size tube is advanced distally after tracheoscope removal. Ventilatory parameters are adjusted as follows: TV was kept constant; ventilatory working pressure was increased in order to overcome the resistance of the small ET tube and to maintain the TV; PEEP ext was reduced in order to keep PEEP tot (PEEP ext + PEEP i) constant; P Plat was continuously monitored.

Table (abstract P057)

	Basal	Final	
	Mean ± SD	Mean ± SD	*P*
PaO_2 (mmHg)	144.4 ± 60	136.8 ± 77	NS
$PaCO_2$ (mmHg)	47.6 ± 16	53.9 ± 18	<0.01
PEEP ext (cmH_2O)	10.4 ± 4.8	2.8 ± 3.8	<0.01
PEEP tot (cmH_2O)	11.2 ± 4.4	11.6 ± 3.7	NS
P Plat (cmH_2O)	31 ± 13.9	32.9 ± 13.3	NS
Peak (cmH_2O)	40.8 ± 8.2	81.3 ± 10.1	<0.01

The wire is then connected with the tracheal cannula and pulled through the trachea till it emerges from the skin. Once the tracheal cannula is correctly positioned, the small ET tube is removed.
Blood gases and respiratory parameters were drawn repeatedly during the procedure. The mean duration of the procedure was 51.6 + 26.9 min. Blood gases and ventilatory parameters at the beginning and at the end of the procedure are shown in the Table.
Conclusions: TLT can be performed in severe ARF patients provided that ventilation is supported during the whole procedure. Small calibre long ET can be safely utilized if ventilatory parameters as PEEP i and P Plat are monitored.

P058

Validation of the esophageal detector device (EDD) in elective and emergency intubation in a medical ICU

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Objective: (i) To confirm the validity of the esophageal detector device (EDD) as an indicator of correct positioning of endotracheal tubes (ETTs) in patients intubated under elective and emergency conditions in a medical ICU. (ii) To establish the positive and negative predictive values sensitivity and specificity of the EDD for correct positioning of ETTs.
Patients and methods: All patients that underwent elective or emergency intubation in a medical ICU during a 4 month period (from August until November 1996) were included in the study. ETT positioning was initially evaluated by auscultation of lung fields and epigastrium during 1 to 2 Ambu-bag ventilations, followed by EDD monitoring. If EDD monitoring was consistent with esophageal ETT placement, the ETT was removed and a new attempt was made by the same or another physician. The technique and the comparison of the EDD with end-tidal carbon dioxide measurements ($ETCO_2$) have been described previously (*Ann Emerg Med* 1996, **27**:595–599) and will not be discussed in this study.
Results: Of 117 intubations in 71 patients EDD monitoring correctly indicated tracheal placement in 94 and falsely indicated esophageal placement in three (sensitivity = 97%). EDD correctly indicated esophageal placement in 20 (specificity = 100%). The positive predictive value (PPV) was 100% and the negative predictive value (NPV) was 87%. All three patients in which the EDD falsely indicated esophageal placement were severely bronchospastic with copious tracheal secretions, possibly creating a vacuum effect. After suctioning of secretions and a further 3 to 4 Ambu-bag ventilations the EDD confirmed correct tracheal intubation in these three patients. No adverse effects or reactions were noted with the use of the EDD.
Conclusion: This study supports the validity of the EDD for confirmation of correct tracheal intubation in the setting of elective and emergency intubation of medical ICU patients. In patients with extreme bronchospasm, excessive copious secretions or lung edema suctioning of secretions and an extra 3 to 4 Ambu-bag ventilations should be done before EDD testing to prevent false negative results. The EDD has excellent specificity, sensitivity, PPV and NPV. In addition and in comparison to $ETCO_2$ monitoring it is cheap and easy to use.

P059

Translaryngeal tracheostomy (TLT): UK clinical experience

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Introduction: Sub-cricoid dilation tracheostomy has gained popularity in intensive care units throughout the world during the past 10 years [1]. We describe our experience with a new and novel method for insertion of a percutaneous tracheostomy minimising the inherent risks of bleeding, misplacement and pneumothorax which have been described with other techniques.
Technique: This percutaneous technique involves the retrograde insertion of a tracheostomy tube via the mouth and then the larynx guided by a transtracheal wire placed under direct bronchoscopic vision

using a Seldinger needle method [2]. Our study involved the prospective collection of data in 40 consecutive patients undergoing this technique in our institution. All tracheostomies were performed by a single operator (JWF), on ventilator dependent patients ranging from 25 to 72 years of age with a variety of underlying pathologies.
No attempt was made to correct any pre-existent coagulopathy in these patients.
Results: All 40 tracheostomies were performed successfully. Mean duration of operative procedure was 16 min. There were no periods of critical hypoxia (< 90%) or arterial hypotension (< 75 mmHg mean). Blood loss was minimal (< 10 ml) in all cases (INR range 1.0–8.4, mean 2.6, platelet range 23–246 × 10^9). Closure of stoma on decannulation was a mean of 2 days with minimal scar.
Conclusion: This pure dilatational and bronchoscopically visualised method is reliable, easy to perform with training and is free from serious complications. We feel that it offers benefits over techniques already available and is worthy of consideration especially in those patients with underlying risk factors.
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P060

Postintubation tracheal injuries in critically ill patients - proposal for an additional prophylactic approach

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The use of endotracheal intubation for respiratory support of critically ill patients is a standard, life saving form of therapy. The lesions produced in the trachea by the erosive or cicatrical response to injury by intubation are still the most common tracheal injuries requiring treatment. It was demonstrated in many studies that there is a pressure necrosis type of injury occuring at points of tube-tissue interfacing. Severe trauma and hypovolemia with tissue hypoperfusion ischemia will markedly shorten the length of `safe intubation', and make tracheal tissue more susceptible to injury. In the setting of critical illness there is a clear analogy between pressure (decubitus) ulcers and tracheal postintubation pressure necrosis injuries. Similarly to decubitus ulcers, most of the tracheal pressure ulcers are due to prolonged, unrelieved pressure on delicate airway structures. When these pressures exceed the capillary-arteriolar blood pressure (ca 30 mmHg) tissue ischemia can lead to a sequence of inflammation-ulceration-granulation and stenosis. Inflation of an endotracheal tube cuff to the minimum pressure that creates a seal during routine positive pressure ventilation (at least 20 mmHg) reduces tracheal blood flow at the cuff site by 75%. Further cuff inflation or arteriolar hypotension can totally eliminate mucosal blood flow.
The concept of the **Double Cuff Pressure Relieving Endotracheal Tube** seems to be a logical response to the analogy between decubitus and tracheal pressure injuries. By simultaneously inflating and deflating Cuff 1 and Cuff 2, as a part of critical care routine, the pressure on delicate tracheal tissue could be intermittently completely alleviated and arteriolar-capillary blood flow at the points of cuff-tissue interfacing restored. Furthermore, the diffusion of frequently used anesthetic nitrous oxide into endotracheal tube cuffs, with consequent increase in the pressure against the tracheal mucosa, could also be easily addressed by this modified endotracheal tube.

P061

Haemodynamic effects of kinetic therapy in critically ill trauma patients

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Background and objectives: The principles of kinetic theraphy and their positive effects on oxygenation have been well established in the last years. Less is known about the haemodynamic effects under continuous rotation in critically ill patients. Facts about the cardiac function, especially the cardiac output, are only based on single measurements with the Swan catheter.

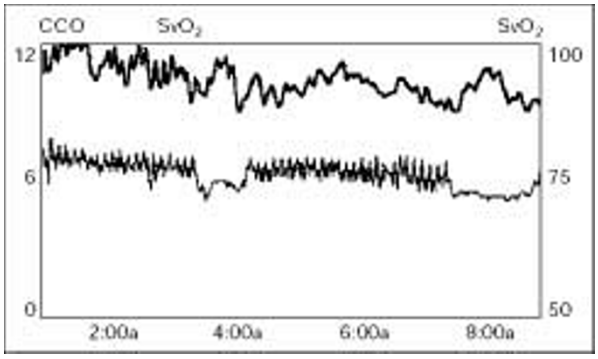

Figure (abstract P061)

Methods: We studied the effects of continuous rotating (Fig left) in 10 patients using the KCI Rotorest bed. All patients were rotated in 60° angulation. During the rotation continuous cardiac output (CCO) was measured with the Baxter Vigilance System. The data were collected and computerised during the whole time the Swan catheter was applied (mean time 4 days). The changes in cardiac output were measured in the printed hardcopies (eg Fig right) of the CCO curves.
Results: In 10 patients, 314 rotation cycles could be measured. A mean number of 32 rotations was measured for every patient. The mean difference in cardiac output (CO) was 700 ml per rotation cycle (100–3000 ml). The higher volumes of more than 2000 ml difference during single rotations were measured in two patients with a septic inflammatory response syndrome (SIRS), which had a CO of more than 12 1/min.
Conclusions: Kinetic therapy has an influence on the cardiac output in critically ill patients. The volume of the cardiac output change seems to correlate with the total CO so that patients with a stable haemodynamic situation have smaller volume changes than patients with a high CO, like in cases of SIRS or sepsis.

P062

Tracheal gas insufflation during CPAP reduces volume and breathing effort in an animal model of acute injury

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Aim of this study was to investigate the effects of tracheal gas insufflation (TGI) during CPAP on gas exchange, ventilation and effort of breathing in sheep with lung injury following injection of oleic acid (OA).
Methods: Ten young female sheep (27.1 ± 4.2 kg) were anesthetized with ketamine, trachotomized and intubated with a 9 mm ID jet Ventilation ETT (Mallinkrodt), with its tip placed 2 cm proximal to the carina. Sheep were ventilated with pressure support ventilation of 5 cm H_2O. PEEP of 5 cmH_2O and FiO_2 of 1.0 (S900C, Siemens). An arterial catheter and a pulmonary artery catheter were percutaneously inserted into the femoral artery and the external jugular vein, respectively. An esophageal balloon catheter (Bicore, Smartcath) was inserted into the left pleural cavity through an intercostal incision. Airway pressure, flow and pleural pressure signals were obtained using a CP100 Pulmonary Monitor (Bicore). Carinal pressure (Pcar) was measured with a transducer connected to the distal side port of the ETT. OA was injected into the right atrium in increments of 0.2 ml every 10 min until a total dose of 0.06 ml/kg was delivered. PaO_2, $PaCO_2$, and lung compliance (CI) were measured before and 2 h following the OA injection. The sheep were then connected to a CPAP circuit. CPAP, and CPAP combined with TGI (CPAP-TGI) were randomly applied for periods of 40 min each. During CPAP-TGI, a humidified (Conchatherm, Hudson Respiratory Care) gas mixture containing 60% O_2 was delivered at a flow of 10 1/min through a

Table (abstract P062)

$n = 10$	PaO_2 (mmHg)	$PaCO_2$ (mmHg)	Vd/Vt	Vt (ml)	RR (b/min)	Vc (l/min)	Dpl (mmHg)
CPAP	88.4 ± 44.5	61.6 ± 11.4	0.75 ± 0.11	93.7 ± 24.2	52.4 ± 20.3	5.1 ± 1.0	19.2 ± 6.1
CPAP-TGI	109.6 ± 66.0	55.3 ± 11.6	0.59 ± 0.16	74.4 ± 27.1	43.1 ± 15.2	3.2 ± 0.9	15.6 ± 5.5
$P <$	NS	0.01	0.01	0.05	NS	0.01	0.05

reverse thrust catheter (RTC) having its tip positioned 1 cm proximal to the tip of the ETT. Throughout both steps the FiO_2 was 0.6, the bias flow was 19 1/min and the PEEP was adjusted in order to achieve an average Pcar of 5 cmH_2O. After each step, hemodynamic, blood gas and mixed expired CO_2 fraction measurements were taken while signals from the CP 100 monitor were recorded by a personal computer. During analysis of stored tracings, tidal volumes (Vt), respiratory rates (RR), minute volumes (Vc) and the pleural pressure swings (Dpl) (ie an index of breathing effort) were computed. Also, the Vd/Vt ratio was calculated.
Results: The injection of OA resulted in a decrease in PaO_2 [431.0 ± 67.1–104.6 ± 40.1 ($P < 0.01$)], and CI [39.3 ± 15.6–10.4 ± 3.17 ($P < 0.01$)] while the $PaCO_2$ increased [46.6 ± 5.4–60.4 ± 11.9 ($P < 0.01$)]. Data obtained during CPAP and CPAP-TGI are shown in the Table.
Conclusions: The injection of OA in spontaneously breathing sheep resulted in lung injury characterized by marked hypoxia, low compliance and hypercapnia. TGI administered during CPAP reduced dead space, allowing reductions in $PaCO_2$, Vt and Vc, and led to a decrease in breathing effort. In patients with acute respiratory failure, adding TGI to CPAP might increase tolerance to spontaneous breathing.

P063

Nasal-airway pressure release ventilation (NASAL-APRV) and nasal-continuous positive airway pressure (NASAL-CPAP): hemodynamic, respiratory and gasometric effects

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This study compared the NASAL-CPAP to a new mode called NASAL-APRV as a non-invasive weaning procedure from mechanical ventilation using nasal prongs, analysing the hemodynamic, respiratory and gasometric effects.
Data were collected in a randomized and prospective protocol, applied to pediatric patients (minimum age, 10 days; maximum age, 10 years 6 months; mean age, 1 year 8 months 12 days), totalling $n = 17$ cases. For each patient the mean airway pressure was kept constant for both modes of ventilation, 4.5 ± 0.65 cmH_2O. In NASAL-APRV the maximum distension pressure ranged from 5 to 8 cmH_2O and the release pressure was always to 0 cmH_2O; release time was 1.0s and release frequency of 15 rpm. NASAL-CPAP was kept between 3 to 5 cmH_2O. FiO_2 was 40%. Statistical analysis: Wilcoxon signed-rank test.

Table (abstract P063)

Variables	NASAL-CPAP		NASAL-APRV		*P*
	Mean	SD	Mean	SD	
HR (beat/min)	136.95	22.66	129.47	24.87	0.0017
MAP (mmHg)	73.94	19.96	72.94	20.02	NS
$ExtO_2$ (%)	23.88	10.8	22.88	9.23	NS
RR (resp/min)	41.65	14.71	36.94	12.79	0.002
pHart	7.39	0.06	7.39	0.05	NS
PaO_2(mmHg)	85.59	29.92	95.65	32.05	0.0052
$PaCO_2$ (mmHg)	37.06	8.27	32.82	6.02	0.0002
$SatartO_2$ (%)	93.47	5.7	94.77	4.91	0.0362

HR, heart rate; MAP, mean arterial pressure; RR, child's respiratory rate.

Conclusions: In the hemodynamic effects there was a significant alteration only in heart rate, lowering in the NASAL-APRV. In the respiratory and gasometric changes there is a significant alteration towards improval both in oxygenation and ventilation, achieved with a better respiratory comfort.

P064

Non-invasive pressure support ventilation (NIPSV) is not very time-consuming for the nursing staff

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Aims of the study: Methods of NIPSV are being proposed more and more for acute exacerbations of COPD (Brochard: *N Engl J Med* 1995, **333**:817–822). Nevertheless, Chevrolet *et al* (*Chest* 1991, **100**:775–782) found that this procedure was very time-consuming for nurses. Objective of our prospective study: to study the amount of nursing care required to treat respiratory failure with NIPSV.
Patients and methods: Forty COPD patients completed the study. Twenty patients had acute exacerbations of their lung disease, with pH = 7.29 ± 0.05. Twenty patients had suspected ventilatory muscle fatigue after weaning from mechanical ventilation. They presented, in 72 h post-extubation, a mark-up of $PaCO_2$ of at least 20% as compared to the value measured in post-extubation, and a respiratory rate > 25 per min. NIPSV (BiPAP® – Respironics; Evita 2 – Dräger) was performed in a sequential mode. For each session of ventilation, it was taken notice of: duration of the session; duration of nursing care required; side-effects observed; improvement, acceptance by the patient.
Results: After a mean duration of sequential ventilatory assistance of 6 ± 3 days, NIPSV was successful in 75% of cases. During the first 24 h of the protocol: 8 ± 3 sessions of NIPSV were performed; the mean duration of a session of ventilation was 48 ± 14 min; the average minutes spent at the bedside directly administering care as estimated by nurses was 10 ± 7. There was a drop in the amount of time nurses spent at the bedside of patients, after the first 24 h of the study. NIPSV was well tolerated and accepted by the COPD patients.
Conclusion: NIPSV, performed with a sequential mode, may reduce the need for tracheal intubation in the failure of COPD patients, and is not very time-consuming for the nursing staff.

P065

Pulmonary function indices in spontaneously breathing subjects

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Background: Assessment of pulmonary gas exchange and adequacy of oxygen supply is complex. At least five different pulmonary indices are available in clinical practice. Modern blood gas analysers allow for calculations of these pulmonary indices. A prerequisite for accurate calculation is a precise determination of the inspired O_2 fraction [FO_2(I)]. In spontaneously breathing patients it is difficult to estimate FO_2(I). The Venturi mask delivers a precise FO_2(I) (fixed performance system), whereas the Large nasal catheter (variable performance system) delivers a variable FO_2(I), which is dependent on the patient's ventilatory pattern. The purpose of this study is to determine the influence of FO_2(I) on five different pulmonary indices.

Table (abstract P065)

	Venturi mask O_2 %			Large nasal catheter O_2/atm l/min					
	24	28	40	0/15	3/12	7.5/7.5	10/5	15/0	30/0
ρO_2 (A-a)(kPa)	3.42	3.68	6.00	3.46	4.49	9.83	6.29	11.32	13.92
ρO_2 (a/A)	0.82	0.83	0.83	0.79	0.83	0.78	0.87	0.82	0.83
ρO_2 [(A-a)/a]	0.22	0.21	0.22	0.28	0.23	0.33	0.15	0.22	0.21
ρO_2 (a)/ PO_2 (I)	62	62	68	59	64	65	70	71	72
*P*shunt	0.02	0.04	0.03	0.04	0.05	0.06	0.06	0.06	0.07

The ρO_2 (ET-a) is increasing with increasing O_2, flow. The highest ρO_2 (ET-a) value (13.92 kPa) is observed when O_2 is supplied via the Large nasal catheter. The pulmonary indices were all within the normal range.

Objectives: (i) To calculate five different pulmonary indices, presuming the end-tidal O_2 tension [pO_2(ET)] to be the best expression of alveolar gas composition. (ii) To generate computer calculations of the five indices referring to the fluctuations of FO_2(I) when a variable performance system delivers O_2.
Data sources: The pO_2(ET) in the airway was continously recorded during the use of different O_2 supply systems and flows in 10 healthy spontaneously breathing volunteers.
Methods: Oxygen was supplied through two different supply systems: Venturi mask and Large nasal catheter. The Brüel & Kjær gas monitor 1304 was used to measure the gas tensions in the airway. The sampling tube of the monitor was connected to a soft 12 CH PVC catheter placed in the subject's upper airway. Simultaneously with the pO_2(ET) recordings blood was drawn from a radialis and analysed by the ABL 520 (Radiometer, Medical).
Results: The SD of the measured FO_2(I) was small when O_2 was supplied through the Venturi mask (40%, SD = 0.9%) and when the subject breathed atmospheric air (SD = 1.1%) but increased with increasing O_2 flows with the use of the Large nasal catheter (30 IO_2, SD = 6.5%). The mean values of the pulmonary indices for the different O_2 flows are summarised in the Table. Normal values: pO_2(a/A)>0.75; pO_2[(A-a)/a] = 0.1– 0.37; pO_2(a)/FO_2(I) = 42–70; *F*Shunt<0.15.
Discussion: As expected pO_2(ET-a) increases with higher FO_2(I) values. The increase in FO_2(I) docs not influence the calculated indices. The *F*Shunt is defined by assuming a fixed-mixed-venous oxygen concentration difference of 2.3 mmol/1. which may not be the case in some clinical situations.
Conclusion: When FO_2 is measured in the airway in a healthy subject the corresponding calculated indices turn out to be in the normal range. Suggestion for the optimal pulmonary index in healthy volunteers, based on estimation of FO_2(I), will be presented by computer generation.

P066

APACHE II score is better than weaning indices in predicting prolonged mechanical ventilator dependence

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Introduction: Spontaneous minute ventilation (V_E), peak inspiratory airway pressure (Plmax), rapid shallow breathing index (f/v_T), relative inspiratory effect (RIE), and the $P(A\text{-}a)O_2$, blood urea nitrogen and gender score (A + B + G) are used in predicting weaning success. Some patients are transferred from intensive care to subacute care facilities when prolonged mechanical ventilation (MV) is anticipated. This prospective. observational study compares the role of weaning indices versus APACHE II score in identifying patients requiring prolonged MV.
Methods: The study included 84 patients referred for weaning assessment, when their underlying acute conditions had stabilized but immediate successful extubation was not expected. Plmax, V_E and respiratory rate were measured. APACHE II score. f/V_T, RIE, and A + B + G were calculated. Prolonged and successful weaning were defined as dependance on MV for ≥ 7 and < 7 days respectively from the day of weaning assessment. Weaning outcome was categorized into three: death, prolonged weaning, and successful weaning. Student's t-test was used to compare differences in means. *P* value < 0.05 was considered significant.

Table (abstract P066)

	Dead	Prolonged weaning	Successful weaning	*P* value *P*1	*P*2
APACHE II	21.2	17.3	12.6	0.0410	0.0010
V_E (l/min)	9.5	9.6	10.3	0.9575	0.4480
Plmax (cm H_2O)	53	44	59	0.2491	0.0169
f/V_T	120	95	87	0.2955	0.5532
RIE	0.406	0.605	0.507	0.1588	0.2877
A+B+G	39	56	54	0.0077	0.6062

*P*1 comparing dead versus prolonged weaning; *P*2 comparing prolonged weaning versus successful weaning

Results: Patients' mean age was 55.9 ± 13.8 years: 42 were male; 42 were black, 41 white and 1 Hispanic. The main causes of the respiratory failure were pneumonia (25) and COPD (17). The patients had been on MV for a median of 9 days before weaning assessment. Eleven (13%) patients died: 22 (26%) had prolonged weaning: 51 (61%) were successfully weaned. The mean APACHE II score and weaning indices are listed in the table.
Conclusions: This study suggests that patients' overall physiologic condition, measured by APACHE II score, is a better predictor of prolonged mechanical ventilator dependence than weaning indices.

