Oral Presentations
Respiratory failure in children and newborns – 414–417

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ACUTE RESPIRATORY DISTRESS SYNDROME IN CHILDREN: INTENSIVE CARE MANAGEMENT AND POST-DISCHARGE OUTCOME

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INTRODUCTION. Acute respiratory distress syndrome (ARDS) carries a high morbidity and mortality (10 to 90 %). It is characterised by non-cardiogenic pulmonary oedema and refractory hypoxaemia of multifactorial aetiology [1]. There are limited data about outcome particularly in children.
METHODS. This retrospective cohort study of 218 patients who met the major risk factors associated with acute lung injury were recruited from a prospectively collected database and represent 18.3 % of 1192 admissions. After full ethics committee approval families of 18 of the 51 survivors were interviewed by questionnaire to assess post discharge quality of life. The patients were admitted between 1 November 1998 and 31 October 2000.
RESULTS. Of the 218, 60 (27.5 %) had developed ARDS. There were 31 males and 29 females with a median (range) age and weight of 9.6 months (1 day – 12.8 years) and 8 kg (0.8 kg – 40 kg). There were 9 deaths giving a crude mortality of 15 %. Pulmonary occlusion pressures were not routinely measured. The admission A-a gradient and PaO_2/FiO_2 ratio [all values in kPa] (median + [95 % CI]) were 37.11 [32.22–41.99] and 20.80 [17.64–24.04] respectively. The non-survivors had a lower PaO_2/FiO_2 ratio (13 [6.69–19.31]) compared to survivors (21.61 [18.03–25.19]) though not significant [p = 0.05] and had a significantly higher A-a gradient (59.88 [47.58–72.18]) compared to survivors (32.38 [27.5–37.26]) [p = 0.003]. 31 patients (51.7 %) were oscillated (Sensormedics 3100A) including all 9 non-survivors. 17 of the 60 (28.3 %) were treated with Nitric Oxide including 5 out of 9 non-survivors (55.6 %). The median [95 % CI] number of failed organs was 3 [2.05–3.95] for non-survivors compared to 1 [0.66–1.34] for survivors [p = 0.002]. There were 32 patients with isolated respiratory failure only 1 of whom died. 8 (88.9 %) of the non-survivors also required cardiovascular support. Of the 18 follow-up patients there was no significant association between severity of disease and post discharge morbidity. 11 (61 %) required further hospital admissions relating to their primary illness and 11 (61 %) reported suffering from continuing distress. 12 (67 %) reported a greater susceptibility to URTI than prior to the development of ARDS.
CONCLUSION. A crude mortality of 15 % compares favourably to published data. The A-a gradient and PaO_2/FiO_2 ratio may be of help in mortality prediction in paediatric ARDS. Multiple organ failure particularly respiratory and cardiac disease is associated with increased mortality. ARDS with isolated respiratory failure carries a good prognosis in children. Further follow-up study of survivors is essential in assessing the impact of ARDS on quality of life in children.
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OPEN LUNG BIOPSY IN CHILDREN WITH RESPIRATORY FAILURE

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INTRODUCTION. The etiology of persisting respiratory failure (RF) in the critical care setting is often obscure. Treatment of the underlying disease process is often empirically instituted. The objective of this study was to evaluate benefits and risks of open lung biopsy (OLB) in children with RF.
METHODS. The charts of all patients with RF who underwent an OLB while in PICU during the last 10 years were reviewed. RF was defined by: 1) requirement of mechanical ventilation with $paO_2/FiO_2 < 300$, or $paO_2 < 60$ torr in room air, and 2) diffuse bilateral pulmonary infiltrates on chest X- ray.
RESULTS. Thirty-one children underwent 33 OLBs. Their median age was 2.1 years (range 3 days-20 years). Ten children were immunocompetent (42 %) and 19 (58 %) were immunocompromised. Diagnosis was nonspecific in 20 (61 %) cases and specific in 13 (39 %, of which 10 were infectious in etiology). A relevant change in medical management resulted from 25/33 (76 %) of the OLBs. In 6 patients, a new, previously unsuspected infectious agent was detected (PCP and CMV pneumonitis), and specific therapy was administered. Antibiotics, antifungal agents or corticosteroids were discontinued in 6 children. In 6 other patients, the OLB contributed directly to the decision to withdraw or withhold life-sustaining treatment. In 32 cases 40 bronchoalveolar lavages (BAL) were performed prior to the OLB. An infectious agent was isolated in the OLB in 10 cases. An earlier BAL failed to detect these agents in 8 of these cases (80 %). In comparing BAL to OLB as a gold standard, BAL had a sensitivity of 27 %, a specificity of 100 % and a predictive positive value of 20 %. Overall, 19 complications that occurred in 15/33 OLBs (45 %) were attributed directly to the procedure. Eleven patients (33 %) suffered air leak, with the pneumothorax appearing immediately after the procedure in all of them. The median duration of air leak was 3 days (range 1–38 days). All the patients required a chest tube following the procedure for a median period of 3.5 days (range 1–44 days). The severity of lung disease (expressed as PaO_2/FiO_2) and the magnitude of positive pressure ventilation (expressed as PEEP and PIP applied prior to the procedure) had no influence on the course of the air leak. The occurrence of air leak did not affect the respiratory status after the procedure. Respiratory deterioration was observed in 7 children (21 %) following OLB. Overall, the PaO_2/FiO_2 values before and after the procedure were not significantly affected (152 ± 67, and 160 ± 86, respectively). Bleeding was observed in one patient who did not require blood product replacement. Mortality was 58 %, with 19 patients having died during their hospitalization (median 7 days, range 1–402 days) after the procedure. Seventeen of these patients died within 30 days of the OLB.
CONCLUSION. OLB is a useful diagnostic procedure that leads to significant changes in medical management and increases the diagnostic yield for infections in children with undiagnosed or persisting RF. OLB should be routinely performed in this group of patients despite the relatively high complication rate.