P067

Biocompatible membranes in acute renal failure (ARF), hope or illusion?

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Introduction: Acute renal failure remains associated with high mortality rates. Different attempts to increase survival have not been successful [1,2]. The use of biocompatible polyacrylonitrile membrane gave promising, but controversial results [3,4]. This paper compares the results of treatment of patients with ARF by hemodialysis using polysulfonate (BC) and cellulose diacetate membrane (BIC).
Patients and methods: In a group of 33 patients with ARF (surgical and medical group, 25 males and 8 females, average age 58.7 ± 8.3 years), polysulfone membrane was used in 14 patients (group BC), and cellulose diacetate membrane in 19 patients (group BIC). On inclusion in the study, there were no significant differences in the severity of the underlying disease between the observed groups. Apache II_0 score was 36.2 ± 9.6 in the BC group, and between the observed groups. Apache II_0 score was 36.2 ± 9.6 in the BC group, and 39.8 ± 9.6 in the BIC group ($P = 0.34$; NS, Student *t*-test). There was no correlation in survival with regard to patients' age. The survival of medical and surgical group of patients was better in the BC group ($P = 0.013$).
Conclusion: The use of biocompatible polysulfone membrane in acute renal failure, along with other measures, represents an advance in the patient management.

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P068

Effects of the continuous venovenous haemofiltration, in the haemodynamic profile of shock septic patients

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Introduction: Septic shock in spite of the new therapeutic strategies. still has a high mortality. There are multiple factors. and we may consider that the main objectives are the recovery of cardiovascular function and haemodynamic stability. Venovenous haemofiltration (CVVH), a technique used in septic patients with renal failure is now proposed in septic shock without renal failure. We studied the haemodynamic effects of the CVVH in septic shock patients that had not responded to high doses of catecholamines.
Materials and methods: We made continuous venovenous haemofiltration in eight patients with septic shock, after trying to control (the situation with fluid replacement and high doses of catecholamines. We used the blood pump MB10, a Gambro poliamide filter FH77 to attain an ultrafiltration higher then 2000 ml/h. We monitored all the patients with a thermodilution catheter, and we evaluated the haemodynamics and the O_2 profile before the beginning of the CVVH, 12–24 h and 24–48 h after.
Results: The data are reported as mean and standard deviation. We made 224 evaluations of the haemodynamic and O_2 profile on the eight patients included in this study.
Conclusion: CVVH improves the haemodynamic function in septic shock patients, confirmed by the rise of PAM, IC and of the LVSWI. Haemodynamic stability after 12 to 24 h of haemofiltration, allowed a reduction in the catecholamines doses, and withdrawal from shock criteria. We think that CVVH may be one valid alternative to control and treat the haemodynamic anomalies in patients with septic shock.

P069

Impact of CVVHD on pulmonary gas exchange measurement

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Aim: To quantify extrapulmonal gas exchange during CVVHD.
Patients and methods: Ten indirect calorimetry (IC) measurements (Deltatrac, Datex, Finland) were done in five stable mechanically ventilated patients requiring treatment by CVVHD (Prisma, Hospal, UK) because of MODS. Dialysate and substitution solutions did not contain bicarbonate. During each IC measurement CVVHD setting was change in 30 min intervals as shown in the table.
Estimated extracorporeal CO_2 losses by CVVHD were calculated as a difference between VCO_2 measured by IC when no CVVHD was performed (period 5) and other periods. The study was approved by Ethics Committee of University Hospital. ANOVA for repeated measurements, paired-*t* test were used for statistical analysis. Values are provided as means ± SD, $P < 0.05$ was considered significant.
Results: Amount of CO_2 removed by pulmonary gas exchange (CO_2 pulm) during the study is shown in the Figure.
Maximal difference in CO_2pulm was measured between no CVVHD (period 5) and CO_2pulm during CVVHD running at maximal parameters (period 3) (292 ± 26 and 263 ± 37 ml/min, respectively, $P < 0.01$). The difference in $C0_2$pulm between periods 5 (no CVVHD) and standard CVVHD setting (period 4) was also significant (292 ± 26 and 268 ± 40 ml/min, respectively, $P < 0.01$). There was no difference in CO_2pulm between periods when no CVVHD was performed (period 5) and only blood was running through the extracorporeal circuit (period 2) (292 ± 26 and 286 ± 46 ml/min, respectively; $P = 0.33$). There was no impact of CVVHD on VO_2 measurement during the study.
Conclusion: During CVVHD treatment indirect calorimetry measurement underestimates VCO_2 due to significant losses of CO_2 into ultradiafiltrate (up to 10% of VCO_2). Measurement of VO_2 by IC seems to be reliable.

Table (abstract P069)

	Period					
	1	2	3	4	5	6
Blood (ml/min)	150	150	150	150	-	150
Dialysis (ml/h)	1000	-	2500	1000	-	1000
Ultrafiltration (ml/h)	1000	-	2000	1000	-	1000

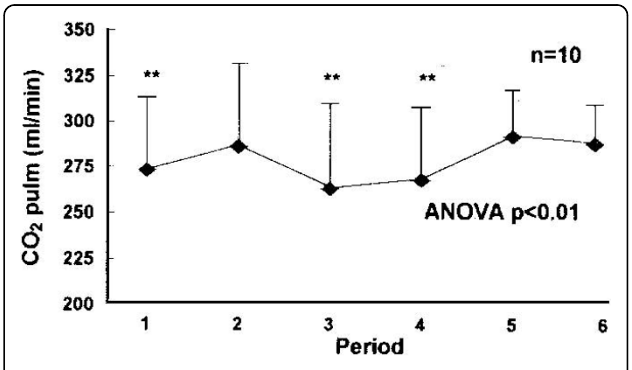

Figure (abstract P069)

P070

Intermittent hemodiafiltration rapidly decreases serum myoglobin levels in rhabdomyolysis

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Introduction: Myoglobin is a pigment protein (MW 17800 D), which forms hematin if tubular pH is low and may cause acute renal failure (ARF). Aggressive fluid therapy, alkalinization of the urine, loop diuretics and mannitol are used in prevention of ARF with varying success. CAVH decreases serum myoglobin levels [1], but is not routinely used. Regardless of the therapy of rhabdomyolysis, the mortality of associated ARF remains high, approximately 30% [2]. The aim of this study was to examine the effect of intermittent 4-h hemodiafiltration (HDF) on serum myoglobin levels.
Methods: HDF was done using predilution technique with AK 100 Ultra equipment, Polyflux 17 hemodiafilter and BiCart 205 acid sodium bicarbonate concentrate (Gambro, Sweden)
Ultrafiltration rate was 167 ml/min, dialysis fluid rate was 333 ml/min and blood pump rate was 250 ml/min. The filtrated fluid was substituted by on-line system of the equipment.
Results: See table.

Table (abstract P068)

n = 8	CI	MAP	PWCP	SVR	PVR	LVSWI	VO_2	DO_2
Before	3.8 ± 0.8	52.2 ± 2.8	15.6 ± 6.3	610 ± 222	117 ± 72	25.5 ± 9	119 ± 43	455 ± 130
12-24 h	4.3 ± 1.4	88 ± 19	14.2 ± 4	999 ± 367	107 ± 37.9	37.6 ± 13.1	158 ± 28	555 ± 246
24-48 h	4.6 ± 0.8	89.3 ± 19.1	17 ± 4.2	766 ± 332	113 ± 51.8	48 ± 15.1	156 ± 18.5	529 ± 95.9

CI, cardiac index; MAP, median arterial pressure; PWCP, pulmonary wedge capillary pressure; SVR, systemic vascular resistance; PVR, pulmonary vascular resistance; LVSWI, left ventricular stroke work index; VO_2, oxygen consumption; DO_2, oxygen and delivery.

Table (abstract P070)

Patient no	Age (years)	s-crea PreHDF (μmol/l)	s-crea PostHDF (μmol/l)	s-myoglobin PreHDF (μg/l)	s-myoglobin PostHDF (μg/l)	Change
1	65	196	131	2622	2292	-12%
2	47	657	403	1647	892	-45%
3	44	476	285	85,500	1699	-98%
4	28	321	316	3427	2500	-27%

Discussion: Hemodiafiltration with predilution technique effectively and rapidly decreases serum myoglobin levels. In rhabdomyolysis associated with severe trauma, metabolic disturbance or intoxication HDF might prove to be effective in prevention or treatment of ARF.

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P071

Evaluation of the predilution technique in reducing the occurrence of bleeding during continuous venovenous haemofiltration in critically ill patients. Efficacy of predilution in reducing the amount of anticoagulation during CVVH

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Background and objectives: Anticoagulation during haemofiltration is one of the major issues. We have to take into account three parameters: bleeding occurrence, filter life, and filter efficiency. The purpose of the study was to assess the efficacy of the predilution technique in reducing the incidence of symptomatic bleeding (by cutting down the amount of heparin) but without avoiding a shorter filter life.
Setting: Intensive care unit of a secondary hospital.
Haemofiltration technique: All these patients were put on continuous venovenous haemofiltration using a Hospal-Prisma-Pump. The membrane was in polyacrylonitrylc (1 m^2 of surface-capillary filter). We exchange 1 l/h without using dialysis.
Protocol: Twenty consecutive critically ill patients were randomised to have either a predilution set or a post-dilution one. Full circuit heparinisation was used to achieve an APTT twice baseline. The vascath site was restricted to the right internal jugular vein. The pump speed was kept at 100 ml/min. Filter efficiency was assessed by the haemopermeability index (HPI). The HPI represent the ultrafiltrate flow divided by the transmembrane pressure. The filter efficiency is lost when the HPI has dropped by 70%. Filter life was measured in hours until the circuit clotted off. Data were analysed using non-parametric statistical methods.
Results: • The median filter life was 38.5 h for the predilution group (n = 10) and 39.3 h for the post-dilution one (n = 10). The difference was not statistically significant ($P > 0.05$).
• Symptomatic bleeding happened in one patient in the predilution group and in four patients in the post-dilution one ($P < 0.05$, highly significant).
• The median amount of heparin used in the predilution group was about 450 U/h and 750 U/h in the post-dilution group ($P < 0.05$, highly significant).
• The median filter efficiency was 32.3 h for the predilution group and 33.9 for the post-dilution group ($P > 0.05$, no statistical difference).
We have also measured the haematocrit, the platelet count, the oncotic pressure and the total calcium in the circuit prior to the filter (after the dilution).
• Median haematocrit was 25.1% in the predilution group and 28.5% in the other group ($P < 0.05$).
• The median platelet count was 116 × 10^9/l in the predilution group and 131 × 10^9/l in the other group ($P < 0.05$).
• The median oncotic pressure was 31.3 mmHg in the predilution group and 37.2 mmHg in the other group ($P < 0.05$).
• No difference was seen in measuring the total calcium between groups.
• Obviously, we measured haematocrit, platelet count, pancreatic pressure and total calcium in the serum and we could not find any statistical difference between groups.
Conclusion: The predilution technique is a good tool for clinicians in the setting of CVVH in critically ill patients at risk for bleeding. It allows the physician to reduce drastically the amount of heparin used without impairing the filter life and the filter efficiency. The mechanism involved seems to be the reduction of the oncotic pressure rather than other systems involving the calcium.

P072

Acute pericardial effusion and renal failure: etiologic diagnosis and outcome

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Objective: To assess the etiologic diagnosis and outcome of acute pericardial effusion (PE) associated to acute renal failure (ARF) or end-stage renal disease (ESRD).
Design: Retrospective study from 1978 to 1996.
Setting: A 10-bed medical/surgical ICU.
Patients: The charts of 17 patients having acute PE and renal failure at ICU admission were reviewed. Diagnosis and severity of PE were echocardiographically defined in all patients. Moderate PE corresponded to no right heart chambers compression (RHCC); severe PE to RHCC without hypotension; and cardiac tamponade to RHCC with hypotension. ARF was defined as follows: in patients without pre-existing renal disease by a serum creatinine value ≥ 150 μmol/l; in patients with previous renal insufficiency by an increase in serum creatinine of ≥ 100% above baseline values. ESRD was defined by chronic hemodialysis requirement.
Measurements and results: Eleven patients had ARF and six ESRD. In ARF group and in ESRD group, mean age was 57.7 and 52.2 years, mean SAPS II was 43.3 and 52.8, number of patients requiring mechanical ventilation was four and two, and number of ICU deaths was four and three respectively. In ARF and in ESRD group, moderate PE was noted in two and one cases, severe PE in three and three cases, cardiac tamponade in six and two cases, and pericardial window was performed in two and four cases respectively. In ARF group 7 patients required dialysis, that was transient in survival patients. PE etiological diagnosis was systemic lupus with extra-capillary glomerulonephritis (n = 2), systemic fibrosis with obstructive renal failure (n = 2), anticoagulation accident with hemodynamic renal failure (n = 2), lung adenocarcinoma (n = 2), adenocarcinoma of undetermined origin (n = 1), systemic polyarteritis nodosa (n = 1), and Wegener granulomatosis (n = 1). In ESRD group, PE etiological diagnosis was uremic pericarditis (n = 5), and prostatic cancer (n = 1).
Discussion: Despite malignancy being claimed as the leading cause of cardiac tamponade, when associated to ARF other etiologic diagnoses must be evoked that prompt specific treatment and could prevent unfavorable evolution. In ESRD patients admitted to ICU, uremia emerged as the most common etiology of PE, and mortality rate is high. These patients should undergo pericardial window to favorise pericardial symphysis, and prevent recidive.

P073

Outcome of intensive care treatment and rehabilitation in multimorbid elderly patients with chronic renal failure

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From a medical and ethical point of view, the question frequently arises whether intensive care treatment in multimorbid elderly patients is justified by its outcome. This applies in particular to patients with chronic renal failure.
Patients and methods: In a descriptive study, 23 consecutive patients (group 1; mean age 71.5 years) with chronic renal failure requiring intensive care treatment and at least three severe accompanying diseases underwent standard geriatric assessment (ICIDH, Barthel Index, Tinetti

test, up & go test, clock completion test) when transferred for rehabilitation. All patients underwent medical rehabilitation for 4–10 weeks after discharge from the ICU. Forty geriatric patients with normal renal function (group 2; mean age 75.5 years) requiring ICU treatment and subsequent rehabilitation served as controls. All patients were reassessed when leaving the rehabilitation center.
Results: In 12 patients of group 1, the rehabilitation measures restored a functional level comparable to that before admission to the ICU. With two exceptions, all patients of group 1 could return to their former environment. The improvement in the Barthel index after rehabilitation was not significantly different from that of the control group (16.3 versus 18.6 points). Lethality was significantly higher in group 1 (16 versus 4%).
Conclusion: Multimorbid elderly patients with end-stage renal disease benefit from ICU treatment and rehabilitation in a similar way as geriatric patients with normal renal function.

P074

New diagnostic peritoneal lavage (DPL) criteria for diagnosing hollow-viscus injuries

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As a result of recent advances in radiological diagnostic procedures, traumatic hemoperitoneum is no longer an absolute indication for emergency laparotomy. By determining the site and extent of abdominal solid organ injuries by computed tomography (CT) and ultrasonography, conservative management can be safely adopted if the patient's vital signs are stable. However, radiological diagnosis alone is not definitive for diagnosing hollow viscus injuries as yet.
As the indications for emergency laparotomy change conceptually, the role of DPL is being transformed. For these reasons, we developed new DPL criteria specifically designed to aid in diagnosing intestinal injury. In the present study, we evaluated the effectiveness of our new DPL criteria.
Materials and methods: Until June 1996, we had performed DPL on 250 blunt abdominal trauma cases at our emergency medical center. We used our new entries to calculate diagnostic accuracy.
Results: Analysis showed that our criteria have a diagnostic sensitivity of 96.6% and specificity of 99.4% for intestinal injury, after exclusion of 57 cases in which DPL was performed within 3 h or 18 h after injury was sustained. In 133 hemoperitoneum cases, emergency laparotomy was performed in only 48; the remaining 85 cases with negative DPL based on the white blood cell count criterion avoided surgery and conservative management resulted in no complications.
Conclusion: Employing our new criteria, DPL can be used to diagnose or exclude intestinal injuries even in the presence of hemoperitoneum.

P075

Effects of therapy with methylene blue on hemodynamics and gas exchange in septic shock

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Introduction: Death of patients from septic shock is usually associated to severe reduction of systemic vascular resistances and severe hypotension despite elevated cardiac output values. The mediator of vasodilatation, nitric oxide (NO), is synthesised by the inducible NO synthase. Excess NO synthesis during septic shock causes abnormal vasodilatation [1].
A possible therapeutic approach is represented by the pharmacological inhibition of the enzyme guanylate cyclase by methylene blue (MB), a long known and safe pharmacological approach for the treatment of nitrate intoxication and methemoglobinemia [2].
The aim of the present study is the evaluation of short term effects of methylene blue on hemodynamics and gas exchange in patients with septic shock.
Materials and methods: We studied five patients (three males, two females, mean age 56.6 ± 16.9, APACHE II 25.8 ± 5.6, SOFA score 13.8 ± 3.0) with septic shock (three post-surgery of aortic aneurysm surgery, one intracerebral bleeding, one encephalitis), informed consent was obtained by patients or relatives. All patients had a Swan-Ganz pulmonary artery and a fiberoptic femoral artery catheter inserted and were monitored with the COLD device (PULSION, München). All variables were measured prior to the injection of an endovenous bolus of methylene blue (3 mg/kg body weight in 10 min) and 20 min and 2 h after bolus administration. Values are indicated as means ± SD, P values < 0.05 were considered as significant.
Results: Mean arterial pressure (MAP) raised immediately after rnethylene blue injection (60 ± 9.2 versus 70.8 ± 11.9), systemic vascular resistances (SVR) raised (938.7 ± 177.9 versus 1262.7 ± 686.9), whereas cardiac index and heart rate did not change. Right ventricle indexed blood volume raised (145.9 ± 16.6 versus 161.4 ± 20.2), whereas left ventricle indexed blood volume was reduced (379.6 ± 158.2 versus 289 ± 211.1). Extra-vascular lung water augmented (8.5 ± 6.3 versus 12.5 ± 11.4). The measured shunt fraction did not change but the PaO_2/FiO_2 index worsened (230 ± 108 versus 219.5 ± 98.3). Two hours after injection of methylene blue MAP, SVR as well as right and left intracardiac volumes remained superior to baseline levels.
Conclusion: In our patients methylene blue induced an increase in systemic vascular resistances and of mean arterial pressure without affecting cardiac output. More difficult remains the evaluation of pharmacological effects on cardiac volumes and on final outcome of these septic shock patients. Further investigations will have to demonstrate effectiveness of methylene blue in the treatment of septic shock.

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P076

Effects of methylene blue on gas exchange and myocardial function in refractory septic shock with acute lung injury

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An important number of patients died in refractory hypotension during the course of septic shock. Methylene blue (MB) increases mean arterial pressure, however cardiac output can decrease and also some effect on gas exchange has been observed.
Objective: The aim of this study was to evaluate the potential side effects on myocardial function and respiratory parameters in patients with refractory septic shock associated to severe acute lung injury (ALI).
Methods: Six consecutive patients with refractory septic shock, mechanically ventilated developing ALI were studied. MB was infused iv (1 mg/kg) in 15 min. Hemodynamics and gasometric values were collected before (baseline) and at 30 min, 60 min, 90 min, 120 min and 180 min after the end of the infusion.
Data = mean ± SE. Statistics: Anova and Student–Newman–Keuls.
Results: See table.
Conclusions: Short-term effects of MB are not deleterious on cardiac performance during refractory septic shock and its use is not limited in patients that developed ALI.

P077

Renal effects of low-dose dopamine in the critically ill

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Objective: To examine the renal effects of low dose dopamine in patients receiving dopamine 2.5 µg/kg/min and no other vasoactive therapy.

Table (abstract P076)

	Baseline	30 min	60 min	90 min	120 min	180 min	*P*
PaO_2 mmHg	85 ± 8	82 ± 7	83 ± 8	80 ± 8	78 ± 8	77 ± 7	NS
SaO_2 %	94 ± 2	95 ± 1	94 ± 1	94 ± 1	93 ± 2	94 ± 2	NS
PaO_2/FiO_2	184 ± 35	1 79 ± 30	176 ± 30	168 ± 27	169 ± 32	171 ± 33	NS
$PA\text{-}aO_2$	255 ± 88	255 ± 86	255 ± 86	255 ± 85	257 ± 85	277 ± 100	NS
Qs/Qt %	15 ± 5	17 ± 2	19 ± 2	22 ± 3	21 ± 4	25 ± 5	NS
$ICI/min/m^2$	4.6 ± 0.5	4.5 ± 0.4	4.5 ± 0.4	4.6 ± 0.5	4.5 ± 0.5	4.4 ± 0.5	NS
IDO_2 $ml/min/m^2$	581 ± 85	556 ± 62	553 ± 65	555 ± 63	536 ± 62	537 ± 60	NS
IVO_2 $ml/min/m^2$	175 ± 30	143 ± 26	132 ± 22	128 ± 25	160 ± 38	144 ± 36	NS
O_2 extraction %	31 ± 5	27 ± 5	25 ± 4	23 ± 4	31 ± 7	28 ± 7	NS

No important differences were observed on gas exchange parameters and myocardial function.

Table (abstract P077)

	Period 1 Mean ± SD	Period 2 Mean ± SD	*P* value
Urine vol (ml)	160 ± 130	222 ± 184	0.04
C_{CR} (ml/min)	62.1 ± 29	69 ± 29.4	0.07
Urine Na conc (mmol/l)	75.2 ± 39.8	66.4 ± 41.5	0.9
Na exc (mmol)	12.2 ± 15.2	13.6 ± 22	0.33
FE_{Na} (ratio)	1.0 ± 1.0	1.2 ± 1.3	0.08

Subjects: Critically ill but stable patients, median APACHE II 13 (range 8–26), with a pulmonary artery catheter placed to assist volume resuscitation
Design: Prospective study.
Methods: Optimal filling was assessed by left ventricular stroke work index (LVSWI) reaching a plateau with serial fluid challenges and recording the pulmonary artery wedge pressure at this optimal LVSWI. We endeavoured to maintain this pulmonary artery wedge pressure throughout the study. The study consisted of two periods of 2 h duration, 1 h was allowed between them for equilibration. Patients were maintained on volume replacement alone for the first period and then dopamine was infused at 2.5 µg/kg/min and continued for the second period. Blood samples were taken at the beginning and end of each period. Urine was collected over each 2 h period for the measurement of volume and calculation of creatinine clearance (C_{Cr}) and fractional sodium excretion (FE_{Na}). Cardiac output studies were also performed during each period.
Analysis: Renal parameters were compared using Wilcoxon signed rank test (stat view 4.5). Statistical significance was taken as a P value < 0.05.
Results: We studied 11 patients, none had to be withdrawn because of hypotension or increasing inotrope requirements.
Conclusion: The above data shows a statistically significant increase in urine volume with low dose dopamine.

P078

Cardiopulmonary dysfunction during porcine endotoxin shock is effectively counteracted by the endothelin receptor antagonist bosentan

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Endothelin 1, an endothelium derived peptide, is the most potent vasoconstrictor known. In experimental endotoxin models as well as in human septic shock, a three- to fourfold elevation of plasma levels of endothelin-1-like immunoreactivity is seen [1]. In a porcine endotoxin shock model, the mixed non-peptide endothelin receptor antagonist bosentan [2] was administered 2 h after onset of endotoxemia (n = 8). Cardiopulmonary vascular changes, oxygen related variables and plasma levels of endothelin-1-like immunoreactivity were compared to a control group only receiving endotoxin (n = 8). Bosentan abolished the progressive increase in mean pulmonary artery pressure and pulmonary vascular resistance seen in controls. Further, bosentan restored cardiac index to pre-endotoxin level by

Table (abstract P078)

Parameter	Group	T0 h	T2 h	T5 h	
Mean arterial pressure (mmHg)	Controls	125 ± 4	64 ± 7	59 ± 6	
	Bosentan	141 ± 7	73 ± 5	61 ± 6	
Mean pulmonary artery pressure (mmHg)	Controls	28 ± 2	35 ± 2	34 ± 2	***
	Bosentan	27 ± 2	34 ± 2	20 ± 1	
Pulmonary vascular resistance index (mmHg kg min/ml)	Controls	182 ± 23	349 ± 52	398 ± 68	***
	Bosentan	155 ± 29	262 ± 47	97 ± 19	
Cardiac index (ml/min/kg)	Controls	111 ± 5	74 ± 6	65 ± 8	**
	Bosentan	130 ± 13	85 ± 10	130 ± 16	
Stroke volume index (ml/beat/kg)	Controls	0.71 ± 0.07	0.43 ± 0.04	0.34 ± 0.06	*
	Bosentan	0.87 ± 0.13	0.52 ± 0.09	0.69 ± 0.09	
Systemic vascular resistance index (mmHg kg min/ml)	Controls	1100 ± 56	830 ± 100	840 ± 69	**
	Bosentan	1100 ± 120	870 ± 100	450 ± 66	
Oxygen delivery index (ml/min/kg)	Controls	18 ± 1	13 ± 1	11 ± 1	**
	Bosentan	19 ± 2	13 ± 1	18 ± 2	

an increase in stroke volume index, improved systemic oxygen delivery and acid base balance, and since mean arterial blood pressure was unaffected, reduced systemic vascular resistance. Endotoxemia increased plasma levels of endothelin-1-like immunoreactivity (from 14 ± 1 to 37 ± 2 pmol/l) and tumor necrosis factor-alpha, the former being further increased by bosentan (from 37 ± 2 to 180 ± 30 pmol/l).

Effects of endotoxin infusion, started at T0 h and bosentan, administered after 2 h of endotoxemia (T2 h), in pigs (n = 8) compared to control pigs (n = 8) not receiving bosentan. Groups are compared at T0 h, T2 h and T5 h. *P < 0.05 and ***P < 0.001 for differences between groups in time-matched between-group contrasts.

In conclusion, in porcine endotoxemia, treatment with the endothelin receptor antagonist bosentan, administered during established shock, abolished pulmonary hypertension and restored cardiac index. These findings suggest that bosentan could be an effective treatment to reverse a deteriorated cardiopulmonary state during septic shock.

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P079

Bosentan restores gut oxygen delivery and reverses intestinal mucosal acidosis in porcine endotoxin shock

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Introduction: Endothelin (ET), the most potent endogenous vasoconstrictor known, is highly produced in septic states. High plasma levels of ET are associated with morbidity and mortality in septic patients. Being a potent vasoactive peptide produced in sepsis, ET may be involved in the pathophysiology of the markedly deteriorated splanchnic circulation seen in septic shock. In this study, bosentan, a non-peptide mixed ET receptor antagonist was utilised in order to attenuate splanchnic blood flow disturbances and counteract intestinal mucosal acidosis in a porcine model of endotoxin shock.

Materials and methods: Sixteen landrace pigs were anesthetised and catheterised for monitoring of regional and central hemodynamics. A tonometer (sigmoid catheter, Tonometrics Inc, MA, USA) was introduced into the ileum and a magnetic flow probe placed around the portal vein. All animals received 20 ml/kg/h of Ringer's glucose throughout the experiment. After baseline measurements, onset of endotoxin challenge (20 μg/kg/h for 3 h) was followed by bosentan administration (n = 8) 2 h later. Eight animals receiving only endotoxin served as controls. The experiments were terminated 5 h after onset of endotoxin challenge.

Results and discussion: As endotoxin infusion reduced cardiac index and systemic oxygen delivery, bosentan treatment restored these parameters to baseline levels. The endotoxin-induced reduction in mean arterial blood pressure remained unaffected by bosentan. The profound reduction in gut oxygen delivery and portal blood flow in response to endotoxin was completely abolished by bosentan administration. Further, bosentan significantly improved a markedly reduced calculated pHi. The endotoxemia induced mucosal-arterial PCO_2 gap was also significantly reduced in response to bosentan administration. There were no apparent differences when monitoring tonometry data as calculated pHi or mucosal-arterial PCO_2 gap, in terms of significance between or within groups. The PCO_2 gap between the mucosa and portal vein was utilised as a monitor of the mucosa in relation to total portal drainage. The mucosal-portal PCO_2 gap was increased in response to endotoxin challenge, illustrating mucosal susceptibility to shock. Mucosal-portal PCO_2 gap was also reduced by bosentan.

Conclusion: Bosentan restored the markedly reduced gut oxygen delivery induced by endotoxin, in parallel with marked improvement of intestinal mucosal acidosis. These findings suggest that endothelin is involved in the microcirculatory disturbances of the gut in endotoxin shock. Bosentan may prove useful in reducing gut ischemia in septic shock conditions.

Table (abstract P080)

	NOR1	PHE	NOR2
MAP (mmHg)	74 ± 4	74 ± 3	73 ± 3
CI (l/min m^2)	4.9 ± 1.4	4.6 ± 1.0	4.9 ± 1.4
DO_2sys (ml/min m^2)	665 ± 152	628 ± 102	669 ± 147
VO_2sys (ml/min m^2)	177 ± 21	175 ± 25	179 ± 24
Qspl (l/min m^2)	1.40 ± 0.24	0.93 ± 0.10*	1.38 ± 0.22
DO_2spl (ml/min m^2)	192 ± 41	126 ± 17*	188 ± 48
VO_2spl (ml/min m^2)	90 ± 9	73 ± 15*	83 ± 9
pHi	7.29 ± 0.08	7.33 ± 0.10	7.31 ± 0.08

All data mean ± SD; *P < 0.05 PHE versus NOR, Friedman-rank sign analysis of variance.

P080

Is β-adrenergic receptor stimulation crucial for splanchnic O_2 availability in septic shock?

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Critical Care 1997, **1(Suppl 1):**P080

Background: Septic shock is characterized by arterial hypotension despite adequate fluid resuscitation, and treatment with vasopressors is current practice [1]. Vasopressors, however, may impair capillary exchange capacity in the splanchnic region [2]. Therefore we tested the effect of replacing noradrenaline (NOR) by phenylephrine (PHE) on splanchnic hemodynamics and O_2 kinetics in septic shock.

Methods: In up to now four patients with hyperdynamic septic shock (CI ≥ 41/min/m^2) all requiring NOR (0.25 ± 0.22 μg/kg min) to maintain mean arterial pressure NOR was replaced by PHE (4.2 ± 3.9 μg/kg min) adjusted to achieve similar systemic hemodynamics. In addition to global oxygen delivery (DO_2sys) and uptake (VO_2sys) (indirect calorimetry) we measured gastric intramucosal pH (pHi) as well as splanchnic blood flow (Qspl), O_2 delivery (DO_2spl) and uptake (VO_2spl) using the indocyanine-green steady state-infusion technique corrected for hepatic dye extraction. Data were obtained after at least 2 h of stable hemodynamic conditions.

Results: See table.

Conclusions: Replacing NOR by PHE selectively reduced Qspl and DO_2spl without influencing pHi. Since VO_2sys remained constant, this fall in Qspl, however, was unlikely to be to due to reduced regional O_2 demands resulting from decreased β-adrenergic receptor-mediated thermogenesis [3]. Suppression of β-receptor stimulation, hence, may cause supply-dependency of VO_2spl in septic shock.

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P081

Does O_2 availability determine hepatic metabolic activity in septic shock?

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Background: In septic shock the hepatic metabolic response to ß-adrenergic receptor Stimulation may not mirror that of splanchnic blood flow (Qspl) and O_2 delivery (DO_2spl) [1], possibly due to hepatocyte heterogeneity associated with metabolic compartmentation [2]. Therefore we investigated if reducing DO_2spl differentially affects metabolic pathways depending on the periportal or perivenous localization.

Table (abstract P081)

	Noradrenaline 1	Phenylephrine	Noradrenaline 2
DO_2spl (ml/min m^2)	192 ± 41	126 ± 17*	188 ± 48
VLac (μmol/min m^2)	615 ± 243	289 ± 128*	541 ± 290
VAla (μmol/min m^2)	226 ± 92	180 ± 60	213 ± 88
VGln (μmol/min m^2)	52 ± 14	35 ± 18	62 ± 19
HGP (μmol/min m^2)	1269 ± 596	942 ± 335*	848 ± 217
MGEX (ng/ml)	33 ± 19	21 ± 6	37 ± 4

All data mean ± SD; *$P < 0.05$ phenylephrine versus noradrenaline, Friedman-test.

Methods: In up to now four patients with hyperdynamic septic shock (CI = 4 l/min m^2) all requiring noradrenaline to maintain mean arterial pressure DO_2spl was selectively reduced without effect on systemic hemodynamics by switching from noradrenaline to phenylephrine. We determined splanchnic lactate (VLac) (enzymatic kit) as well as alanine (VAla) and glutamine (VGln) (liquid chromatography) clearance rates from Qspl and arterio-hepatic venous content difference, hepatic glucose production rate (HGP) from the appearance rate of stable isotope-labelled 6,6-D_2-glucose (ion-selective mass spectrometry), and monoethylglycinexylidide (MGEX) formation (immunofluorescence polarization).
Results: See table.
Conclusions: Reducing DO_2spl leads to decreased HGP probably due to decreased precursor flux and clearance. While the cytochrome P450 IIIA dependent MGEX formation located in the perivenous region returned to baseline levels after restoration of DO_2spl, HGP, a highly O_2 consuming pathway of the periportal region, remained depressed such as recently demonstrated during ventilation with PEEP [3]. Oxygen supply, hence, may determine hepatic metabolic activity and compartmentation in septic shock.

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P082

Influence of dopexamine on leukocyte adherence and vascular permeability during endotoxemia in rat mesenteric venules

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Critical Care 2001, **1(Suppl 1):**P082

Introduction: Dopexamine is a β2-adrenoceptor agonist with dopamine 1 and 2 receptor properties. It was recently shown that dopexamine was able to preserve the hepatic ultrastructure in a porcine sepsis model [1]. It seemed likely that the anti-inflammatory properties of dopexamine were associated with β2-adrenoceptor properties. The adherence of leukocytes to the vascular endothelium is an important step in the development of sepsis. The objective of this study was to investigate whether pretreatment with dopexamine could attenuate leukocyte adherence to venular endothelium and influence vascular permeability in post-capillary venules of the rat mesentery during endotoxemia.
Materials and methods: Male Wistar rats were laparotomized under pentobarbital anesthesia and mesentery was exposed under an in vivo videomicroscope. Endotoxemia was induced by infusion of 2 mg/kg/h lipopolysaccharides (LPS). Leukocyte adherence (LA) and vascular permeability (VP) in postcapillary mesenteric venules were determined before (0 min) and 120 min after induction of endotoxemia. Capillary leakage was determined by measuring the extravasation of FITC-labeled albumin given prior endotoxemia. Venular wall shear rate was calculated by measuring mean erythrocyte velocity and venular diameter. Group B ($n = 8$) was treated with dopexamine (2.5 μg/kg/h). The infusion was started 30 min prior endotoxemia. Group A ($n = 8$) only received an equivalent volume of NaCl. Group C ($n = 8$) was treated with dopexamine (2.5 μg/kg/h), as well, but the β2-effect was antagonized by the β2-adrenoceptor antagonist ICI 118551. Data are mean ± SD. Statistical analysis was performed using two-way ANOVA followed by Scheffe's test.
Results: In the group treated with NaCl (group A) the number of adherent leukocytes increased from 4 ± 1 per 100 μm venule length at 0 min to 13 ± 1 at 120 min. In the dopexamine group (group B) LA increased from 4 ± 1 per 100 μm venule length at 0 min to only 8 ± 2 at 120 min, showing a significant difference between the groups after 120 min ($P < 0.01$). In the dopexamine + ICI 118551 treated group (group C) LA increased, as well (4 ± 1 at 0 min and 8 ± 2 at 120 min), but was significantly lower compared to group A ($P < 0.01$). Venular wall shear rates were significantly higher in the groups treated with dopexamine (groups B and C). Vascular permeability expressed as ratio of graylevels of the video frame in and outside of the investigated venule increased in the NaCl-treated rats from 7 ± 1% at 0 min to 48 ± 12% at 120 min. In the dopexamine group it increased, as well, but only from 8 ± 2% to 30 ± 12%, showing a significant difference between the groups at 120 min ($P < 0.01$). In group C the ratio increased from 9 ± 1% to 38 ± 12%. This was significantly higher compared to group B.
Discussion: Dopexamine is able to attenuate leukocyte adherence and vascular permeabilty in post-capillary venules during endotoxemia. The beneficial effect of dopexamine on leukocyte adherence could not be antagonized by the β2-adrenoceptor antagonist. This suggests that a higher wall shear rate caused by a higher blood flow in the venules is mainly responsible for the lower LA. However, the attenuating effect of dopexamine on vascular permeability during sepsis is apparently a β2-adrenoceptor mediated process.

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P083

Monoethylglycinexylidide (MEGX) as an early predictor of liver dysfunction in severe sepsis

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The development of demonstrable liver dysfunction in severe sepsis is associated with high rates of mortality. Lidocaine metabolite MEGX has proven to be a highly sensitive indicator of hepatic dysfunction, especially in the field of liver transplantation. The present study aimed to assess the prognostic value of MEGX formation kinetics in predicting liver dysfunction in patients with severe sepsis, and compared it with other oxygenation indices as well as gastric mucosal pH (pHi).
Twenty-seven patients meeting the criteria for severe sepsis as defined by Bone *et al* were prospectively evaluated. Patients with hemodynamic instability, high liver enzymes (> 2 × normal) and bilirubin levels (> 3 mg/dl), coagulation disorders, and gastrointestinal bleeding were not included. A gastric tonometer (TRIP, Tonometrics, Worchester, MA) was introduced in all patients in place of a standard nasogastric tube. Gastric pHi was calculated as previously described. Oxygen delivery (DO_2) was calculated by the simplified formula $DO_2 = CI \times CaO_2$, and oxygen consumption (VO_2) was determined by indirect calculation of the product of CI and arteriovenous oxygen content difference. Plasma aspartate aminotransferase, alanine aminotransferase, bilirubin and arterial lactate levels were determined by using enzymatic method. The serum MEGX concentrations were determined using an automated fluorescence polarization immunoassay (TDX, Abbott, Chicago) before and 15 min after an iv injection of 1 mg/kg lidocaine. Liver dysfunction indices (bilirubin > 3 mg/dl, liver enzymes > 2 × normal) were recorded until discharge or death. Effectiveness in predicting liver dysfunction was compared by calculating the sensitivity and specificity for each variable (lactate, pHi, MEGX). To evaluate the accuracy with which of these variables were able to discriminate between those %. In ROC curves constructed to compare the ability of the variables to discriminate two patient groups, MEGX displayed the greatest predictability of liver failure development in regard to lactate and pHi. Relating these variables to survival patients who developed clinically demonstrable liver dysfunction (LD+) and those who did not (LD-), receiver operating characteristics (ROC) curves were constructed. Values of the measurements given as median (25th per cent, 75th per cent) were compared by the Mann-Whitney U test.

MEGX values were the only parameter that showed a significant difference when comparing the two groups (LD+, LD-), Sixty-three per cent of the patients had MEGX values below 90 μg/1 which is a limit indicated as an impaired liver function. MEGX cut-off at 60 μg/l had a prognostic sensitivity of 84% and a specificity of 100, no significancy was determined in any of the parameters. No correlation was found between MEGX or pHi and oxygen derived variables, and there was also no significant difference in hemodynamics and oxygen derived variables either between LD+ and LD- groups, or in survivors and non-survivors.
Our data demonstrated that MEGX formation kinetics is an early bedside procedure to dynamically assess hepatic functions. This test might be an early sign showing the hepatic insult in severe sepsis when the global circulatory and splanchnic circulation indices are in normal range. More research is essential in order to see whether this parameter can guide therapeutic strategies for preventing liver hypoxia or metabolic impairment in the very early phase of sepsis.

P084

N-acetylcysteine (NAC) decreases liver lactate levels in septic shock patients shown by magnetic resonance spectroscopy

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Introduction: NAC was shown to improve the global oxygen consumption in sepsis and toxic liver failure. Very little is known about its effects on liver lactate levels under experimental conditions nothing to our knowledge in septic shock patients. The purpose of this study was to examine these effects using proton magnetic resonance spectroscopy (1H-MRS).
Methods: Nine patients with septic shock participated in this institutionally approved study (written informed consent by the relatives). 1H-MRS measurements were performed at 1.5 Tesla (Magnetom Vision Siemens) with a Steam sequence. A repetition time of 3000 ms and two different echo times of 135 and 270 ms were used to differentiate fatty acid signal from lactate signal. After the initial spectra, the patients received NAC (150 mg/kg bw). Forty-five minutes after this infusion a second measurement followed. Statistical analysis was performed by the Wilcoxon matched pairs signed rank sum-test.
Results: The median age was 66 (range: 37–90 years) and the median APACHE III score was 49 (range: 22–72). Following NAC infusion lactate levels showed a significant median decrease of 45% (range: 16-83%: $P = 0.018$). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) did not change significantly within the first 24 h. The oxygenation index intermittently significantly increased ($P = 0.0277$) and then returned to baseline values within the first 24 h.
Conclusions: The decrease in liver lactate levels may demonstrate the improved liver blood flow and function after NAC application. However, the deterioration of the oxygenation index may limit NAC therapy in patients with an increased inspiratory oxygenation fraction.

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P085

Effects of nitric oxide on hemodynamic changes and metabolism following acute hepatic inflow occlusion in pigs

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The purpose of this study was to examine the effects of nitric oxide on systemic hemodynamics and oxygen metabolism following acute hepatic inflow occlusion. Fourteen mongrel pigs received solvent (control group, $n = 4$), the nitric synthesis inhibitor N^G-nitro-L-arginine methyl ester (L-NAME group, $n = 5$), or the substrate for nitric oxide synthesis L-arginine (L-arginine group, $n = 5$) 30 min before hepatic inflow occlusion. Following 30 min of hepatic ischemia, all livers were reperfused. While all pigs in the control group and L-arginine group survived more than 7 days after reperfusion, two of five pigs in the L-NAME group died during hepatic ischemia period. However, venous oxygen saturation was significantly lower during and after ischemic period, oxygen extraction ratio was significantly higher during hepatic ischemic period in L-NAME group, and systemic vascular resistance was also significantly higher 5 and 15 min after hepatic inflow occlusion. Furthermore, lactate/pyruvate ratio was significantly higher during hepatic ischemic period in L-NAME group. In summary, inhibition of nitric oxide synthesis resulted in maintaining higher arterial blood pressure, but aggravated tissue oxygenation during and after hepatic inflow occlusion. We conclude that nitric oxide appears to decrease arterial blood pressure, but improve the tissue oxygenation in acute hepatic inflow occlusion and reperfusion.

P086

Predictive value of interleukin 6 (IL-6) and gastric intramucosal pH (pH-i) levels in splanchnic ischemia during major abdominal surgery

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Introduction: Abdominal surgery activates monocytes, macrophages and endothelial cells resulting in elevated blood levels of different interleukins, which are directly correlated to the entity of surgical stress [1]. The present study investigates the effects of splanchnic ischemia on plasma concentrations of interleukin-6 (IL-6) and the predictive power of IL-6 levels for post-surgery complications to occur.
Patients and methods: We have studied 12 patients scheduled for major abdominal surgery and informed consent was obtained from all patients. All patients were treated with H2 receptor antagonists before surgery. Gastric intramucosal pH (pH-i) measurements and arterial blood probes for IL-6 dosage were realised after standard anaesthesia induction and prior to the start of surgical procedure (TI), every 60 min after TI during surgery (Tla, b, etc), immediately after extubation (T2), and after 1 h (T3), 2 h (T4), 24 h (T5) and 48 h (T6) after T2. Patients with and without complications during and after surgery were identified and mean values and standard deviation of IL-6 and pH-i for this two patient groups were calculated and plotted on a Cartesian diagram with cut-off points of 7.32 for pH-i and of 300 pg/ml for IL-6. Mean values of pH-i and IL-6 were evaluated with the Mann-Whitney test, P values < 0.05 were considered as significant.
Results: Patient with complications demonstrated significantly lower values of pHi (7.19 ± 0.113 versus 7.39 ± 0.096) and significantly higher values of IL-6 (596.7 ± 687 versus 65 ± 43.5) during surgical intervention compared to patients without complications.
Five out of seven plotted values of patients with complications during or after surgery are located in the lower right quadrant of the diagram (pH-i < 7.32, IL-6 > 300 pg/ml) and eight out of nine plotted values of patients without complications are located in the upper left quadrant of the diagram (pH-i > 7.32, IL-6 < 300 pg/ml). The differences between the two groups are statistically significant ($P = 0.0029$).
Conclusion: Our results suggest that splanchnic ischemia during major abdominal surgery, measured by pH-i, is associated to increased levels of IL-6. Those patients with higher IL-6 levels during and immediately after major abdominal surgery seem to have a higher probability to develop complications.