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DETECTION OF VENTILATOR-INDUCED OVERDISTENSION IN CHILDREN

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INTRODUCTION. Different methods have evaluated ventilation-induced overdistension (OD) in dynamic conditions. The volume-pressure curve model based on constant flow inflation and fitting to a second order polynomial (SOPE) was validated against the quasi-static low-flow inflation technique (1). Using the volume-dependant single-compartment model (VDSCM) it was shown that a contribution of the volume-dependent elastance component to the total elastance (%E2) > or = 40 % was predictive of OD (2). %E2 was not affected by the ventilation mode or tracheal tube resistive pressures. We aimed to compare the VDSCM with the SOPE (used as the reference method) to predict OD.

METHODS. Flow (V') and pressure (Pao) measured at the Y-piece from (1) were reanalysed by multiple linear regression to fit the VDSCM (Anadat software, RHT-Infodat, Montreal, Canada): $Pao = (E1 + E2 \cdot V) \cdot V + Rrs \cdot V' + EEP$; $\%E2 = [E2 \cdot V / E1 + (E2 \cdot V)]100$ where V is tidal volume, E1 + (E2 · V) total respiratory system dynamic elastance, E1 the volume-independent elastance and E2 · V the volume-dependent elastance, Rrs dynamic respiratory system resistance and EEP the alveolar pressure at end-expiration. Results are medians (range). Non-parametric tests were used when appropriate with significance level taken at $p < 0,05$. Qualitative agreement between SOPE and VDSCM classifying for OD was assessed by kappa value.

RESULTS. 18 children, 10 males, 8 females, aged 0.7 years (0.2–14.3), weighing 7.4 kg (3–60), including 6 with ARDS, 7 with other respiratory and 5 with non-respiratory diseases were studied. Among 8 patients classified by SOPE as having OD, 6 had a %E2 > or = 40 % yielding a kappa value of 0.77. Ten patients had no OD whatever the method. The respiratory mechanics parameters were (OD vs. non-OD): total elastance 0.32 $cmH_2O \cdot mL\text{-}1$ (0.01 to 1.28) vs. 0.91 (0.22 to 2.12) (p = 0.41), %E2 45 % (4 to 58) vs. 3 (-156 to 39) (p = 0.002), Rrs 0.04 $cmH_2O \cdot mL\text{-}1 \cdot sec\text{-}1$ (0.01 to 0.06) vs. 0.11 (0.003 to 0.07) (p = 0.28) and EEP 7.9 cmH_2O (0.6 to 19) vs. 2.1 (0 to 6.2) (p = 0.02).

CONCLUSION. VDSCM showed good agreement with SOPE in detecting OD in ventilated children. A significant difference in %E2 between OD and non-OD patients was evidenced. Like SOPE, estimating %E2 does not interfere with patient ventilation. As it is not affected by the ventilation mode, %E2 might be more useful for clinical monitoring of OD.