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Table (abstract P087)

MAP (mmHg)	Time to response (s)	Time to peak pCO_2 (s)	Peak ΔpCO_2 above baseline (mmHg) (r = 0.8)	Area ΔpCO_2 above baseline (r = 0.85)
10	44 (6)	174 (2)	43 (5)	6461 (561)
20	62 (9)	175 (7)	32 (6)	4801 (662)
30	36 (9)	173 (10)	35 (6)	4978 (845)
40	39 (15)	173 (11)	23 (3)	3816 (580)
50	60 (9)	155 (4)	6 (1)	901 (259)
60	66 (13)	176 (9)	4 (1)	571 (157)

Table (abstract P088)

	τ	$T_{1/2}$	R^2
Gas system			
5% Tonocap	3.12	2.16	0.997
10% Tonocap	3.56	2.46	0.985
5% Saline	7.37	5.11	0.973
10% Saline	10.6	7.38	0.969
Fluid system			
5% Tonocap	4.41	3.06	1.00
10% Tonocap	3.63	2-51	0.991
5% Saline	8.15	5.65	0.990
10% Saline	8.45	5.85	0.985

P087

Continuous measurement of gut luminal pCO_2 in an animal model — a sensitive index of reduced perfusion

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Critical Care 1997, **1(Suppl 1):**P087

The sensitivity of gastric tonometry to fluctuations in mucosal perfusion is limited by long equilibration periods (minimum 30 min with saline). Delayed detection of splanchnic ischaemia may negate any benefit from subsequent improvements in splanchnic oxygen delivery. Continuous luminal pCO_2 measurement for prompt detection and quantification of mucosal ischaemia could make gastric tonometry a more valid therapeutic end point. We tested the sensitivity of one continuous system to graded brief reductions in gut perfusion.

Five Sprague-Dawley rats (430–r510 g) were anaesthetised with intraperitoneal sodium pentobarbitone and ventilated with 100% oxygen via tracheostomy to a $paCO_2$ of 30–r50 mmHg. Distal aortic pressure was monitored invasively, and a Paratrend 7™ sensor inserted into the ileal lumen. Normal saline was infused at 3 ml/h, and isoflurane titrated to a mean aortic pressure of 80–r100 mmHg. Distal aortic pressure was reduced to predefined levels for 2 min intervals by digital elevation of an aortic silk sling above the coeliac artery, with intervening recovery periods to allow restabilisation of luminal PCO_2. Measurements were downloaded every 2 s to a data acquisition system. Data are mean (SEM).

Conclusions: Continuous luminal pCO_2 measurement by the Paratrend 7™ was highly sensitive and rapidly responsive to brief reductions in aortic pressure. The peak pCO_2 elevation above baseline and area of the CO_2 elevation curve above baseline both correlated significantly with insult severity. Combined with continuos arterial blood gas analysis, the technique could be used to monitor pHi or the luminal-arterial pCO_2 gradient real-time and provide a better therapeutic end point in the individual patient.

P088

A comparison of the response of the tonocap and saline tonometry to a change in CO_2

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Introduction: Gastrointestinal tonometry has proven to be a useful technique to evaluate gut mucosal perfusion. The most commonly used method is saline tonometry which does not allow rapid assessment of gut luminal CO_2 and is subject to sampling errors. The Tonocap (Tonometrics Division, Instrumentarium Corp, Helsinki, Finland) is a new device which can be used with the established tonometric catheters. The Tonocap fills the tonometer balloon with air rather than saline. Following an equilibration period, the gas is automatically sampled, measured with an infra-red sensor and PCO_2 and calculated intramucuosal pH (pHi) are displayed. We studied the in vitro response of the Tonocap and traditional saline tonometry to a step change in PCO_2.

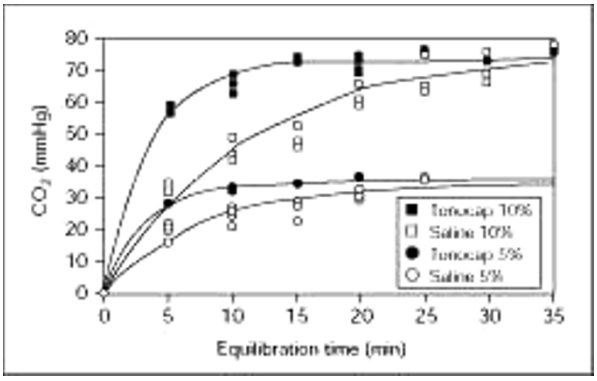

Figure (abstract P088)

Methods: Two TRIP sigmoid tonometers (Tonometrics Division, Instrumentation Corp, Helsinki, Finland) were placed in an air tight test chamber. In one set of experiments, the chamber was perfused with saline in a closed circuit with a roller pump and a membrane oxygenator. The oxygenator allowed for rapid change of PCO_2 in the fluid. In the other set of experiments, the chamber was flushed with calibration gas. The two systems mimic the clinical situations of a fluid filled viscus or a gas filled viscus. The CO_2 in the chamber could be fully changed from 0 to 5 or 10% within 60 s in the saline system, and 30 s in the gas system. One catheter was connected to the Tonocap, the other was filled with 2.5 cc saline that was analysed with an IL1610 blood gas analyser. CO_2 readings were taken at different times of equilibration after a step change in CO_2 from 0. Between each reading, each catheter was flushed to eliminate CO_2 in the dead space. CO_2 versus equilibration time was fit to an exponential function and a time constant was derived.

Results: A plot of CO_2 equilibration time is shown for the gas circuit. The time to reach half of the final CO_2 value ($T_{1/2}$) and the exponential time constants (τ) are shown in the table. The CO_2 response curves were significantly different between saline and Tonocap methods by linear regression in each CO_2 level (P = 0.0001).

Conclusion: The Tonocap responds approximately twice as fast as saline tonometry to a step change in CO_2. This should translate to a quicker detection of changes in intraluminal CO_2 and incracellular acidosis in patients, thereby leading to more expedient intervention to correct the underlying perfusion deficit.

Table (abstract P089)

Mucosal pCO_2 (mmHg)	50	60	80	100	120	140
pHi conventional	7.30	7.22	7.10	7.00	6.92	6.86
pHi new	7.34	7.29	7.12	6.94	6.72	6.33
Mucosal plasma [lactate] (mmol/l)	1.5	1.5	8.1	15.5	23.5	30.5

P089

A new algorithm for the determination of intramucosal pH and mucosal plasma lactate concentration

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Critical Care 1997, **1(Suppl 1):**P089

The conventional calculation of gastric intramucosal pH (pHi) makes the invalid assumption that mucosal and arterial plasma bicarbonate concentrations are identical. Mucosal bicarbonate concentrations exceed arterial during aerobic O_2–CO_2 exchange, causing underestimation of intramucosal pH. Conversely, because of locally reduced bicarbonate concentrations, the conventional calculation significantly overestimates intra-mucosal pH in regional mucosal lactic acidosis, as shown by direct intramucosal pH measurement in animal models of splanchnic ischaemia. Accurate pHi calculation is important since mucosal acidosis is the probable cause of loss of barrier function in gut ischaemia.

We devised an algorithm eliminating arterial bicarbonate from the calculation by: (i) determining the aerobic and anaerobic components of the arterial-mucosal pCO_2 gap using an equation for the Dill nomogram: (ii) introducing a factor quantifying the fall in base excess (BE) which accompanies anaerobic pCO_2 elevation (determined in vitro by anaerobic addition of lactic acid to blood): (iii) applying the Siggaard-Andersen algorithm to derive mucosal end-capillary pH from the calculated mucosal BE.

The pHi was estimated by the new and conventional algorithms tor mucosal pCO_2 values ranging from normal to those associated with severe intramucosal acidosis, assuming [Hb]= 15 g%, SaO_2 = 97%, arterial pCO_2 = 40 mmHg, BE = 0 meq/l and plasma (lactate) =1.5 mmol/l.

Results: See table.

Conclusion: The new pHi values appear valid, exceeding conventional in mild aerobic mucosal acidosis, and in severe acidosis closely resembling directly measured pHi during mesenteric ischaemia. Lactate estimations provide additional information about the gut wall redox state. The algorithm requires experimental evaluation.

P090

Monitoring of electrical activity of small bowel in patients with generalized peritonitis

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Critical Care 1997, **1(Suppl 1):**P090

Objective: To define the range of normal values of electromyography (EMG) parameters, to study their changes in favourable and unfavourable run of postoperative period, to study the possibility of automatization of EMG.

Subjects: We examined 41 peritonitis patients (10 died) with different etiology (in sum 122 observations).

Methods: The PEG-8 electrode was placed on the serosa of small bowel 50 cm distal of Traiz ligature during operation. The EMG curves were registered by `Mingograft-81' and processed manually. The EMG curves from eight patients were amplified (I-400) and recorded into IBM PC/AT-386. The frequency and amplitude of slow waves (FSW and ASW), standard deviation of duration of slow wave (SDDSW), the percent of spike activity (SA), amplitude of spike activity (ASA) were calculated, stored in special file and statistically analysed (*t*-test, elementary statistic and histogram methods were used).

Table (abstract P090)

EMG parameter	FSW (/min)	SDDSW (c)	ASW (μV)	SA (%)	ASA (μV)
Mean value	11.32	0.55	189	27	117
Range of norm	10.30–12.34	0.33–0.77	98–280	5–49	0–240

Results: EMG curves of 14 patients recovered from peritonitis with restored bowel function were examined. On the base the ranges of normal values of EMG parameters were obtained.

The unfavourable prognostic signs were the values of SDDSW more than 0.9 c (dysrhythmic EMG curve) and values of FSW less than 9/min. In patients with severe peritonitis the significant growth of ASW was found. The significant differences of SA and ASA between patients with mild and severe peritonitis, favourable and unfavourable outcomes were not established ($P > 0.05$). Based on our data the working market of automized system for registration and interpretation of EMG was elaborated.

Conclusion: The obtained data can help in objective estimation of EMG activity of small bowel in peritonitis.

P091

Distribution of intracapillary hemoglobin O_2 saturations in gastric mucosa, gastric outer wall and skeletal muscle in septic shock

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Introduction: Alterations in capillary density associated with a heterogeneity in microcirculatory blood flow in the intestine and skeletal muscle are found after both endotoxin infusion and cecal ligation and perforation leading to areas of hypoxia.

Objectives: To investigate the effects of septic shock on spatial distribution of intracapillary hemoglobin O_2-saturations ($cHbO_2$) and relative hemoglobin concentrations [rel(Hb)] in gastric rnucosa, gastric outer wall and skeletal muscle tissue.

Methods: Eight domestic pigs of either sex were studied. After surgery and a 90 min recovery period baseline data sets were collected. Septic shock was then induced by a bolus infusion of *E coli*-endotoxin followed by a continuous infusion. All measurements were repeated at 60 min intervals over a time frame of 8 h.

Empho (*E*rlanger *M*icrolightguide Spectro*pho*tometer): Gastric mucosal $cHbO_2$ spectra were recorded via a fibreoptic probe at the greater curvature at five sites. Gastric outer wall $cHbO_2$ values were collected from the stomach surface through a ventral recloseable laparotomy, and skeletal muscle $cHbO_2$ values were assessed in a foreleg muscle preparation. $cHbO_2$ values obtained were classified into three ranges: critical (0–10%), reserve (11–50%) and normal (51–100%).

Results: At baseline the $cHbO_2$ gradients exhibit a homogeneous oxygenation profile at the five measuring sites within the organs. Between organs, however, $cHbO_2$ distributions were different. In the mucosa 20, 75 and 5% of the recorded $cHbO_2$ values were found in the critical, reserve and normal range, whereas the gastric outer wall distributions were 2, 30 and 67%. In skeletal muscle 0.34% of the $cHbO_2$ were in the critical, 25 and 74% were in the reserve and normal range. In septic shock (1 h), the incidence of $cHbO_2$ values below 10% increased from 20 to 47% in the mucosa and from 2 to 4% in the outer wall, whereas no change could be detected in the skeletal muscle in this range. The incidence of $cHbO_2$values between 11 to 50% dropped from 75 to 52% in the mucosa, but increased from 30 and 25% to 67 and 46% in the outer wall and skeletal muscle, respectively. The incidence of the normal range values decreased from 6, 67 and 74% to 0.5, 28 and 53% in mucosa, outer wall and skeletal muscle. After 4 h of septic shock distributions of $cHbO_2$ were unchanged in all organs compared to 1 h values, but as septic shock continued the oxygenation profile progressively shifted to lower values primarily in the mucosa whereas in the skeletal muscle values below 10% $cHbO_2$ only appeared after 8 h of shock. The relative hemoglobin concentrations changed from 0.79, 0.72, 0.72 at baseline to 0.57, 0.43, 0.52 after induction of shock and 0.37, 0.23, 0.53 at 8 h of shock (mucosa-outerwall-muscle).

Conclusion: In septic shock the shift of HbO_2 distribution to critical values is mainly found in the gastric mucosa and to a lower extent in the gastric outer wall. In skeletal muscle, however, $cHbO_2$, although also shifted to lower values, were always maintained within the normal or reserve range for 7 h of shock. Only after 8 h did critical values appear. These findings are supported by the changes in the rel(Hb). Thus, it appears that septic shock causes critical $cHbO_2$ in the gut, a non-vital organ suffering from redistribution of flow, but barely in the skeletal muscle, an organ of locomotion.

P092

Long-term follow-up study in liver resection patients receiving a haemoglobin-based oxygen carrier

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Introduction: Since improvement in purification of stroma-free haemoglobin solutions enables the production of cell-free oxygen carriers which are free of toxic side-effects on liver and kidneys, clinical interest in such material has been aroused during the last years. Animal models have shown that ultrapurified polymerized bovine haemoglobin (HBOC-201) is free of severe hepato-renal side-effects and provides excellent tissue oxygenation [1–3]. The present prospective study was designed to examine safety and tolerance of HBOC-201 applied during haemodilution in patients prior to liver resection.
Methods: After approval of the ethics committee and written informed consent, 12 patients (6 male and 6 female, mean age 59 ± 10 years) undergoing elective liver resection randomly received either 0.4 g/kg HBOC-201 (Biopure MA, group 1) or 3 ml/kg of hydroxyethylstarch 70,000/0.5 (B Braun, FRG, group 2) after autologous blood donation of 1 l. Blood chemistry, haematology, coagulation profiles, urinalysis and immunologic samples were taken on the day before surgery, on days 1-4, 7 and 14 after surgery as well as 3 months after the operation. All values were statistically analysed using ANOVA and Mann-Whitney U-test with $P < 0.05$ considered as significant.
Results: Demographic characteristics, blood loss, time of operation and duration of hospitalization did not differ between groups. No allergic or other adverse reactions occurred during infusion of HBOC-201. The mean intravascular half-life of HBOC-201 was 8.5 h, no free haemoglobin was detectable in urine over time. Due to the operation, all patients of both groups showed temporary but reversible rises of liver enzymes and bilirubin but no changes in coagulation profiles or creatine. No IgE antibodies to HBOC-201 were seen. The Figure shows the mean concentrations of IgG to HBOC-201.
Discussion: The single application of a moderate dose of HBOC-201 was well tolerated in patients undergoing liver resection surgery. However, in spite of the very low IgG titers 14 days after the application of HBOC-201, it remains unclear at the moment if a second administration of the material may cause any immunological reactions.
References

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P093

Microvascular gut oxygenation measured by Pd-porphyrin phosphorescence during severe hemorrhagic shock and low volume resuscitation with DCLHb™ in pigs

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Introduction: Diaspirin crosslinked hemoglobin (DCLHb™, Baxter Healthcare Corp) is a hemoglobin based blood substitute which has been demonstrated to restore systemic blood pressure following hypovolemic shock at a low dose in pigs. In this study microvascular pO_2 of the pig gut (pO_2microv) was measured with a light guide attached to a phosphorimeter and using Pd-porphyrin quenching of phosphorescence [1], during shock and resuscitation. Resuscitation with DCLHb™ was compared to resuscitation with a combination of crystalloid and colloid.
Methods: Ten pigs (16 kg) were anesthetized, and ventilated with 33% O_2 and 67% N_2. Catheters were inserted, a length of ileum was extracted from the peritoneal cavity, and the fibre of a phosphorimeter placed on the serosa of the last 10 cm of the ileum. During preparation, Pd-porphyrin bound to albumin was injected intravenously. After stable baseline (BL), a severe hemorrhagic shock was induced by withdrawing 40 ml/kg (50% of circulating blood volume) of blood over 1 h. After 45 min of shock (ES) all pigs were randomly assigned to two groups. Resuscitation was performed over 20 min with either DCLHb™ (10%, 5 ml/kg) (DCLHb, $n = 5$) or a combination of lactated Ringers' solution (75 ml/kg) and gelofusine (15 ml/kg) (coll/cryst, $n = 5$). Observations were made every 15 min for 2h after resuscitation. Pd-porphyrin measurements were performed every 20 s.
Conclusion: Low volume resuscitation with DCLHb™ in pigs results in a more sustained improvement of microvascular pO_2, measured by Pd-porphyrin phosphorescence, compared to resuscitation with a combination of large volume colloid and crystalloid.
Reference

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P094

Peri-operative changes of haemodynamics and oxygen transport in patients undergoing haemodilution with bovine haemoglobin

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Critical Care 2001, **1(Suppl 1):**P094

Introduction: Haemodynamic reactions following infusions of haemoglobin solutions have been shown in several animal experiments and may be of clinical concern. There is some evidence that vasoconstriction is a function of impurities of haemoglobin solutions. As a consequence, purification and chemical modification of haemoglobin should reduce adverse circulatory reactions. In animal models, ultrapurified polymerized bovine haemoglobin (HBOC-201) appears to be free of severe side effects. The present prospective study investigates haemodynamic changes and oxygen transport parameters in patients undergoing pre-operative haemodilution with HBOC-201 in comparison to hetastarch.
Methods: After institutional approval and written informed consent, 12 patients (6 m and 6 f, mean age 59 ± 10 years) underwent pre-operative haemodilution prior to elective liver resection. After induction of general anaesthesia, patients received an arterial line, a central venous and pulmonary catheter. Haemodynamic parameters and blood gases were measured before and after patients donated 1 l of their own blood and received 1 1 of Ringer's lactate (RL). Following haemodilution, patients were randomly allocated to receive either 0.4 g/kg HBOC-201 (Biopure, MA, group 1), or an equal volume of 6% hetastarch 70,000/0.5 (B Braun, FRG, group 2) plus 1 l of RL within 30 min. Haemodynamic and blood gas measurements were performed every 10 min during infusion of HBOC-201 or hetastarch, at the beginning of surgery and 4 h after arriving at the ICU. Values were tested using ANOVA and Mann-Whitney U-test with $P < 0.05$ considered as significant.
Results: Demographic characteristics did not differ between groups. In contrast to group 2, the mean arterial blood pressure increased by 18% over baseline in group 1. While the pulmonary vascular resistance did not change in both groups, the systemic vascular resistance (SVR) increased to a maximum of 42% over baseline in group 1. Cardiac output (CO), mixed-venous oxygen content and oxygen delivery were lower in the HBOC-201 group. In contrast, arteriovenous oxygen difference and oxygen extraction ratio were higher in group 1 than in group 2, even on the ICU. Free haemoglobin reached a maximal concentration of 1.0 ± 0.2 g/dl 30 min after the HBOC-201 infusion was started.

Discussion: In spite of ultrapurification of HBOC-201, the present haemodynamic data are consistent with different studies which show increased SVR and decreased CO following application of haemoglobin solutions. However, the long-lasting increase of oxygen extraction after HBOC-201 infusion which is provided by the low oxygen affinity of this compound may overcome potential adverse haemodynamic side effects.

P095

The variation of volume expansion after infusion of hydroxy ethyl starch 6% in critically ill patients

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Critical Care 2001, **1(Suppl 1):**P095

Background and objectives: Knowledge of the volume expanding effect of colloids is essential in many intensive care unit (ICU) patients. This volume expanding effect is usually evaluated by indirect methods [eg arterial blood pressure, central venous pressure, pulmonary capillary wedge pressure (PCWP), cardiac output, hematocrit and diuresis], albeit these methods only correlate poorly to direct measurements. The scarce amount of data so far available is mainly due to the rather cumbersome methods for direct determination of circulating blood volume (CBV) in ICU patients. We have used a modification of the carbon monoxide (CO) method for estimation of CBV enabling quick bedside determinations. The aim of this study was to evaluate the interindividual variation of volume expansion during the first 8 h after infusion of 500 ml HES 6% in critically ill patients.
Methods: In 20 consecutive patients admitted to the ICU requiring mechanical ventilation and volume expansion. In each patient 500 ml of HES 6% was infused during a period of 30 min. The CBV was measured immediately before the infusion and hourly for 8 h. During this period all efforts were made to keep the fluid balance unchanged.
Results: The mean volume expansion measured immediately after infusion 500 ml HES 6% was 476 ± 310 ml (2SD). The corresponding values after 4 and 8 h were 241 ± 248 ml (2SD) and 104 ± 358 ml (2SD), respectively. The coefficient of variation of the method for estimation of CBV was 3.6%.
Conclusion: The large interindividual variation of the volume expansion after infusion of HES 6% in critically ill patients illustrates the difficulties in optimizing colloid therapy without a direct measurement of the CBV.
Reference
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P096

Changes to cardiac output and left ventricular work indices following a 200 ml bolus of 20% albumin

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Objectives: We have previously described a technique for the measurement of vascular permeability (the Albumin Distribution Index, ADI) which entails the bolus administration of 200 ml of 20% albumin solution. This hypertonic solution causes a fall in ionised calcium levels, possibly reducing contractility, and in the septic patient with myocardial depression theoretically might lead to left ventricular overload and dysfunction. This study set out to investigate to what degree this occurs.
Design: Prospective observational study.
Subjects: Fifteen adult patients with clinical septic shock, median APACHE II score 17 (± 3), mean age 47 (± 16) years, with pulmonary artery catheters in situ.
Methods: Pulmonary artery wedge pressure (PAWP) and cardiac output measurements in triplicate were taken immediately before, then 1, 5, 15 and 30 min following the infusion of 200 ml of 20% albumin (BPL, Elstree) over a 90 s period. Cardiac index (CI) and left ventricular stroke work index (LVSWI) were calculated for each set of measurements.
Results and statistical analyses: See table.
Conclusion: Cardiac output and left ventricular stroke work were improved in this group of septic patients following the administration of 200 ml of 20% albumin. This suggests that septic patients are normally below their optimal filling pressures, and that the administration of this albumin bolus does not overload them.