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N-ACETYLCYSTEINE IN THE TREATMENT OF NEONATAL RESPIRATORY DISTRESS SYNDROME

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INTRODUCTION. Discrepancy between enhanced free-radical activity and existing low antioxidant potential may represent an important mechanism of secondary lung injury in premature new-borns with acute respiratory failure [2]. Different studies have demonstrated that N-acetylcysteine (NAC) might be a promising compound either for the prevention or the treatment of acute lung damages such as acute respiratory distress syndrome (ARDS) [1,3]. In a randomised clinical study we evaluated the effect of the treatment with NAC in the pre-term new-borns with respiratory distress syndrome (RDS).
METHODS. 48 pre-term infants with a confirmed diagnosis of RDS at the moment of randomisation were involved into the study. They randomly received either 100 mg/day NAC (n = 23) or placebo (n = 25) in a continuous intravenous infusion starting within the first 8 hours of life for 5 days.
RESULTS. There were no significant differences between the groups in a prevalence of perinatal risk factors and numbers of infants with severe RDS (grade III or IV). Mean birth weight and gestational age of the infants who were treated with NAC were accordingly 1632.61 ± 372.92 g and 31,44 ± 1,88 weeks in comparison with 1433.27 ± 406.09 g and 30.42 ± 2.15 weeks in the control group ($p > 0,05$). The all new-borns in both groups were treated with mechanical ventilation. 19 (83 %) infants in the treatment group and 18 (71 %) newborns in the control group received nasal CPAP-therapy. Exogenous surfactant was not used in any case. Overall survival rate was 63 % for the infants in the treatment group and 33 % for the new-borns from the control group ($p < 0,05$). The incidence of such complications as persistent pulmonary hypertension syndrome and chronic lung disease were lower among the infants who were treated with NAC but the differences were clinically not statistically reliable (accordingly 4 % and 14 % in the treatment group versus 18 % and 44 % in the control group, $p > 0,05$). Administration of NAC allowed using CPAP significantly longer (21.91 ± 17.40 versus 8.23 ± 6.83 hours; $p < 0,01$) and avoiding early tracheal intubation. It also reduced the duration of mechanical ventilation after reintubation and significantly shortened the total period of IMV and CPAP support (accordingly 137.64 ± 73.31 versus 269.80 ± 212.74 hours; $p < 0,01$). These results are in agreement with the data preliminary obtained for the adult patients with ARDS [3].
CONCLUSION. In this comparatively small randomised study we found a significant difference in outcome between NAC and placebo-treated premature new-borns with RDS. Our results suggest that intravenous NAC treatment during 120 hours reduced overall mortality rate and total duration of ventilatory support in pre-term new-borns with RDS who were not treated with exogenous surfactant.
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Oral Presentations
Clinical sepsis: What is up-to-date – 418–422

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HOSPITAL MORTALITY FOR ICU ADMISSIONS WITH SEVERE SEPSIS IN ENGLAND, WALES AND NORTHERN IRELAND

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INTRODUCTION. The PROWESS trial suggested a 6.1% reduction in 28-day all-cause hospital mortality following intensive care in patients with severe sepsis treated with recombinant human activated protein C [1]. Given this result and given that some admissions may stay longer than 28 days in hospital, the current ultimate hospital mortality rate was investigated for admissions with severe sepsis, diagnosed within 24 hours following admission to the intensive care unit (ICU), in England, Wales and Northern Ireland.
METHODS. The ICNARC Case Mix Programme Database was examined to identify admissions with severe sepsis meeting a modification of the SCCM/ACCP criteria used in the PROWESS trial [1]. Ultimate hospital mortality was defined as death at ultimate discharge from hospital following intensive care. Ultimate hospital mortality for admissions with severe sepsis in the first 24 hours in ICU was compared with that for all admissions. For admissions with severe sepsis, ultimate hospital mortality was investigated by age, number of organs failing, sex and month of admission to ICU.
RESULTS. 61,874 admissions to 92 ICUs were investigated for the period 1996–2000. 2,894 (4.7%) were readmissions to the ICU within the same hospital stay and were excluded. 15,764 (26.7%) had severe sepsis in the first 24 hours in the ICU. Ultimate hospital mortality for all admissions was 30.1%; ultimate hospital mortality for admissions with severe sepsis was 44.7% (with 18.9% of non-survivors dying after 28 days in hospital). For admissions with severe sepsis, ultimate hospital mortality increased with age, from 13.9% (0–9 years) to 59.8% (80 + years) [Pearson Chi-Square = 1047.3, 16 d.f, $p < 0.001$]. Ultimate hospital mortality for admissions with severe sepsis also increased with the number of organs failing, from 19.4% (one organ) to 84.4% (five organs) [Pearson Chi-Square = 1990.3, 8 d.f, $p < 0.001$]. The particular organs involved were associated with differing ultimate hospital mortality: renal failure was associated with a 71.1% ultimate hospital mortality, haematological failure 60.8%, metabolic acidosis 51.8%, respiratory failure 48.8% and cardiovascular failure 46.7%. There was little evidence for variation in ultimate hospital mortality by sex (43.9% – men versus 45.4% – women, $p > 0.1$) or by month of admission (41.4% – May to 46.8% – January, $p = 0.07$).
CONCLUSION. Ultimate hospital mortality for admissions with severe sepsis in the first 24 hours in the ICU was 1.5-fold greater than that for all admissions. Ultimate hospital mortality was greatest for admissions with renal or haematological organ failure, and increased with the number of organs failing.
REFERENCE. Bernard GR, et al. Efficacy and safety of recombinant human activated protein C for severe sepsis. New England Journal of Medicine 2001;344: 699–709.