Table (abstract P096)

	Pre	1 min	5 min	15 min	30 min
CI	4.6 ± 1.2	5.1 ± 1.4**	5.1± 1.3**	5.0 ± 1.4**	5.1± 1.3**
CI(%Δ)		11 ± 13	11 ± 12	8 ± 10	11 ± 12
LVSWI	45 ± 13	57 ± 18***	58 ± 18***	55 ± 16***	55 ± 15***
LVSWI (%Δ)		27 ± 17	29 ± 16	24 ± 17	24 ± 16
PAWP	13 ± 3	17 ± 4***	16 ± 4***	15 ± 4***	15 ± 3***

Paired *t*-tests, pre versus 1 min, 5 min,15 min and 30 min. $^{***}P < 0.001$, $^{**}P < 0.01$.

P097

Optimisation of high risk surgical patients improves mortality in clinical practice

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Introduction: Deliberately increasing oxygen delivery (DO_2) in the peri-operative period has been shown to improve survival for high risk surgical patients, in several randomised, controlled, trails [1].
Design, subjects and methods: A prospective study evaluating the efficacy of increasing peri-operative oxygen delivery in high risk surgical patients, to greater than 600 ml/min/m^2 with dopexamine hydrochloride, in routine clinical practice
Results: Expressed as medians with 25%, 75% centiles.
Conclusions: An 11.9% 28 day mortality rate compares favourably with historical controls and clinical trials. This study confirms that the technique of increasing DO_2 in the peri-operative period is both practical and beneficial in routine clinical practice.
Reference
1. Boyd O, Grounds RM, Bennett ED: *JAMA* 1993, **270**:2699-2707.

Table (abstract P097)

Number of patients	50
Age years	72 (64, 76)
Sex male/female (%)	62/38
Number of high risk criteria	1.9
APACHE III score	65 (50, 80)
Admitted pre-op/postop (%)	88/12
Elective emergency (%)	54/46
Baseline DO_2	492 (439, 562)
Pre-operative DO_2	639 (522, 693)
Postoperative DO_2	488 (368, 735)
Number of patients achieving DO_2 > 600 ml/min/m^2	25
Number of patients achieving DO_2 > 600 ml/min/m^2 without dopexamine	12
ICU length of stay days	2.8 (2, 6.3)
Hospital length of stay days	24 (12, 48)
Mortality prediction ratio from APACHE III (%)	31(7,50)
28 Day mortality rate (%)	11.9

Table (abstract P98) Contents of the six parenteral nutritions

	1	2	3	4	5	6
G 50% (ml)			500	500	650	600
G 30% (ml)	750	750				
IL 20% (ml)	500		500			
M 20% (ml)		500		500	500	600
H 25 (ml)	500	500	500	500	750	750
N (g)	12.8	12.8	12.8	12.8	19.2	19.2
G/L (%)	47/53	48/52	50/50	50/50	57/43	50/50
C/N	148	147	156	155	119	124
Kcal G + L	1900	1884	2000	1984	2284	2381

P098

Twenty-nine day study of stability for six different parenteral nutrition mixtures

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Aim of the study: Parenteral nutrition is often peri-operative. It can be realized with packages containing different nutrients. Knowledge of the stability of these mixtures is necessary. The aim of this study is to test the stability of six parenteral nutrition mixtures, fitted to different pathologies.
Materials and methods: The mixtures are not supplemented. The packages are made of EVA (Nutripoches NPP235; Pharmacia). They contain (Table) glucose (G50 or G30%: Aguettant and Cooper Lab), amino acids (Hyperamine 25® B Braun Medical SA), and lipids consisting of medium chain and long chain triglycerides (20% Médialipide® B Braun Medical SA) or only long chain (20% Intralipide® Pharmacia). The Central Pharmacy of the hospital fills the packages in a clean room under a laminary horizontal flux hood. The packages are filled with nutrients under nitrogen pressure. Two packages of each type are forwarded by air freight in a cold box to the stability control laboratory within 24 h after manufacture. They are stored in a refrigerator at 4 ± 1°C (circulating air) during 28 days, then 24 h at room temperature. The stability tests are performed at Dl, D3, D7, D10, D14, D21, D28, D28 + 24 h. The tests are: visual macroscopic (with and without homogenization) and microscopic controls (dilution = 1 : 10, increase: × 500 and × 1000), granulometric analysis (Coulter Counter TA II with a 50 µm aperture tube, dilutions = 1 : 100,000 and 1 : 1000), controls of pH, osmolality and conformity to the formulae. Results are given compared to mother emulsions.
Results: There is no macroscopic destabilization from D1 to D29 (no change in the colour or aspect of the mixtures). They are microscopically identical with the D1 mother emulsions. There is neither granulometric destabilization nor break of the emulsion incompatible with a normal therapeutic use. Conformity to the formulae, osmolality and pH are not significantly different from D1 to D29.
Conclusion: All the stability tests comply: the controlled mixtures are stable during a long storage period: 28 days at 4°C temperature, plus 24 h at room temperature.

P099

The effect of nutrition and severity of illness on blood vitamin concentrations in critically ill patients

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Objectives: To measure blood vitamin concentrations after admission to ICU and to assess the effect of our standard nutritional regimen and the severity of organ failure on subsequent vitamin concentrations.

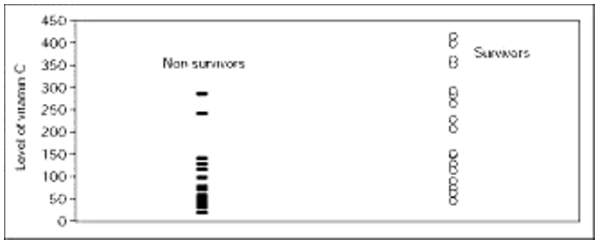

Figure (abstract P099)

Method: Blood vitamin concentrations were measured in 42 ventilated patients following admission and thereafter twice weekly for the duration of their ICU stay. Parenteral nutrition with vitamin supplementation (daily Solivito N and Vitlipid N) or enteral nutrition was instituted independently by the clinicians according to their normal practice. Data were collected to allow calculation of Sepsis Score and Organ System Failure Score. Vitamins A, D, E, red cell thiamine and leucocyte vitamin C were measured using standard laboratory assays.
Results: Baseline vitamin A concentrations were below the normal range in 59% of patients. However, in those patients with renal failure (dialysis or creatinine > 300 µmol/1) baseline and subsequent concentrations were up to four times the upper limit of the normal range.
Baseline vitamin C levels were below the normal range (119–301 nmol/10^8 wbc) in 77% of the group of non-survivors (median 63 nmol) and in 43% of the group of survivors (median 146).
This difference is not statistically significant in this pilot study given the number of patients involved. Vitamin C levels failed to reach the normal range over the study period (4-31 days) in both groups. Baseline vitamin E (alpha tocopherol) concentrations were below the normal range in 50% of patients, but reached the normal range in the majority of patients over the study period. Vitamin D2, D3 and red cell thiamine concentrations were within the normal range for nearly all patients throughout the study. Thiamine levels were supranormal in patients given parentrovite for a history of alcoholism. There was no correlation between vitamin concentrations, either on admission or during the study, and severity of illness as measured by the Sepsis Score or Organ System Failure Score.
Conclusions: The initial low concentrations of vitamin A in critical illness may be explained by concurrent low concentrations of serum retinol binding protein, a negative acute phase protein, although this was not measured in the study. However, with the onset of renal failure, vitamin A reaches high concentrations strongly suggesting supplementation should be reduced, in view of potential toxicity.
Both vitamin C and E levels were low on admission and may reflect low concentrations in the general population, reduced intake with the onset of illness, increased requirement or increased utilization. The standard regimen of supplementation was not sufficient to bring leucocyte vitamin C concentrations into the normal range for `healthy individuals'. The data suggests we should give more vitamin C, and possibly vitamin E, on admission to ICU and higher maintenance doses of vitamin C. Further studies will show if this has any effect on blood concentrations or on outcome.

P100

Nutritional parameters in patients with severe catabolism due to trauma or sepsis

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Our previous studies indicate that in critically ill patients ICF-I levels are reduced to a greater extent in septic (S) than in trauma (T) subjects.

However, it is well known that IGF-I levels depend on nutrition as well as on somatotrope secretion. Aim of the present study was to verify the levels of IGF-I and other nutritional parameters such as albumin (A), prealbumin (PRE-A), transferrin (TRA) and retinol-binding-globulin (RBG) in septic patients [n = 11, age (mean ± SEM) 56.1 ± 2.7 years, BMI 25.2 ± 0.9 kg/m^2] and in trauma patients (n = 13, age 42.4 ± 4.1 years, BMI 25.0 ± 0.8 kg/m^2) after ICU admission. Both groups were characterized by similar scores of catabolism (SAPSII and MOF score) and underwent similar artificial nutrition. Nutritional parameters were evaluated on day 1, 3, 5 and 7 after ICU admission. Both in S and in T, IGF-I, A, PRE-A, TRA and RBG levels on day 1 of ICU admission were lower than the normal range. Basal IGF-I levels in S were lower than those in T (82.9 ± 13.0 versus 127.0 ± 16.4 μg/1, P < 0.05). IGF-I levels increased on day 7 to a lower (P < 0.05) extent in S (110.3 ± 9.5, P < 0.05 versus day 1) than in T (211.4 ± 25.5, P < 0.01 versus day 1). Basal A and RBG levels in S (3.0 ± 0.2 g/dl and 2.8 ± 0.9 mg/dl) were similar to those in T (3.2 ± 0.1 g/dl and 3.1 ± 0.3 mg/dl); in both groups A levels did not show variations up to day 7 while RBG showed a trend toward increase (P < 0.05 in S). Basal PRE-A and TRA levels in S (10.9 ± 2.5 mg/dl and 108.8 ± 10.7 mg/dl) were lower (P < 0.01) than those in T (17.8 ± 1.4 mg/dl and 168.7 ± 8.3 mg/dl). PRE-A and TRA levels did not show significant variations up to day 7 persisting lower (P < 0.05) in S than in T.
In conclusion, our results further demonstrate that, in spite of similar score of catabolism, in critically ill patients the reduction of IGF-I, PRE-A and TRA levels is more marked in septic than in trauma patients. These findings indicate that the influence of nutrition and/or somatotrope function on ICF-I synthesis and release varies among different catabolic states.

P101

Activity of GH/IGF-I axis in catabolic patients with sepsis or trauma

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Increased GH together with decreased IGF-I levels suggesting a peripheral GH insensitivity in critically ill patients have been reported by some but not by other authors. To clarify the activity of GH-IGF-I axis in catabolic states, basal and GHRH-stimulated GH secretion and IGF-I levels have been evaluated in patients with sepsis [SEP, n = 11; age (mean ± SEM) 56.1 ± 2.7 years] or trauma (TRA, n = 13; age 42.4 ± 4.1 years) on 1st, 3rd, 5th and 7th day after ICU admission, during artificial nutrition. SAPS II and MOF scores overlapped in both groups. Basal GH and IGF-I levels were also assayed in 24 normal subjects (NS, age 48.1 ± 4.3 years), 54 adult hypopituitaric patients with severe GH deficiency (GHD, age 44.8 ± 2.3 years), 19 patients with anorexia nervosa (AN, age 18.6 ± 0.6 years) and 12 patients with liver cirrhosis (LC, age 50.4 ± 2.8 years). In GHD, basal GH levels were lower than in NS (0.3 ± 0.1 versus 1.4 ± 0.2 μg/l, P < 0.01); similarly, IGF-I levels were markedly reduced and lower than in NS (68.6 ± 6.1 versus 213.5 ± 15.4 μg/l, P < 0.01). AN and LC basal GH levels were similar (10.0 ± 2.8 and 7.7 ± 2.1 μg/l) and higher than in NS (P < 0.01). AN and LC IGF-I levels were similar (70.4 ± 9.1 and 52.4 ± 10.5 μg/l), lower than in NS (P < 0.01) while overlapping with those in GHD. On the 1st day of ICU admission basal GH levels in SEP (0.7 ± 0.3 μg/l) and TRA (1.8 ± 0.6 μg/l) were similar to those in NS. IGF-I levels in SEP were lower than in TRA (82.9 ± 13.0 versus 127.0 ± 16.4 μg/l, P < 0.05) and both lower than in NS (P < 0.01). IGF-I levels in SEP were similar to those in GHD, AN and LC which were lower than in TRA (P < 0.01). GH levels in SEP and TRA remained similar up to the 7th day. In both groups the GH response to GHRH on the 3rd day was nearly abolished, clearly lower than in age-matched NS (GH peak, 2.5 ± 1.2 versus 10.5 ± 1.9 μg/l, P < 0.01). During parenteral nutrition, IGF-I levels increased both in SEP and TRA (P < 0.05 and P < 0.01, respectively). However, on the 7th day, IGF-I levels in SEP were clearly lower than in TRA (110.3 ± 9.5 versus 211.4 ± 25.5 μg/l, P < 0.01), overlapping the latter with those in NS.
In conclusion, in severe catabolic conditions due to trauma and furthermore to sepsis, IGF-I levels are markedly low and similar to those in GHD. Somatotrope secretion is also impaired in both these catabolic conditions. Therefore, in patients with severe catabolism due to trauma or, particularly to sepsis, peripheral GH insensitivity and somatotrope insufficiency could both severely impair the activity of GH-IGF-I axis. Finally, artificial nutrition clearly increases IGF-I levels in post traumatic but not in septic catabolic states.

P102

A retrospective review of the intensive care management of diabetic ketoacidosis

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Critical Care 1997, **1(Suppl 1):**P102

Introduction: Diabetic ketoacidosis (DKA) remains a common complication for patients with diabetes mellitus. Despite a relatively low mortality of 2-5 % [1] there remains a substantial morbidity.
Design, methods and patients: All patients who had been admitted to intensive care at St George's Hospital, over a 3 year period, with a primary admitting diagnosis of diabetic ketoacidosis, were retrospectively reviewed from the notes and ICU charts. All patients were treated with similar recognised management plans tor DKA [1].
Results: Expressed as mean (± SEM). Twenty-nine patients were identified with a mean age of 42.3 (± 2.9) years, an APACHE III score of 58.4 (± 3.9) and a predicted mortality of 2.5 (± 0.6)%. The length of stay on the ICU was 3.16 (± 0.6) days.
Conclusions: Despite recognised management plans for DKA there is still a substantial morbidity for these patients. Although the arterial pH return to normal within 24 to 36 h there is still a significant metabolic acidosis, despite an absence of ketones in the urine, normal serum lactate levels and normal blood sugar levels. It is unclear whether this metabolic acidosis has any clinical relevance as the mortality is so low, or if it is reflecting inadequate treatment regimes.
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P103

Postoperative complications following cardiac surgery with cardiopulmonary bypass

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Critical Care 1997, **1(Suppl 1):**P103

Introduction: Cardiac surgery using cardiopulmonary bypass (CPB) is associated with a low mortality, and planned hospital stays of less than 7 days imply a low incidence of major morbidity. We challenge this notion, having observed considerable morbidity attributable to low grade organ dysfunction; the purpose of this study was to quantify postoperative morbidity.
Methods: A retrospective analysis of prospectively collected data on all adult cardiac surgery patients presenting at the Duke Heart Center

Table (abstract P102)

Admission	
pH	7.12 (± 0.06)
Base excess	-20.8 (± 3.9)
Lactate (mmol/l)	1.67(± 0.37)
24 h	
pH	7.31 (± 0.02)
Base excess	-10.9 (± 1.9)
Discharge	
pH	7.4(± 0.02)
Base excess	-5.7 (± 1.6)

The overall hospital mortality for this group was 0%.

Table 1 (abstract P103) Demographics

	CABG	Valve	Combined	Male	Female	Total
n = %	2106	309	186	1652	949	261
	81%	12%	12%	7%	36%	100%

The range of Hlos in survivors is 5-112 days; the mean is 8; the median 6; the mode 5 and the standard deviation 7.4 days. Twenty-five percent of patients stay longer than 8 days.

Table 2 (abstract P103) Mortality and morbidity

	Died	Lived	Anycomp	No comp	Total
n = %	91	2509	964	1637	2601
	3.50%	96.50%	37%	63%	100%

Overall, complications occurred in 37% of patients. Arrhythmias (predominantly atrial) rank highest but of the 10 commonest complications resulting in a Hlos > 7 days, seven are non-cardiac. Regarding organ specific complications, the five commonest prolonging Hlos > 7 days rank: cardiac, lung, renal, brain, gut.

1993-1995. Thirty-one named complications were recorded and described as patients cardiac or non-cardiac (further ascribed to specific organs) and the hospital lengths of stay (Hlos) associated with each named complication was noted.

Results: See tables.

Discussion: The median and mode Hlos support the impression that the postoperative course is uncomplicated and routine. However, morbidity following cardiac surgery (37% of patients) is common and a significant proportion is non-cardiac. Of note, 25% of patients remain in hospital > 8 days, most with some manifestations of organ dysfunction. The caremap structure for postoperative cardiac patients at Duke aims to limit Hlos to < 7 days; to stay beyond 7 days at Duke is invariably associated with serious morbidity, so for a significant minority of patients, recovery from cardiac surgery is far from uneventful. The incentives for interventions designed to reduce such morbidity and its associated increased cost are huge [1].

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P104

Cardiac arrhythmias post-esophagectomy as the second day complication

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Introduction: We observed by the second day, cardiac arrhythmias in most of the patients undergo to esophagectomy. The main anomalies were ventricular arrhythmias with and without haemodynamic dysfunction.

We tried to find a relationship between those arrhythmias and the electrolyte variations in the first 48 h after the operation.

Materials and methods: A retrospective study was performed in 28 patients admitted after esophageal surgery, during a 2 year period. Data collected for all patients included age, SAPSII, and the occurrence of acute arrhythmias. In all patients was analysed blood levels of calcium, phosphorus, magnesium, potassium and pH. The patients were divided in two groups: A, with 'malign' ventricular arrhythmias; B, without arrhythmias. We compared and analysed the outside of the normal range (referrable laboratorial values at our institution) for the blood. Data are reported as mean and standard deviation.

Results: See table.

Conclusion: It is well known that post-operative electrolyte and water metabolism imbalance is a common cause of cardiac rhythm disturbances. In this study we were able to verify that patients with cardiac rhythm disturbance had the lowest median blood levels of calcium and phosphorus on admission at the ICU. Twenty-four hours after the admission the same ions still remain at low blood levels. Concerning the other ions, there was no differences between the two groups, and the values were in the normal range. However, present data do not permit to establish a strong causal relationship between this rhythm disturbance and the electrolyte imbalance, because some patients of the lowest ion levels (group A) exhibit normal levels after surgery. We think, therefore, that further investigation is needed to understand the cardiac rhythm disturbance at the second day after esophagectomy.

Table 1 (abstract P104)

n = 28	Age	Saps II	Arrhythmia	Mortality
A (n = 14)	66.8 ± 9.8	30.5 ± 7.7	EVbs (multifocal)	7.1%
			VT;VF	(2 patients)
B (n = 14)	64.6 ± 11.3	26.2 ± 9.9	—	—

Table 2 (abstract P104)

	Calcium			Phosphorus		
	0	24	48	0	24	48
A	7.1 ± 0.3	7.89 ± 0.66	8 ± 0.72	2.78 ± 0.78	3.3 ± 0.7	2.46 ± 0.8
B	7.42 ± 0.8	8.2 ± 0.5	8.5 ± 0.4	3 ± 0.6	3.2 ± 0.3	2.5 ± 0.9

Table 3 (abstract P104)

	Magnesium			Potassium		
	0	24	48	0	24	48
A	1.48 ± 0.5	1.77 ± 0.29	1.61 ± 0.4	3.57 ± 1.18	3.22 ± 0.4	3.1 ± 0.2
B	1.38 ± 0.2	2 ± 0.44	-	3.34 ± 0.3	3.27 ± 0.3	3.08 ± 0.4

P105

APACHE-II-score-based identification of an escalating systemic inflammatory response syndrome (SIRS) early after cardiac surgery with the assistance of the cardiopulmonary bypass (CPB)

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Multiorgan dysfunction syndrome (MODS), sepsis and septic shock are the leading causes of death in the postoperative phase after cardiac surgery assisted by the cardiopulmonary bypass (CPB). The APACHE-II score has been validated for identifying patients at risk of developing MODS in the intensive care unit and was used in this study to detect post-pump inflammatory response. Using the APACHE-II score on the first postoperative day, in a monocenter patient population of the years 1988–1990, a risk stratification for sepsis after cardiac surgery had been achieved (Pilz *et al: Chest* 1994, **105**:76–82). Three groups had been discerned: an APACHE-II score ≥ 19–23 described a patient group at risk of developing sepsis with a mortality of 14%; an APACHE-II score ≥ 24 implied a very high mortality of 76%; patients with a score < 19 had a low risk of developing sepsis.