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INCIDENCE AND OUTCOME OF SEVERE SIRS AND SEPSIS IN AUSTRALASIAN INTENSIVE CARE UNITS: PROVISIONAL RESULTS OF A PROSPECTIVE STUDY OF 3689 PATIENT EPISODES

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INTRODUCTION. Sepsis and the resulting organ dysfunction remain common causes of ICU admissions and death. Despite decades of research no specific treatment has established itself in routine clinical practice and treatment remains supportive. Sepsis is a priority area of the ANZICS binational research strategy that seeks to define epidemiology and current practice, to conduct prospective controlled studies and further improve mortality in Australasian ICU practice. This study, a prospective epidemiological study to document the incidence and outcome of severe Systemic Inflammatory Response Syndrome (SIRS) and Sepsis in Australasian ICUs, is the first phase of that research strategy.
METHODS. 21 Australian and New Zealand ICUs screened all patients admitted during a three-month period. Published definitions were used to identify patients with SIRS and organ dysfunction (severe SIRS), and sepsis with organ dysfunction (severe sepsis), detailed data was collected for the duration of the ICU stay in these patients. All patients were followed to 28 days after onset of severe SIRS/sepsis (SS/S), 28-day all cause mortality was the main outcome measure. Other data collected included admission APACHE II score, daily SOFA score, microbiology data, and cause of death. Where patients with SS/S died the treating ICU Specialist was asked to state if they considered the death definitely or possibly preventable by a new effective treatment for sepsis
RESULTS. 3689 admissions involving 3548 patients were screened. 1805 episodes of SS/S occurred in 1653 patients. 46.6% of patients screened suffered at least one episode of SS/S. 652 (39.4%) of episodes were due to infection, 50.0% of these were due to pulmonary infection. Median APACHE II score was 19 for patients without SS/S and 21 for patients with SS/S. Mean ICU LOS was 5.03 days, 2.92 for patients without SS/S, 7.41 for patients with SS/S. Overall mortality was 15.2%, 28-day all-cause mortality for patients with SS/S was 32.4%. 45.2% of deaths were due to sepsis with multi-organ dysfunction, 21.8% of deaths were due to neurological injury. In patients with SS/S who died, the death was considered definitely preventable in 2.4% of cases and possibly preventable in 23.1% of cases.
CONCLUSION. This prospective dataset confirms a high incidence of severe SIRS and sepsis in Australasian ICUs. The mortality rate, comparable with the control group in the recent Activated Protein C study [1], is unacceptably high. Our study further documents that 45.2% of deaths were due to sepsis with multi-organ failure with 25.5% of all deaths judged potentially preventable. These data will aid the design of future sepsis studies by the ANZICS Clinical Trials Group.
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CONTINUOUS INFUSION OF METHYLENE BLUE IN HUMAN SEPTIC SHOCK: A CONTROLLED, RANDOMIZED STUDY

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INTRODUCTION. In septic shock, enhanced generation of endogenous nitric oxide (NO) contributes to myocardial depression, hypotension, and hyporeactivity to vasoconstrictors (1). The circulatory failure promotes tissue hypoxia and the multiorgan dysfunction syndrome, ultimately causing increased mortality (2). We have evaluated the effects of continuous infusion of methylene blue (MB), an inhibitor of the NO pathway (3), on haemodynamics and organ functions in human septic shock.