This risk stratification was renewed in 1996 in another center in a university setting. So far in 223 patients, who had undergone elective open-heart surgery from June to October, APACHE-II score was determined on the morning of the 1st postoperative day and correlated with

mortality: 28-day-mortality amounted to 3.8% in patients with a score < 19; 12.5% in patients with a score of ≥ 19–23; and 31.2% in patients with a score ≥ 24 (21 patients still in validation process). These APACHE-II score (≥ 24)-identified high-risk patients significantly differed from patients with a score < 19 in the duration of the extracorporeal circulation (score < 19: 98.1 ± 35.4 min; score ≥ 19–23: 120.1 ± 64.1 min; score ≥ 24: 134.8 ± 41.1 min), the duration of mechanical ventilation in the ICU (score < 19: 26.1 ± 58.6 h; score ≥ 19–23: 78.6 ± 74.7 h; score ≥ 24: 145.7 ± 139.7 h) and age (score < 19: 62.4 ± 9.1a; score ≥ 19–23: 62.5 ± 12.4a; score ≥ 24: 69.8 ± 4.6a) of the patients. The groups were not significantly different with respect to the average pre-operative NYHA degree of heart failure.
Conclusion: The APACHE-II score on the morning of the 1st postoperative day after elective cardiac surgery with CPB allows for a risk stratification. In the patient population investigated, the APACHE-II score (≥ 24)-defined high-risk group had a better prognosis than the patients with the same score values examined in 1988–1990.

P106

Postoperative inotropic treatment after combined beating heart coronary surgery and transmyocardial laser revascularization

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Introduction: Patients with contraindications to CBP and coronary anatomy unsuitable for CABG can be treated by means of transmyocardial laser (TMLR) combined with beating heart coronary surgery. We evaluated the efficacy of enoximone (E) in improving postoperative hemodynamics.
Methods: Ten patients, mean EF 38%, undergoing the combined procedure, were randomized into two groups, one receiving E (group A, 5 patients), and one dopamine (D) (group B, 5 patients). TEE and thermodilution were performed after induction of anaesthesia (T0), after sternal closure (T1), on arrival in ICU (T2), and 12 h later (T3). Drugs were titrated in both groups until achievement of haemodynamic end points (CI > 2.6 l/min/m^2; WP < 18 mmHg; TEE-EF > 35%).
Results: No differences were observed at T0 and T1 between the two groups. Group A showed a better myocardial performance than group B at T2 and T3 (EF 49 ± 9% versus 42 ± 7%, $P < 0.05$, and CI 3.3 ± 0.4 l/min/m^2 versus 2.8 ± 0.2 l/min/m^2, $P < 0.05$, at T2; EF 50 ± 8% versus 44 ± 8%, $P < 0.05$, and CI 3.4 ± 0.6 l/min/m^2 versus 3.0 ± 0.1 l/min/m^2, $P < 0.05$, at T3).
Discussion: E improves cardiac function more than D in patients undergoing combined beating heart CABG and TML revascularization. Such better haemodynamics does not affect postoperative outcome in our experience.

P107

Correlation between QT interval and serum level of calcium

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Introduction: The first reported association between long QT interval syndrome and structural disease in the heart was demonstrated by James, Froggatt and James in 1964 (*Quart J Med* 1964, **33**:361–385). A high incidence of long QT interval in critically ill patients has been showed previously (*Intensive Care Med* 1996, **22**:S85). Some causes of long QT interval are electrolyte disturbances, antiarrhythmic and non-antiarrhythmic drugs.
The aim of this study is to evaluate the correlation between serum level of calcium and QT interval in intensive care patients.
Patients and methods: We studied 30 patients (18 men and 12 women) aged more than 12 years old (mean = 52.5 years old) admitted to the intensive care unit. All patients were monitored by the Multi-Function Monitoring System 'Dina Scope DS-330' (Fukuda Denshi Company). Serum electrolytes were determined along their treatment in the intensive care unit. Electrocardiogram (ECG) was recorded daily. The QT interval was correct for the heart rate (QTc) using the Bazett formula (*Heart* 1920, **7**:353). The upper limit of QTc was 0.424 s for men and 0.440 s for women.
Results: Nineteen patients (63.33%) had QTc intervals above the normal limit and 11 (36.67%) had normal values. The most frequent electrolyte disturbance was related with calcium level. From 19 patients of the abnormal QTc group, 12 patients (63.16%) had hypocalcaemia (serum level below 8.5 mg/dl). In the normal QTc group (11 patients) only four patients (36.36%) had hypocalcaemia.
Although there was a high incidence of hypocalcaemia in the abnormal QTc group, according to the Chi-Square test it was not statistically significant (Chi-Square of 2.00).
Conclusion: Our results showed that the most frequent electrolyte disturbance associated with long QT interval was hypocalcaemia. However, our data was not statistically significant. In the future studies with larger groups we might find a significant correlation.

P108

Increased risk due to ventricular arrhythmias after transmyocardial laser-revascularisation? Preliminary results

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Critical Care 1997, **1(Suppl 1):**P108

Introduction: Transmyocardial laser-revascularisation (TMLR) is a new and promising method for the treatment of angina pectoris in patients with no other therapeutic options. We investigated the incidence of ventricular arrhythmias (VA) before, immediately after and 4 months after TMLR.
Methods: In this ongoing, 24 h study Holter monitors were applied immediately before, 48 h after and 4 months after TMLR-surgery and analysed using Hellige-Marquette 4000 software. We registered ventricular premature beats mean (VPB), ventricular couplets, triplets and ventricular tachycardias (VT).
Results: We included 16 patients so far, mean age 64.8 (± 7.9) bypass surgery previous to the TMLR. Mean echocardiographic ejection fraction was 45%. The table summarizes the results of our patients, values are given as median and minimum/maximum.
Conclusion: Our preliminary data suggest a temporary increase of ventricular premature beats in the early phase after TMLR, but no increase of ventricular tachycardias.

P109

Is serum myoglobin an early marker of reperfusion in thrombolysed AMI?

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Background and objectives: Since early reperfusion of an occluded artery proved to be the essential mechanism of the improved prognosis and mortality reduction, better prediction of successful thrombolysis had become a priority.
Our study aimed to prove that serum myoglobin determination allows better prediction of blood flow re-establishment.
As successful reperfusion causes an earlier release of biochemical markers of myocardial necrosis, we supposed that early and repeated dosage of serum myoglobin would permit a better prediction of recanalisation.
Methods: We studied the serum myoglobin levels in 47 patients presenting an AMI: 37 intravenous patients were treated by thrombolysis

Table (abstract P108)

	VPB/ 24 h	Couplets/ 24 h	Triplets/ 24 h	VT/ 24 h
Before TMLR	135 (16–1452)	5 (0–235)	0 (0–94)	0 (0–575)
48 h after TMLR	301 (7–1654)	3.5 (0–43)	0.5 (0–26)	0.5 (0–76)
4 months after TMLR	226 (12–1930)	3 (0–91)	0.5 (0–17)	0 (0–13)

(rTPA); five by emergency TGA; and four patients presented a contraindication to either one methods. Thirty-two from 37 patients were reperfused during the first 90 min, five were not.
Results: A fourfold increase in the first 90 min is a good predicting factor of reperfusion (78% sensibility, 89% positive predicting value, 40% specificity, 25% negative predicting value). The low results for specificity and negative predicting value are probably due to the small number of non-reperfused patients.
Conclusion: Determination of serum myoglobin levels during the first 90 min of an AMI treated by intravenous thrombolysis may accurately identify successful reperfusion if used in association with the other reperfusion predicting factors (resolution of the ST-segment elevation, pain resolution, arrhythmias), but larger series are necessary before generalisation of this technique. Thus, lower cost and rapid assay device make this method interesting for early assessment of myocardial reperfusion.

P110

Troponin T as myocardial ischemia marker to guide therapy with positive inotropes in septic shock patients

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Introduction: Tissue ischemia and organ failure are considered to be main reasons for the high mortality in septic patients. In the past years therapy of septic shock has changed. The therapeutic goal is no longer a supranormal DO_2 (DO_2 > 600 ml/min/m^2), but the sole therapy of low-output-failure (LOF) with positive inotropes to avoid myocardial ischemia [1,2]. It was investigated whether therapy guided by a myocardial ischemia marker troponin T is superior to the sole LOF therapy or the DO_2 guided therapy [3].
Methods: Thirty septic patients were included (following informed consent of the relatives) in this prospective randomized institutionally approved study. If the patients achieved a DO_2 > 600 ml/min/m^2 by volume replacement alone they were excluded from the study. In case of required catecholamines, they were randomly allocated to three therapeutic groups: DO_2 (> 600 ml/min/m^2); LOF (CI 2.5-3.0 l/min/m^2); troponin T guided; CI > 2.5 l/min/m^2 and DO_2 > 600 ml/min/m^2 until the bedside troponin T test (semiquantitative rapid assay, Boehringer Inc) was positive with consecutive reduction of inotropic therapy to the prepositive level. Measurements were performed three times a day: hemodynamic and oxygen transport related variables, blood sampling, electrocardiogram and in case of no contraindications a transesophageal echocardiography. Statistics: Kruskal-Wallis-test.
Results: Basic patient characteristics did not differ between groups.
Conclusions: The myocardial ischemia marker troponin T differed significantly between groups. In the LOF and troponin T guided group lower maximal troponin T values were observed than in the DO_2 group. The ICU stay was significantly shorter in the troponin T guided group. Whether these results and the in tendency reduced mortality in the LOF and troponin T guided group are associated with these therapies require further investigation.

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P111

Serum lactate: a poor predictor of postoperative mortality in paediatric cardiac surgery

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Critical Care 1997, **1(Suppl 1):**P111

Introduction: Initial serum lactate > 4.5 mmol/l has been found to predict mortality in children following cardiopulmonary bypass for open heart surgery [1]. Since in our experience initial lactate varies widely in both survivors (S) and non-survivors (NS), we hypothesized that persistent hyperlactataemia, or hyperlactataemia in combination with base deficit, might better predict postoperative mortality.
Design: One hundred and ninety-three children, median age 7 months (inter-quartile range 0.5-63 months) were operated on for congenital heart disease over a 1 year period. One hundred and forty-four patients were selected on the basis of surgical complexity. Sequential serum lactates (mmol/l) were measured prospectively at 0, 6, 12, 18 and 24 h. Mean blood pressure, base deficit, bypass time, complications, length of ICU stay and outcome were recorded. Complicated postoperative course was defined as the presence of: seizures; INR/APTT > 3 or AST > 4× normal; and peritoneal or haemodialysis. Data were analysed on 124 patients by Spearman rank correlation, Mann-Whitney and Fisher's exact test. In 19 patients there were insufficient data.
Results: Nine patients died (7.3%) and the postoperative course was complicated in 30 patients (NS and S) by seizures (n = 4), liver dysfunction (n = 16) and dialysis (n = 16).
There was considerable overlap in initial lactate values between the S and NS groups. Initial lactate was significantly (P = 0.0002) elevated in non-survivors (median 8.66, range 1.9-17.6 mmol/l) compared to survivors (median 2.17, range 0.55-13.6 mmol/l), as was lactate at 6, 12, 18 and 24 h. Median 6 h lactate was 5.59 mmol/l in non-survivors (range 2-17.1 mmol/l) and 1.13 mmol/l in survivors (range 0.41-7.42 mmol/l). Twenty-two patients (17.7%) with initial lactate > 4.5 mmol/l survived to discharge. Using ROC analysis, an initial lactate level of 6 mmol/l had the best predictive value for mortality.

Table (abstract P110)

	DO_2		LOF		TropT guided	
Age (years)	59 (37-73)		52 (18-76)		64 (54-75)	
ICU-stay (days)	16 (2-67)		17(3-38)		*12(4-36)	
Mortality	8/10		4/10		5/10	
	Baseline	Max	Baseline	Max	Baseline	Max
APACHE III	66 (48-85)	98 (85-116)	64 (31-105)	80(43-124)	63 (38-97)	95(59-100)
ST-SD (mV)	0.0	1.0	0.0	0.3	0.0	0.5
	(0.0-1.4)	(0.4-2.8)	(0.0-1.7)	(0.0-1.8)	(0.0-1.5)	(0.0-1.5)
TropT (ng/ml)	0.07	*0.43	0.17	*0.30	0.08	*0.12
	(0.05-0.16)	(0.11-7.82)	(0.03-5.93)	(0.06-10.79)	(0.02-0.16)	(0.03-0.17)
TEE (H/D/A)	86/18/5		51/4/2		42/3/1	

Mean (range); frequency: APACHE III (Acute Physiology and Chronic Health Evaluation-score); ST-SD, ST segment depression; Trop T: troponin T test (quantitative ELISA, Boehringer Mannheim Inc); TEE, traneasophageal echocardiography; H, hypokinesis; A, akinesis; *P = 0.05 (between groups).

Table (abstract P111) Predictive value of initial postoperative serum lactate > 6 mmol/l

	Sensitivity	Specificity	PPV	*P* value (Fisher's)
Mortality	78%	83%	32%	0.0003
Complications	50%	90%	68%	< 0.0001

Sequential lactate fell significantly only in survivors (non-parametric ANOVA, $P < 0.001$) but persistent hyperlactatatemia, ie initial and 6 h lactate > 6 mmol/l, predicted mortality with a positive predictive value (PPV) of only 50%. Postoperative lactate correlated poorly with total bypass time ($r = 0.23$) and initial base deficit did not correlate significantly with either bypass time or initial lactate. Indeed, the presence of hyperlactataemia with base deficit, ie initial lactate > 6 mmol/l plus base deficit > 4 mmol/l, predicted mortality with PPV of only 38%.

Conclusion: Initial lactate levels vary widely in both survivors and non-survivors following complex paediatric cardiac surgery and have low predictive value for mortality. Serum lactate determination may be useful in predicting postoperative complications.

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P112

Blood gas and electrolyte analysis in prehospital emergency medicine – first experiences

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Critical Care 2001, **1(Suppl 1):**P112

Background: Oxygenation and ventilation are important factors in the treatment of prehospital emergency patients. With non-invasive methods such as pulse oxymetry and capnometry the ability to obtain reliable measurements assessing oxygenation and ventilation can be limited by abnormal physiologic states commonly seen in emergency patients. In addition optimization of the electrolyte status, especially potassium and ionized calcium is important in the treatment of arrhythmias and cardiac failure. During resuscitation, knowledge of the pH is essential for correcting acidosis by giving bicarbonate.

Methods: Arterial blood was drawn from 21 prehospital emergency patients (age 16 to 90) at the site of the emergency. Blood gases and electrolytes were analysed immediately with three new, portable blood analysing devices ('IRMA', Diametrics).

Results: In 19 of the 21 cases the knowledge of the blood gases, pH and electrolytes was considered to be helpful for the emergency physician. The therapeutic consequences were intubation or the decision that no intubation is necessary, correction of ventilation, puffering with bicarbonate and substitution of electrolytes (potassium, calcium).

Conclusion: There are several indications for the use of a blood analysis in prehospital emergency situations. If we define prehospital emergency medicine as an early intensive care medicine, the knowledge of a few parameters (blood gases, pH, electrolytes, lactate) is essential for diagnosis and therapy.

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P113

Reliability and accuracy of continuous blood gas monitoring

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The current method for blood gas measurement consists of intermittent blood sampling and analysis in a remote laboratory. The drawbacks of this method include the need lor heparinized syringes, wasted blood during sampling and testing, and wasted time due to sample transportation and result reporting. Continuous (in vivo) blood gas (CBG) measurement has the potential to eliminate all these drawbacks. However, its reliability and accuracy need clinical validation. We performed this prospective study to determine whether or not CBG monitoring was reliable and accurate. We hypothesized that the CBG technology was less reliable and less accurate than the laboratory blood gas (LBG) method. Between September and November of 1996, new admissions to the SICU requiring mechanical ventilation were studied. Upon placing an arterial catheter, a CBG sensor (Paratrend-7, Biomedical Sensors, Malvern, Pennsylvania and High Wycombe, England) was calibrated, inserted and connected to a Paratrend blood gas monitor. The patient's subsequent management was guided by the CBG data. Whenever the CBG values were used for therapy, they were also recorded on the data collection sheet. A simultaneous LBG value was also obtained and recorded. Additional data collection included the duration of CBG sensor use, the time saved by CBG monitoring, and problems with the arterial line, CBG sensor, and the laboratory. The results were analysed by descriptive statistics and Student *t* test. A P value of < 0.05 was considered to be significant.

Using 17 CBG sensors in 13 patients, 1478 h of CBG monitoring was carried out. Ninety-six pairs of CBG and LBG values were available for comparison. The mean pH, $PaCO_2$ (Torr) and PaO_2 (Torr) by CBG and LBG measurements were 7.40, 43.1 and 122.6 and 7.41, 41.4 and 120.5, respectively and the differences between them were significant. CBG sensors were placed in the femoral artery in eight patients and four of them required a second sensor. In five patients, CBG sensors were placed through the radial artery. Six of 12 femoral and four of five radial artery sensors had problems with either pH or PaO_2 measurements. The mean durations for the femoral and the radial arterial sensors were 100 + 85(SD) and 56 + 103(SD) h, respectively. CBG monitoring saved 35 min per therapy decision or 50.8 h during the study period.

Conclusion: Continuously measured blood gases are as accurate as the laboratory measured blood gases. They shorten therapeutic decision time. Their reliability can be improved by using the femoral artery for sensor placement.

P114

Continuous arterial blood gas monitoring in pediatric patients: analysis of prolonged monitoring using the Paratrend 7 system

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Introduction: Continuous blood gas monitoring is a new addition to the intensive care unit. The Paratrend 7 contains sensors to measure pH and PCO_2, an electrode to measure PO_2, and a thermistor to measure temperature. The entire apparatus can be placed via a 20 gauge arterial catheter. Because the initial proposed life span of the sensor was 72 h, those children who had it in place greater than this period form the basis of this analysis.

Methods: Patients who had a sensor in place greater than 72 h were identified. Matched values of the arterial blood gas and the sensor were compared for pH, PCO_2, and PO_2 via bias and precision. Variation over time was calculated using partial and Pearson's correlation analysis. If significant drift of the values of the sensor was noted by the clinician, an in vivo calibration was performed.

Results: Twelve patients had the sensor in place for a mean of 138.0 ± 45.4 h (range 74–238 h). The mean age of the children was 7.1 years (range 14 months to 21 years). All but one of the sensors were placed via the femoral artery. The bias/precision values were for pH 0.0034/0.0292, PCO_2 -1.87/6.22, PO_2 1.97/25.0. The Pearson correlation/partial correlation values were for elapsed time for pH 0.963/0.964, PCO_2 0.931/0.931, and for PO_2 0.806/0.8109. There were no complications from prolonged sensor use. All the arterial lines showed adequate blood pressure waveform display and ability to draw blood specimens during the entire life of the sensor. Calibration of the oxygen sensor was performed 14 times, every 54.9 ± 35.7 h.

Conclusion: The Paratrend 7 continuous blood gas monitor can be safely used for as long as 10 days without any complications. For pH and PCO_2 no degradation in accuracy is noted over this time period. The accuracy of the oxygen sensor should be confirmed every 24–36 h via comparison to the arterial blood gas value.

P115

Air bubbles and co-oximetry — a pilot study

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Introduction: The pre-analytical error potential of air bubbles contaminating blood gas samples has been well recognized for blood gas tension and pH measurements [1], and is thus considered in present recommendations for blood gas sample handling [2]. The effect of air contamination on the oxygen saturation of haemoglobin (HbO), measured by co-oximetry, has however, scarcely been appreciated [1]. With increased reliance on directly measured HbO for the evaluation of blood oxygen content [3,4], a closer look at possible errors of this parameter is warranted. This study was undertaken to estimate the early effect of graded air contamination in conditions simulating pre-analytical sample handling in clinical practice.
Methods: A. Serial analyses (blood gases/co-oximetric saturation, ABL505 +OSM3, Radiometer Medical AS, Denmark) of fresh heparinized venous or arterialized venous blood from three study participants. Blood was drawn as batches (one batch per series), divided into graded aliquots in blood gas samplers, immediately capped with or without the inclusion of air corresponding to the syringe tip dead space (approx 0.05 ml), and analysed consecutively for 25 min following capping and storage in various conditions (table). All first samples were analysed immediately for reference; all samples were agitated for 10 s immediately before analysis.
B. Screening of arterial blood samples, referred to the ICU for analysis, for air bubbles. If present, bubble volume and air volume fraction (ie of total sample volume) was measured (as plunger displacement) on evacuating the bubble before analysis.
Results: A. Twenty-eight series (n = 7) from each participant were analysed. Reference HbO was (mean ± SD) 0.55 ± 0.10 for venous and 0.92 ± 0.03 for arterialized venous samples. Air contamination regularly (although unpredictably) increased measured HbO within minutes after preparation; apparently, errors increased as a function of haemoglobin oxygen affinity, storage temperature, air volume fraction and sample agitation (Fig). Compared to changes in HbO. Changes in pH and blood gas tensions were small. The limited number of data for each series and the wide spread of HbO values, particularly in venous samples, precludes closer statistical analysis.
B. When present (n = 14), air bubbles had a volume of (median/IQR/range) 45/40–111/23–398 mm^3 constituting a volume fraction of 7.2/3.8 15.4 /2.9 33.8%.
Conclusion: Present recommendations for pre-analytical blood gas sample handling may be inadequate in relation to co-oximetry. The error potential of air contamination on measured HbO in hypoxaemic blood appears much greater than errors on gas tensions and should be respected when evaluating such samples (eg mixed venous, or possibly hypoxaemic arterial samples). Optimally (ie concerning HbO), samples with subatmospheric oxygen tensions should be immediately purged of all air, stored on ice and analysed as soon as possible; improvements in blood gas samplers to minimize air trapping and facilitate purging of air might be worthwhile. Further systematic studies are ongoing.

Table (abstract P115) Scheme of analysis series

Blood volume (air volume fraction)	2.0 ml (0%)	0.5 ml (10%)	1.0 ml (5%)	2.0 ml (2.5%)	3.0 ml (1.7%)
Iced storage, undisturbed	+	+	+	+	+
Room temperature storage, undisturbed	+	+	+	+	+
Room temperature storage, agitated	0	+	+	+	+

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P116

Does the SUPPORT study of the effectiveness of right heart catheterization represent all patients who receive pulmonary artery catheters?

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Objective: To review the pulmonary artery catheter (PAG) use, examining mortality, SICU length of stay, and demographics of patients with and without PACs in comparison to those of the recent SUPPORT study on right heart catheterization effectiveness [1].
Design: Retrospective analysis of data extracted from a comprehensive database archived from a computerized ICU clinical record.
Setting: Surgical intensive care unit (SICU) of a tertiary university medical center.
Subjects: All SICU patients admitted over a 5 month period (June–October 1996).
Results: During the period under analysis, 554 patients were admitted to the SICU. Fifty-seven percent were male and 43% were female. The average age was 56 (range 16–100). Of the 554 patients, 141 patients received 202 PACs (25% of admissions). Fifty-eight of these patients were trauma patients, most of whom did not have ARDS or MOSF. This is in contrast to SUPPORT trauma patients, in whom the presence of ARDS or MOSF was a requirement for study entry [2]. The average duration of PAC insertion was 2.6 days (range 0–11.7 days). The average SICU length of stay (LOS) was 8.9 ± 11.6 (median = 4) days (range 0–66 days). This compares favorably with both the SUPPORT PAC patients (mean ICU LOS = 14.8 days, 25th percentile = 5 days, median = 9 days) and the SUPPORT non-PAC patients (mean ICU LOS = 13 days, 25th percentile = 4 days, median = 7 days). Forty-seven of the 554 patients died in the SICU (overall mortality 8.5%), but 26 of the 141 SICU PAC patients died (18.4%). Yet this compares quite favorably with not only the SUPPORT PAC patients (37.5%, 30-day mortality, $P < 0.00001$ by χ^2 analysis) but even the SUPPORT non-PAC patients (32.8% 30-day mortality, $P < 0.001$). Indeed, the difference in mortality between the SICU PAC patients and either SUPPORT group (PAC or non-PAC) was greater than the reported minor difference in mortalities between the PAC and non-PAC SUPPORT patients.
Conclusion: The recent SUPPORT study of the effectiveness of right heart catheterization purports to demonstrate an adverse outcome in patients in whom PACs were used. However, the original SUPPORT study population consisted of critically ill patients, most of whom had at least one established organ failure, and the use of PACs in acutely injured burn and trauma patients was specifically excluded. The better outcomes in our SICU PAC patients (even better than the SUPPORT non-PAC patients) could result from an intrinsically better prognosis due to lower acuities or from the proactive use of PAGs to forestall the onset of organ failures. A well conducted randomized, controlled clinical trial of PAC use in all ICU patients is clearly warranted. In the interim, we emphasize that it appears that the SUPPORT study does not represent PAC effectiveness in all ICU patients.

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P117

Hemodynamic effects of kinetic therapy in critically ill trauma patients

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Background and objectives: The application of the pulmonary artery catheter (PAC) has been well established in the treatment of haemodynamic

unstable patients in the last 20 years. A new variation of the PAC is available now. These systems use the thermodilution with heat for the calculation of the cardiac output and are able to generate out of these data a continuous cardiac output curve. The computed data which can be visualised on a monitor, provide the surgeon with an 'on-line' monitoring of this important haemodynamic parameter. The fluid and drug management of the polytrauma patient in the initial trauma phases could be one of the fields in ICU therapy where by this new device may be beneficial.

Methods: To evaluate the diagnostic and therapeutic impact of the continuous cardiac output (CCO) measurement for the haemodynamic unstable polytrauma patient we initiated a prospective pilot study. The Baxter Vigilance System was used for measuring the continuous cardiac output. Patients were scored on the first day for Injury Severity Score (ISS) and APACHE II. The CCO was used no later than 5 h after the initial treatment in 10 polytrauma patients. The CCO values were controlled three times a day by the conventional 'cold' thermodilution technique. Continuous SVO_2 measurement was carried out in addition. As outcome parameters were chosen days on ventilation, days on the ICU and days in hospital. The results were compared with the same parameters evaluated of 50 polytrauma patients who were not treated by the CCO method on the same ICU unit. The treating ICU physicians were asked in a standardised questionnaire whether or not there was an impact of the CCO measurement on their therapy.

Results: Group I represents the CCO patients (n = 10), group II the control group without CCO monitoring (n = 50). The mean age of group I was 42 years, of group II, 29 years. Mean ISS: group I, 50; group II, 38. Mean APACHE II: group I, 17.5; group II, 14. Mean days on ventilation: group I, 10; group II, 7. Mean days on ICU: group I, 18; group II, 8.5. Mean time in hospital (days): group I, 24: group II, 19.5. In group I, two patients (20%), in group II, six patients (12%) died during their stay in hospital. The catheter was in use for a mean time of 3 days (2–20). Seven different surgeons were working with the system. The unique opinion was that the CCO device had a significant impact on their decision making in the fluid or drug management of the study patients.

Conclusion: Even regarding the greater severity of illness in group I it is still too early to state that the use of the CCO measurement can reduce the mortality in polytrauma patients. Our first experience, however, suggests that these devices may become an important improvement in the management of haemodynamics in the early trauma phases. We are now working out a more extensive prospective study to prove the assumption.

P118

Can clinicians reliably estimate cardiac output in children?

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Background and objectives: The acquisition of a reliable, repeatable, relatively non-invasive method for measuring cardiac output (CO) and hence cardiac index (CI) in children remains elusive. Because of this many clinicians involved in the provision of paediatric intensive care tend to rely on clinical and basic haemodynamic parameters when caring for the critically ill child. At our institution, we routinely use femoral artery thermodilution to measure cardiac output in critically ill children. We wished to evaluate different clinicians' abilities to estimate CI in children and to see if estimates improved with time when results of objective measurements were known.

Patients and methods: One hundred and twelve estimates of CI were made by 27 clinicians on 36 patients, median age 34.5 months (interquartile range 4.8–90.8 months). Clinicians originated from a variety of paediatric sub-specialities, including intensive care, cardiology and anaesthetics, and ranged from consultant to senior house officer (SHO) level. Before estimating cardiac index, clinicians were exposed to all clinical and laboratory data available on the patients, and were allowed to make a physical examination. They were initially asked to estimate the category of cardiac index (high ≥ 5 l/min/m^2, high-normal 4.0–4.9, low-normal 3.0–3.9 and low < 3.0), and then the absolute value. Concurrently, five consecutive measurements were made, and then averaged using femoral artery thermodilution (COLD® Z-021, Pulsion Medical Systems, Munich). One clinician, who made all thermodilution measurements, estimated CI prior to measurement. This was to test if positive feedback improved estimation ability over time.

Results: Measured CI ranged from 1.39-6.84 l/min/m^2. Overall, there was poor correlation between absolute measured and estimated CI (r = 0.24). There were slight differences between levels of seniority and accuracy of estimation: Consultants r = 0.19; Fellows r = 0.38; SHOs r = 0.04. For categorical estimation of CI, the kappa statistic was 0.09 and weighted kappa 0.169, both indicate a poor strength of agreement. Furthermore, the clinician who was aware of previous CI measurements showed no improvement in his ability to estimate CI with time.

Conclusion: Clinical estimation of cardiac output is unreliable in paediatric practice. This unreliability is spread across disciplines and levels of seniority.

P119

A comparison of bioimpedance and continuous thermodilution measurement of cardiac output in ICU patients

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Objective: Bolus thermodilution is the standard bedside method of cardiac output measurement in the ICU. The Vigilance monitor (Baxter Healthcare Corporation) uses a modified thermodilution pulmonary artery catheter with a thermal filament (CCO/SvO_2/VIP Catheter model 746H8F) to give a continuous readout of cardiac output. This has been shown to correlate well with the gold standard dye dilution method with a mean difference of -0.01 and r^2 = 0.97 [1].

Bioimpedance cardiography using the NCCOM 3 monitor (Bomed Medical Mfg Ltd) offers a non-invasive means of continuous cardiac output measurement and has shown reasonable correlation with the bolus thermodilution method.

However, it is difficult to ensure contemporaneous measurement when comparing the continuous bioimpedance method with the intermittent bolus thermodilution method. We therefore investigated the agreement between the continuous bioimpedance and continuous thermodilution methods, thereby enabling simultaneous measurements of the two techniques.

Design: Prospective observational study.

Subjects: Seven patients requiring pulmonary artery catheterisation for cardiac output monitoring on the General ICU.

Methods: A continuous thermodilution pulmonary artery catheter was inserted into each patient and the bioimpedance electrodes were applied. Each patient was monitored for study purposes for approximately 6 h, with acquisition of simultaneous paired cardiac index (CI) data at 1 min intervals.

Results: A total of 2390 paired data points were analysed on SPSS for Windows 3.1 and a Bland-Altman plot [2] was constructed. There was poor correlation (r^2 = 0.0107) between the two methods of cardiac output measurement. The mean of the differences was -0.161 with a standard deviation of 1.158.

Conclusion: The NCCOM 3 bioimpedance monitor gives poor agreement with the well validated Vigilance continuous thermodilution monitor in a mixed group of General ICU patients and therefore the bioimpedance method cannot be recommended tor cardiac output monitoring in this situation.

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P120

A comparison of central venous pressure (CVP) in the superior vena cava and common iliac vein in critically ill patients

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Introduction: The measurement of CVP via the femoral route using a long catheter placed, under electrocardiographic guidance, in the inferior vena cava, close to the right atrium has been shown to accurately reflect superior

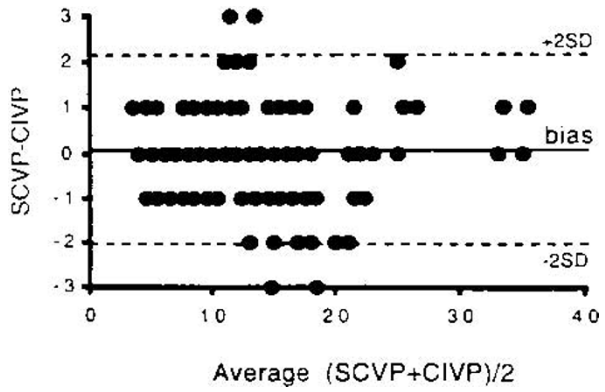

Figure (abstract P120)

vena cava pressure (SVCP) in critically ill adults [1]. We assessed the possibility of using widely available and more easily placed short catheters (15-20 cm in length), placed via the femoral route, to measure CVP.

Objective: To compare common iliac venous pressure (CIVP) with SVCP in critically ill mechanically ventilated patients. To document the effect of PEEP, mean airway pressure (MAP) and intra-abdominal pressure (IAP) on the difference between CIVP and CSVP.

Design: Randomised, blinded comparison. Twenty consecutive ICU patients requiring femoral catheterisation.

Methods: Pressure recorded from the femoral catheter (CIVP) was compared with pressure from the internal jugular or subclavian central venous catheter (SVCP). Correct position was confirmed by radiograph. Random order, simultaneous measurements of CSVP and CIVP were made in a blind fashion at hourly intervals for 6 h. PEEP, MAP and IAP were measured at the same time intervals.

Results: One hundred and forty pairs of measurements in 20 patients were compared. Paired measurements of CSVP and CIVP were compared using the method of Bland and Altman (Fig). The bias was 0.1 mmHg (95% CI 0.1 mmHg). The differences were distributed around the mean with a standard deviation of 1.1 mmHg. The limits of agreement are therefore 2.2 mmHg above or below the mean value (95% CI 0.2 mmHg). The effect of PEEP, MAP and IAP was assessed by comparing each parameter with the difference between CSVP and CIVP. Regression analysis showed no difference between CSVP and CIVP with increasing PEEP, MAP or IAP.

Conclusion: For clinical purposes CVP measured in the common iliac vein can replace standard intrathoracic CVP measurements in mechanically ventilated patients.

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P121

Measurements of mean systemic filling pressure in normal subjects during general anesthesia

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Mean systemic filling pressure (Psf) is identified as the equilibrium pressure in the systemic circulation when the blood flow is zero. Psf might be an index of the effective filling of the circulatory system [1,2]. Aim of this study was to test a simple method to measure Psf in a population of anesthetized patients under conditions of intact circulation and during mechanical ventilation. Modeling the systemic circulation as a pipe of constant resistance we have assumed the venous return (Qv) to be proportional to the difference between arterial pressure (Pa) and central venous pressure (Pcv). According to Guyton's venous return equation: Qv = (Psf-Pcv)/Rsf. Rsf.d. is the resistance downstream to the site in the circulation where blood pressure is equal to Psf. For the systemic flow, Qs = (Pa–Psf)/Rsf.u (where Qs is the cardiac output and Rsf.u is the resistance upstream). Since Qv = Qs, then Pa = Psf+(1+Rsf.u/Rsf.d)-(Rsf.u/Rsf.d) × Pcv. If Rsf.u. Rsf.d and Psf are constant [2], then Pa is linearly related to Pcv, and Psf can be computed from the regression line Pa versus Pcv, at Pa = Pcv. In eight patients undergoing elective surgery (ASA I-II, weight 68.8 ± 12 kg, age 59.5 ± 14 years), with no previous history of cardiovascular and pulmonary diseases, anesthesia was induced by pentobarbital and maintained with isofluorane (0.4%) and nitrous oxide, while neuromuscular blocking agents were atracurium or pancuronium bromide. The averaged hemodynamic baseline was: HR 85.2 ± 21.6 bpm; Pa 84.6 ± 13.8 mmHg: Pcv 5.26 ± 2.08 mmHg. Airway pressure, flow, Pa and Pcv traces were simultaneously measured, recorded and digitalized on a data acquisition system (Colligo, Elekton, Italy). In order to induce changes in Pcv and consequently in Qv, at least five end inspiratory pauses (IP) were performed after inflation of different tidal volumes (Vt), applied in a random order. The Vt ranged from 8.2 ± 2 ml/kg to 26.0 ± 10 ml/kg. We have measured the fall in Pa and the rise in Pcv caused by IP. At each step Pcv and Pa were measured during the IP, when the fall in Pa reached a plateau, ie after a mean time of 9.1 ± 3.7 s.

Results: (i) In each patient, as shown in the graph, we found a linear relation between Pcv and mean Pa (average R was: 0.93 ± 0.06). (ii) Average Psf was 19.21 ± 3.54 mmHg.

Conclusions: In the anesthetized patients we found a linear relation between Pa and Pcv during the inspiratory hold as in previous laboratory studies, where the Psf measurements were validated utilizing standard venous return curve [2]. Therefore, we conclude that this method is a reliable technique to estimate mean systemic filling pressure.

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P122

Epinephrine application via a conventional endotracheal airway and via the Combitube™ in esophageal position in an animal model

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Background: Early administration of epinephrine plays an essential role in the management of cardiac arrest patients. A new emergency airway, the Esophageal Tracheal Combitube™, provides rapid airway management when endotracheal intubation is not possible. The aim of our study was to compare plasma concentrations and the cardiovascular effects of epinephrine after application via a conventional endotracheal airway and via the esophageal lumen of the Combitube™.

Methods: Fourteen juvenile swine were randomly assigned to two subgroups: group A received an endotracheal tube, group B a Combitube™ in esophageal position. In part I of the study, epinephrine (group A, 0.05 mg/kg; group B, 0.5 mg/kg) was administered via the respective tube during spontaneous beating of the heart. In part II, 3 min after induction of ventricular fibrillation, CPR was started and 5 min later epinephrine (group A, 0.1 mg/kg; group B, 1.0 mg/kg) was administered. Plasma epinephrine levels were measured 1, 2, 3, 5, 7, 10, 15 and 30 min after application. Systolic arterial pressure and cardiac output in part I, and $ETCO_2$ and coronary perfusion pressure in part II were recorded.

Results: In part I increased levels of plasma epinephrine and systolic arterial pressure were maintained significantly longer in group B when compared to group A. In part II, no significant differences between the groups were found with regard to plasma epinephrine levels and hemodynamic parameters.

Conclusion: Epinephrine applied via the esophageal lumen of the Combitube™ in a 10-fold higher dosage than recommended for endotracheal application has similar effects on plasma epinephrine levels and hemodynamic parameters compared to endotracheal administration. The prolonged intensive care support delivered also to patients with apparent poor prognosis in the first days allows to partially overcome the frequent criticism that early withdrawal of treatment results in a self-fulfilling prophesy of poor outcome. In fact, at day 7 patients with

better prognosis have been already clearly identified, while in C-patients, in spite of some CNS functions improvement (respiration, brain stem reflexes), the outcome remained the same as earlier predicted.

P123

Mechanism of blood-flow promotion during thoraco-abdominal compression-decompression CPR and standard CPR in man - preliminary results

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Background: CPR with thoraco-abdominal compression-decompression (TACD) enhances coronary perfusion and resuscitability in animal studies.
Aim of the study: To observe aortic pressure (AoP), right aterial pressure (RAP) and mitral valve ((MV) position during CPR with a new, manually operated device to administer TACD in order to detect the operative mechanism of blood flow promotion and compare it to standard CPR (sCPR) with a mechanical device (Thumper®).
Methods: Included were 11 adult patients with witnessed cardiac arrest brought to the emergency department under chest compressions. Arterial and venous catheters were placed to monitor AoP and RAP continuously, the MV was visualized by transesophageal echocardiography (TEE). RAP < AoP in the compression phase indicates that blood-flow promotion is most likely due to cardiac pump, if RAP = AoP in the compression phase chest pump is most likely operative [1].
Results: In all patients TEE was performed during TACD-CPR and in four patients during both sCPR and TACD-CPR. In 10 patients catheters could be placed. For MV position and the relation between AoP and RAP in the compression phase see the table.
Conclusions: It appears that in both sCPR and TACD-CPR, the prevailing mechanism of blood-flow promotion is by means of thoracic pump. The MV-position during the compression phase of CPR cannot be used to differentiate between thoracic or cardiac pump mechanism.

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P124

Outcome prediction in patients after out-of-hospital cardiac arrest cannot be improved by prolonging observation

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Neurologic prognosis after out-of-hospital cardiac arrest has important implications for delivery of intensive care, with the aim to assure the best opportunities for recovery without prolonging futile treatment. The prognostic value of several neurologic signs has already been assessed in previous studies [1,2]. A too short period of full active treatment is, however, frequently reported as a possible important limitation of many study designs.
We investigated in a retrospective study outcome predictors for post-anoxic coma; all patients had homogeneous and complete treatment for at least 7 days. Only patients aged 18-80 years, admitted with post-anoxic coma without concomitant neurologic disorders, and who survived at least 24 h were included. At a follow up examination 6 months or more after ICU admission, the 23 patients were assigned to three outcome groups; almost complete neurologic recovery (A); moderate-severe disability (B); dead without regaining consciousness-vegetative state (C). In this analysis the outcome groups A (six patients) and B (five patients) are considered together and compared to patients of group C (12 patients).
Routinely performed neurologic tests, known to be potential outcome predictors were collected at four different times: at 6 h after successful CPR (T0), at 24 h (T1), on the 3rd day (T2) and on the 7th day (T3). Sensitivity

Table (abstract P124)

	T0	T1	T2	T3
GCS > 4				
TCC (%)	69	78	78	82
Sensitivity (%)	73	100	100	100
Specificity (%)	67	58	58	64
Motor response to pain				
TCC (%)	60	87	78	77
Sensitivity (%)	56	100	100	100
Specificity (%)	64	75	58	55
Spontaneous motility				
TCC (%)	61	83	83	83
Sensitivity (%)	45	73	91	100
Specificity (%)	75	92	75	67
Seizures				
TCC (%)	59	83	74	83
Sensitivity (%)	30	0	0	0
Specificity (%)	50	67	50	67
Cranial nerve reflexes				
TCC (%)	75	62	61	57
Sensitivity (%)	100	90	100	100
Specificity (%)	44	30	25	10

Table (abstract P123)

	Standard CPR (compression phase)			TACD-CPR (compression phase)		
Patient no	MV position	RAP-AoP relation	Blood flow pump	MV position	RAP-AoP relation	Blood flow pump
1	-	RAP = AoP	Thoracic	Closed	RAP = AoP	Thoracic
2	-	-	-	Open	-	-
3	Open	RAP = AoP	Thoracic	Closed	RAP = AoP	Thoracic
4	-	RAP = AoP	Thoracic	Closed	RAP < AoP	Cardiac
5	-	RAP = AoP	Thoracic	Open	RAP = AoP	Thoracic
6	-	RAP = AoP	Thoracic	Closed	RAP = AoP	Thoracic
7	-	RAP = AoP	Thoracic	Closed	RAP = AoP	Thoracic
8	-	RAP = AoP	Thoracic	Closed	RAP = AoP	Thoracic
9	Closed	RAP = AoP	Thoracic	Closed	RAP = AoP	Thoracic
10	Open	RAP = AoP	Thoracic	Open	RAP = AoP	Thoracic
11	Closed	RAP < AoP	Cardiac	Closed	RAP < AoP	Cardiac

and specificity of each test in predicting a good outcome and total correct classifications (TCC = efficiency of prediction) are reported in the table.
Consistent with the results of previous investigations [1] our results show that: (i) it is mostly impossible to state a correct prognosis from a very early evaluation (T0); (ii) data reported at 72 h support the prognosis obtained at 24 h without adding any new information. The single best predictor of good outcome is motor response to pain, also GCS > 4 is a good predictor, but with lower specificity. Conversely the persistence of seizures is associated in all cases with poor prognosis.
The prolonged intensive care support delivered also to patients with apparent poor prognosis in the first days allows to partially overcome the frequent criticism that early withdrawal of treatment results in a self-fulfilling prophesy of poor outcome. In fact, at day 7 patients with better prognosis have been already clearly identified, while in C-patients, in spite of some CNS functions improvement (respiration, brain stem reflexes), the outcome remained the same as earlier predicted.

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P125

Withdrawal of ventilation from the dying child

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Objectives: To document the beliefs and practices of UK paediatric intensive care (PICU) consultant medical staff in withdrawing ventilatory support from children who are terminally ill, but not brain-dead. Whilst all dying children should be treated individually, there is little in the literature to guide doctors in the manner and sequence in which ventilation should be discontinued [1]. Better understanding of current clinical practice may help formulate a rational and compassionate approach to withdrawal of ventilation.
Design: Questionnaires were posted to ninety-three consultants involved in the day-to-day management of children in 19 paediatric and 14 mixed adult/paediatric intensive care units in the UK. Questions related specifically to the withdrawal of ventilatory support from dying children beyond the neonatal age-group (1 month to 16 years). There were 73 respondents (78%).
Results: Thirty-one (42%) respondents preferred extubation to terminal weaning, including nine (12%) who continue paralysis during extubation. Of the latter group, four were paediatricians, and six had withdrawn ventilation from five or more dying children in the last year. Twenty-four (33%) respondents preferred terminal weaning, 14 of whom decreased the FiO_2 as the first step. Consultants who graduated after 1980 were no more likely to practice extubation than their older colleagues ($P = 0.78$, Fisher's exact test). Eighteen respondents (25%) gave no preference. Thirty-six (49%) used a higher than standard dose of sedative during the process of withdrawal.
Conclusion: Once a consensus has been reached that death is inevitable, and that further prolongation of life is not only futile but intolerable, then the principal concern of the doctor should be the comfort of the child and family. Withdrawal of ventilation should be carried out with dignity, humanity, and concluded as rapidly as possible. Extubation was the preferred method of withdrawal in our survey, with a significant minority of respondents who continue paralysis.

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P126

Cost-effectiveness of a paediatric retrieval service

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Introduction: Paediatric intensive care is expensive and accounts for a large share of inpatient expenditure. Recently, it has been claimed that not only is transfer of critically ill children best performed by specialist paediatric retrieval services (PRS) [1,] but the use of such services should reduce the health care costs of these patients [2]. We report the effect a PRS has had on cost-effectiveness within the PICU, specifically: the median cost per survivor (CPS) and non-survivor (CPNS) and the effective cost per survivor (ECPS) within defined mortality risk intervals. Predicted mortality was calculated from the patients admission PRISM score, for both retrieved (R) and non-retrieved (NR) patients during the period 1 January 1994-31 December 1995. ECPS was determined by summing the total costs incurred within each mortality risk interval and dividing the sum by the total number of survivors.

Table (abstract P126)

	Non-retrievals (n = 88)				Retrievals (n = 255)			
Mortality risk intervals	$N^0/(^*)$	CPS	CPNS	ECPS	$N^0/(^*)$	CPS	CPNS	ECPS
<1%	17/0	1526	N/A	2220	47/0	1757	N/A	3252
1-5%	40/1	2248	5577	3352	99/0	2433	N/A	4486
5-15%	12/0	2759	N/A	3130	62/6	3905	5015	5870
15-30%	6/1	4434	4930	7657	23/5	3019	3143	6180
>30%	13/6	3956	4390	8114	24/10	4293	3145	14,544

Patients and methods: Guy's Hospital has a 120 bedded children's hospital, with 16 PICU beds. Each retrieval team incorporates two doctors, the lead clinician being either a Consultant or Fellow together with a resident, and one nurse. Since January 1995, the unit has had the ability to run two PRS simultaneously.
Results: The table shows the median costs incurred for CPS and CPNS. The ECPS is also given. All costs are in pounds Sterling (£). Costs were allocated from the use of patient TISS points. The value of a TISS point in 1994 and 1995 was £34.70 and £33.80 pounds, respectively. N^0 records the number of patients within each mortality risk interval and (*) denotes deaths.
The mean predicted risk, the standardised mortality ratios (all less than 1) and the median length of PICU stay (days) for NR versus R patients were not significantly different within comparable mortality risk intervals (data not shown).
Conclusion: We can find no supportive evidence to show that surviving patients retrieved by specialist staff do indeed have reduced health care costs; to the contrary the trend is towards them being more costly.

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P127

SPARC: an integrated prehospital and hospital resuscitation tool to aid in the immediate care of sick and injured children

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Background: Accurate selection and calculation of drug dosage in treating sick or injured children is often difficult as it depends on estimating the weight of the child. A device has been developed to remove calculation errors and use of inappropriate drugs.
Aim: Validation of the SPARC* system for the resuscitation of children.
Participants: Eighty-nine clinicians of all grades in the three specialties dealing with paediatric emergencies (A&E medicine, paediatricians and anaesthetists).
Settings: Four hospitals in the north east of England.
Method: Each participant was given two paediatric resuscitation scenarios (septic fitting child and a cardiac arrest from tricyclic poisoning). A series of treatment related randomised questions were given. For each question the weight of the child was provided. The participants were offered the device to aid in dosage selection.
Measurements: Time to response/accuracy of response/ previous experience/use or otherwise of the device/previous resuscitation training.

Results: Junior staff using this device, without previous experience or training were accurate in treatment suggestions. There was no significant difference in response time between those middle grades with experience and training and untrained, new SHOs.
Conclusion: This study suggests that inexperienced doctors without previous training using SPARC will be able to initiate critical interventions rapidly and accurately before the arrival of more senior staff. This device removes inaccurate weight estimation. It hastens response time to critical events. Our impression of this device is that it is a useful addition to emergency care involving drug therapy.
*SPARC: Standard Paediatric Aid to Resuscitation Cards: a series of A4 cards (with identical layout) list the drug dosage and sequence of drugs for the emergencies in childhood that demand immediate specific treatment. This is accompanied by a weight estimation tape which has previously been validated.

P128

Are paediatric submersion incidents preventable?

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Background: Because drowning is one of the leading causes of accidental death in children in civilized countries, we have studied the epidemiology and the preventability of severe submersion incidents in Finland.
Patients: A 10-year retrospective study of all the victims of severe submersion incident under 16 years of age who either required admission to the paediatric intensive care unit (PICU) or died in the Province of Uusimaa.
Results: Of the 62 submersion victims 16 were female and 46 were male. Their ages ranged from 0 to 15 years and the median was 3.7 years. Fifteen patients were declared dead at scene without CPR. Five of the 24 patients in whom CPR was initiated had intact survival. Altogether 28 survivors had good neurological outcome and two had severe disability. Thirty-one patients died during the first 24 h and one died later. The annual rate of drownings per 100,000 persons under 16 years of age was 1.3. Seventy-seven per cent of the submersion incidents took place when children were left without adult supervision for a moment or children were playing themselves close to a waterway or in water. Seventy-one per cent of all submersion incidents occurred in freshwater bodies, 21% in swimming pools or baths and 8% in other places. The cause of submersion incident was a fall into water in 31, swimming or bathing in 15, a fall through ice in six, a homicide committed by child's own mother in five, negligence in three and miscellaneous in two cases.
Discussion: Our results show that many of these submersion incidents could have been prevented by not leaving infants or toddlers without adult supervision even for a brief period in water or close to bodies of water. Earlier recognition of mother's need for psychiatric care and keeping children away from thin ice could have also prevented few incidents.
Conclusion: The probability of intact survival of nearly drowned children receiving CPR was not better than 21%. Because most of the submersion incidents appear to be preventable, investment in prevention programs would probably be the best and cheapest way to reduce mortality in paediatric submersion incidents.

P129

Emergency medical hypnosis: a useful adjunct in the suturing of children

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Background: Analgesia, anaesthesia and sedation have all been used singly and in combination for the suturing of children's minor lacerations in the emergency room. Failure of such techniques often result in a child receiving further distress and potential risk of a general anaesthetic. Alternative techniques including music, fairy tales and play therapy have been used to help district children during such procedures. Hypnosis (formal medical relaxation: FMR) has been reported anecdotally to be successful but no prospective randomised trials have been published. If hypothesis is successful the child will remain calm content and immobile without restraint throughout the procedure resulting in complete compliance and successful closure of wounds in the ER.
Aim: To assess the efficacy of FMR on children requiring suturing of wounds in the emergency room.
Population: Fifty children aged between 5–12 with wounds requiring suture.
Exclusions: any child with: head injury; depressed level of consciousness; on epileptic or other neuropharmaeological drugs; need for opiate analgesia.
Setting: An urban paediatric ER which sees more than 25,000 children per year.
Method: Children randomised into two groups: *Control*: Wounds sutured in the standard manner (warm 2% lignocaine, paediatric nurse and parents in attendance. Emergency medicine resident suturing). *Experimental*: The standard manner and formal medical relaxation. The experimental group was sutured by the chief resident (senior registrar).
Measurements: Behavioural (CHEOPS) and Visual Analogue Scales were used prior to, during and post-procedure to assess level of activity.
Results: The CHEOPS score fell during the procedure where FMR was employed in over 75% of cases. Children and parent satisfaction was recorded as higher in the FMR group. Further results to follow.
Conclusion: This pilot study in the use of hypnosis in the ER has been shown to be statistically significant. To further validate it, a double blind trial will be required.

P130

Sudden increase in ICU-mortality rate: a look behind the stage applying continuous quality improvement

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Continuous quality improvement (CQI) implies regular evaluation of and reaction to a variety of parameters (`indicators'). We examined 238 consecutive patients admitted to our newly chaired 8-bed medical ICU in 1995 in terms of severity of organ failure at admission, mortality rate (MR %), and the relation of ventilator therapy (VD) for survivors (S) versus non-survivors (N), and compared the results with our patients of 1994 (n = 215) as well as, prospectively, with all consecutive patients of 1996.
Results: See table.
ICU-MR as well as the VD for non-survivors increased (31% to 56%) during 1995. In search for the cause of this finding the incidence of three- and four-organ failure at admission was found to be elevated. These effects were reversible during the first 9 months of 1996.
Conclusions: (i) The increase in MR was due to a significant change in case mix (more frequent admission of patients with late-stage-MOF including liver failure and extremely poor prognosis) during 1995 rather than to improper therapeutic skills of personnel. (ii) This increased long-term supply of life-support (VD) for patients with poor prognosis. (iii) Revision of admission policy and information campaigns referring to manage organ failure in earlier stages were able to reverse our efficiency to the original extent.

Table (abstract P130)

	ICU-MR		MOF (0-4 organ failure)		Ventilator days (VD)	
	S	N	0-2	3-4	S	N
1994	161	54 (25%)†	178	37 (17%)†	1039	469 (31%)†
1995	149	89 (37%)*	176	62 (26%)*	722	927 (56%)*
1996	123	46 (27%)	122	47 (28%)*	544	356 (40%)*†

Chi square, Bonferroni-Holm corrected; $^{*}P < 0.05$ versus 1994, $^{\dagger}P < 0.05$ versus 1995.

P131

Social and hygienic characteristics of sudden mortality among rural population of South Ural with low density of settlement

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The problem of sudden mortality is a very complex topic of emergency medicine. The aim of this study was to evaluate the reasons of sudden death among rural population of South Ural with rare settlement. The obtained data were verified by conventional statistical methods. Males of following age groups predominated: 30–39, 40–49, 50–59 and 60–69 years (81.3% of men suddenly died). In addition, a group of boys died before 1 year was stood out (7.1%). More older groups (40–49, 50–59, 60–69, 70 and older) were demonstrated among equivalent women population (74.4%). A portion of girls suddenly died before 1 year was 13.5% ($P < 0.01$). Thus, men of able-bodied age (30–39 years) had a higher risk of sudden death than women of the same age. On the contrary, sudden death occurred with a higher rate among females between 50–70 years old. Cardiovascular disorders led to sudden death in 81.2% of cases among males versus 73.7% among females ($P < 0.05$). Mortality due to respiratory diseases was 13.5% in women and 8.9% in men, respectively. Digestive disorders were revealed in 4.29% of males versus 3.3% of females ($P < 0.05$). Perinatal pathology resulted in sudden death in 3.38% of females and in 1.27% of males. Infectious and parasitic diseases as a cause of death were less prevalent in the female population (1.27%). Females with urogenital disorders, pregnancy and labor complications developed this state in 4.4%. These data suggest that sudden death among rural population mainly results from cardiovascular and respiratory diseases.

P132

Aggressive treatment, outcome and long time neurologic and pulmonary complications of lethal hydrogen sulphide (H_2S) intoxication

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Introduction: Hydrogen sulphide poisoning can occur in industrial/occupational (oil refining, viscose rayon manufacturing, vulcanization of rubber, hydrochloric acid in farm wells, leather industry, sewage cleaning, roofing asphalt tanks, etc), recreational (cleaning of hot spring reservoirs, caves, sulfur springs, etc), or hospital (plaster of Paris, etc) settings. The first reports date from the 17th century where city sewage cleaners were found dead in the vicinity of the sewers. At a concentration of 0–25 ppm H_2S has a specific odour of rotten eggs. This odour is an unreliable marker since at higher concentrations (> 100 ppm) the gas rapidly causes paralysis of (the olfactory system resulting in anosmia. At concentrations > 50 ppm symptoms are characterized by mucositis (conjunctivitis, upper airway irritation), nausea and dizziness, at > 200 ppm pulmonary edema can occur, at > 500 ppm neurologic problems arise (agitation, seizures followed by coma), at > 1000 ppm sudden death can occur. Main target organs are the central nervous system (CNS) and the respiratory system. Acute high dose intoxication mainly results in CNS problems whereas chronic lower dose intoxication results in acute lung injury (ALI) or acute pulmonary edema, the latter carrying a worse prognosis. There is still a great controversy in the literature about the best treatment and little is known about long time CNS and pulmonary complications in survivors.
Patients and methods: Five male patients, mean age 39 ± 11 years, working in the petroleum refining industry were admitted to the ICU of a 600 bed teaching hospital with acute H_2S poisoning. Two patients were exposed to concentrations of 9000 ppm (nine times the lethal dose), three others to > 1000 ppm. The following parameters were obtained on admission in the ICU: Glasgow Coma Score (GCS), arterial blood gases, LDH, lactate, anion gap (AG), hemoglobin, white blood cell (WBC) count, platelet count, and chest X-ray. Treatment consisted of intubation (ETT) and mechanical ventilation (MV) if GCS < 6, antidotes: sodium nitrite ($NaNO_2$) 3% (10 ml iv/15'; = 300 mg), sodium thiosulfate (NaS_2O_3) 25% (50 ml iv/30'; = 12.5 g), and steroids iv (methylprednisolone 2 g on admission followed by tapering dose over 7–14 days) in all patients. In cases of ALI euphylline (250 mg iv), broad spectrum antibiotics (with coverage of anaerobics) with prostaglandin E1 (continuous infusion starting at 5 up to 30 ng/kg/min) were added. Bronchoscopy with broncho-alveolar lavage (BAL) and peripheral biopsies were done in the MV patients. End-points were mortality treatment related morbidity and long-term complications (CNS, pulmonary). Values are mean ± standard deviation.
Results: The GCS was 6.6 ± 5, the GCS was 3/15 in three patients and these were intubated and mechanically ventilated. pH was 7.32 ± 0.11, pO_2 151 ± 90 mmHg (with an FiO_2 of 84 ± 17%), pCO_2 was 43.2 ± 11.7 mmHg, LDH 599.6 ± 585.7 IU/l, lactate 14.06 ± 19.46, AG 17 ± 3 mEq/l, hemoglobin 14.4 ± 0.8 g/dl, WBC 9.7 ± 3.6 × 10^9/l, platelets 220 ± 39 × 10^6/l. Carboxyhemoglobin and methemoglobin levels (performed in two) were normal. Chest X-ray showed bilateral nodular opacities in two patients (with GCS 3/15 and MV) and unilateral involvement in one. CT scan confirmed the presence of large airway disease in two but showed no evidence of roundglass opacities or bronchieetasis. BAL fluid showed raised WBC: mainly polymorphonuclears (PMN) in two during the early phase and mainly macrophages in one (after 24 h), RBC were raised in the BAL-fluid after 24 h. Side-effects of the antidote treatment were minor and transient nausea, agitation sweats, fall in blood pressure. One patient died on day 6 (GCS 3/15 on the spot, immediate CPR, acute fulminant pulmonary edema developed on day 1 as well as a central diabetes insipidus, MODS developed on day 3). Neurologic sequelae in form of a Claude Bernard Horner syndrome were noted in one case. Pulmonary sequelae were seen in three cases: bronchial hyper-reactivity in two (one of which had reactive airway disturbance syndrome), and chemical pneumonitis with bronchiolitis obliterans and fibrosis in the third. Lung function tests showed an FEV of 77 ± 22.7%, FEV/VC 73 ± 7.3%. TLC 83 ± 15%, DL_{co} 86.5 ± 12.5. Under treatment with beta-2-mimetics and inhalation steroids lung function tests returned to normal in all except one (fibrosis) patient. All patients could go back to work after 5 ± 5.4 months.
Conclusions: Hydrogen sulphide intoxication at concentrations of > 1000 ppm are rarely seen. On the basis of our findings we recommend aggressive treatment in these cases with oxygen supplements by face mask or via ETT + MV (if GCS < 6), antidotes (Na-nitrite, Na-thiosulfate) in appropriate doses, and steroids iv. In the MV patients with opacities on chest X-ray or CT scan euphylline, broad spectrum antibiotics and prostaglandin E1 iv should be added. This treatment resulted in a mortality of only 20% in five cases of lethal dose intoxication. Neurologic sequelae are rare. A worse prognosis (mortality and pulmonary complications) can be expected in those cases presenting with acute pulmonary edema. With appropriate treatment (beta-2-mimetics, inhalation steroids) quality of life and lung function tests returned to normal in the majority of survivors.

P133

High dose intravenous clonidine is superior to intravenous clomethiazole in severe alcohol withdrawal syndrome (delirium tremens)

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Background: Delirium tremens develops in 3–15% of all alcoholics under acute withdrawal. At present the treatment consists mainly of sedatives and symptomatic therapy. In addition to benzodiazepines, neuroleptic drugs and carbamazepine, clomethiazole is widely used. Catecholamine turnover in the central nervous system increases in delirium tremens with corresponding clinical signs. Clonidine reduces the sympathetic tonus in the region of the nucleus of the tractus solitarius.
Methods: Ninety-two patients (11 female, 81 male) reaching > 10 points (median 14, 10–23) on a symptom scale of max 25 points were treated in an open, randomized study with high dose clonidine (n = 43; 46 years; average dose 2.3 ± 1.4 mg/day) or clomethiazole (n = 48; 43 years; average dose 5.2 ± 2.5 g/day). Criteria for the evaluation of efficacy were the duration of treatment (days) to normalisation of clinical symptoms, the necessity of parenteral nutrition after 5 days of treatment, the possible mobilisation of the patients and their delirium specific concomitant medication. Clinical examinations with scoring were done twice daily. Examinations for adverse events and overall tolerability were done daily, laboratory tests at baseline and termination of the study.
Results: See table.

Table (abstract P133)

	Clonidine	Clomethiazole
Initial dose	0.56 ± 0.22 mg	0.78 ± 0.56 mg
Maintenance dose	2.2 ± 1.5 mg/day	5.2 ± 2.5 mg/day
Duration of treatment		
≤ 2 days	14 (32.6%)	7(14.6%)
3-5 days	22 (51.2%)	22 (45.8%)
6-10 days	3 (7.0%)	12 (25.0%)
Non-responder (≥ 10 days)	4 (9.3%)	7 (14.6%)
Enteral nutrition day 5	20 (46.5%)	12 (25%)
Mobilisation		
Regular respiration	35 (81.4%)	27 (56.3%)
Regular bowel function day 2	24 (55.8%)	36 (75%)
Regular bowel function day 4	24 (55.8%)	39 (81.3%)
Additive sedatives necessary	36 (83.7%)	24 (50%)

Both drugs were effective in the treatment of alcoholic delirium. Eighty-four percent of the patients on clonidine compared with 60% on clomethiazole reached normalisation of symptoms within 5 days ($P < 0.01$). There were less non-responders with clonidine. On day 4 of treatment only 19% of the patients on clonidine had respiratory complications compared to 44% on clomethiazole ($P < 0.013$). In contrast, bowel function was a problem in 44% of patients on clonidine compared to 19% on clomethiazole on day 4 ($P < 0.012$). More patients on clonidine needed additional sedative measures. The global clinical assessment of efficacy at the end of treatment was better for clonidine. Nevertheless in clonidine six serious adverse events were documented, but only two in clomethiazole treatment. Hypotension and bradycardia were main adverse reactions with clonidine whereas clomethiazole led to excessive bronchial hypersecretion.

Conclusions: In treatment of delirium tremens clonidine is superior to clomethiazole with regard to duration of therapy and respiratory function. The clonidine dose used (2.3 mg/day) was higher as recommended (1.5 mg/day) in alcohol withdrawal. The tolerability of clonidine was better rather than the tolerability of clomethiazole.

P134

The urinary ratio of 5-hydroxytryptophol and 5-hydroxyindole-3-acetic acid in patients with chronic alcohol misuse

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Background: The pre-operative detection of patients with chronic alcohol misuse is decisive for decreasing the peri-operative morbidity [1]. However, only 16% are detected in clinical routine [2]. Conventional laboratory parameters have only low sensitivity and specificity [3]. New markers seems to be superior [3]. The urinary ratio of 5-hydroxytryptophol (5-HTOL) and 5-hydroxyindole-3-acetic acid (5-HLAA) inverts due to alcohol consumption [4]. Measurement of the urinary 5-HTOL/5-HLAA ratio could show alcohol consumption the evening prior to operation in a high risk group, which is not possible by determining the blood alcohol concentration. The aim of this study was to determine the pre-operative 5-HTOL/5-HLAA ratio in patients with continuous alcoholic misuse.

Materials and methods: Forty-two patients, scheduled for a tumor resection of the upper digestive tract, participated in this institutionally approved study having received written informed consent prior to operation. The patients were assigned to the chronic alcohol group by meeting the criteria of `The Diagnostic and Statistical Manual of Mental Disorders' (DSM III R) and by consuming = 60 g ethanol daily. In cases of alcohol dependence, pharmacoprophylaxis was administered to counteract postoperative alcohol withdrawal syndrome. The urine samples were taken pre-operative, determined by gas chromatographic-mass spectrometric (5-HTOL) [4,5] and high-performance liquid chromatography (5-HIAA) [4,5]. The 5-HTOL/5-HIAA ratio was calculated. Statistics: Mann-Whitney U-test.

Results: See table.

Table (abstract P134)

	Chronic alcoholics (n = 22)	Non-alcoholics (n = 20)	P
Age (years)	52 (36-74)	62 (47-06)	0.072
Ethanol consumption (g/day)	100(60-700)	0 (0-20)	0.000
5-HTOL/5-HIAA-ratio (pmol/nmol)	18.6 (1.8-1082.8)	8.0 (3.5-11.2)	0.000
CDT (U/l)	14.4 (2-66.9)	2.5 (2.0-11.30)	0.000
MCV (fl)	95.3 (85.2-106.0)	92.3 (84.5-98.3)	0.010
?-GT (U/l)	20 (7-61)	23 (6-55)	0.400
ICU stay (days)	7 (2-83)	3 (2-26)	0.009

Median (range); CDT = carbohydrate-deficiency transferrin; MCV = mean corpuscular volume; ?-GT = gamma-glutamyl-transferase; ICU = intensive care unit.

Conclusions: The urinary ratio of 5-HTOL/5HLAA could improve per-operative detection of high-risk patients, who are posteratively in danger of developing alcohol relation complications. This subsequently leads to a prolonged ICU stay.

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