METHODS. Twenty patients diagnosed with septic shock and hospitalized in a multidisciplinary ICU of an 850-bed university hospital during 1998–2000 were enrolled in a prospective controlled study. Patients were randomized 1:1 to receive either MB (MB group) or isotonic saline (control group), adjunctive to conventional treatment. MB was administered as an intravenous bolus injection (2 mg/kg), followed 2 h later by infusion at stepwise increasing rates of 0.25, 0.5, 1, and 2 mg/kg/h that were maintained for 1 h each. During infusion, mean arterial pressure (MAP) was maintained between 70 and 90 mm Hg, while attempting to reduce concurrent adrenergic support with norepinephrine and/or epinephrine and/or dopamine. Hemodynamics and organ function variables were assessed over a 24-h period, and the survival rate at day 28 was noted.

RESULTS. Infusion of MB prevented the stroke volume and the left-ventricular stroke work indexes from falling and increased MAP. Compared with the control group, MB reduced the requirement for norepinephrine, epinephrine, and dopamine by as much as 87, 81, and 40%, respectively. Oxygen delivery remained unchanged in the MB group and decreased in the control group. MB also reduced the body temperature and the plasma concentration of nitrates/nitrites. Leukocytes and organ function variables such as bilirubin, alanine aminotransferase, urea, and creatinine were not significantly affected. Platelet count decreased in both groups. Five patients treated with MB survived vs. three patients receiving conventional treatment.

CONCLUSION. Continuously infused MB as an adjuvant treatment to patients with septic shock counteracts myocardial depression, maintains oxygen transport and reduces adrenergic support as compared with conventional treatment alone. The infusion of MB appears to have no adverse effects on the selected organ function variables. Our findings warrant confirmation by a larger clinical trial of MB infused in a dose-titrated manner.

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MEDIATORS RESPONSE AFTER P55 SOLUBLE TNF RECEPTOR FUSION PROTEIN INFUSION FOR SEPSIS AND SEPTIC SHOCK

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INTRODUCTION. The effect of inhibitors of inflammatory pathways on sepsis and septic shock was tested in numerous clinical trials. In the present study, we investigated the effects of Ro45–2081, Lenercept®, a recombinant soluble TNF receptor p55 fused to an immunoglobulin heavy chain "IgG1", on the balance of inflammatory mediators in septic patients.
METHODS. Septic patients were randomly assigned to receive either Lenercept® or placebo in a multicenter study (1). In order to assess the effects of treatment on the inflammatory response, circulating levels of TNF-α, IL-6, $TNFsR_{75}$ and IL-1Ra were measured before and after the treatment in patients enrolled in our center. Statistical significance was assessed by a Kruskal-Wallis test followed by Dunn's multiple comparison test if significant.
RESULTS. 29 patients received the drug while 28 the placebo. The two groups were comparable in age, sex and diagnostic distribution. There was no difference in mortality between the two groups. A significant rise in the total TNF-α level was observed in treated patients, compared to patients who received placebo. There was no difference in the levels of other inflammatory mediators between the two groups. We confirmed that patients with a basal IL-6 level higher than 1000 pg/ml had a significantly increased mortality. Stratification for infectious source, type of bacteria and severity of sepsis did not identify any special subgroup regarding mediator responses.

	Placebo median (min-max) | n	Treated median (min-max) | n	p (Kruskal-Wallis, then Dunn's)
Baseline	84 (5–2830) | 28	74 (2–1270) | 29	NS
Day 1	69 (8.4–2880) | 28	82 (4.5–1530) | 29	NS
Day 2	56 (7.3–680) | 25	149 (14.7–2700) | 28	< 0.05
Day 3	48 (3–178) | 24	157 (29–1910) | 28	< 0.001
Day 7	29 (5–61) | 23	196 (117–640) | 24	< 0.001
Day 14	24 (2–62) | 19	222 (66–830) | 24	< 0.001

Circulating TNF-α levels in patients (pg/ml) and number of patients in each group (n).

CONCLUSION. The significant rise of total TNF- α level in treated patients did not affect the cytokine patterns when compared to patients receiving placebo. We suggest that the treatment by Lenercept®, led to a protracted half-life of TNF- α in these patients, without modifying the global inflammatory balance. This might account for the lack of efficiency of this treatment of septic patients.
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MORTALITY REDUCTION ASSOCIATED WITH RECOMBINANT HUMAN ACTIVATED PROTEIN C [DROTRECOGIN ALFA (ACTIVATED)] IN PATIENTS WITH SEVERE SEPSIS AS ASSESSED BY MARKERS OF DISEASE SEVERITY

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INTRODUCTION. In a phase III, double-blind, placebo-controlled trial (PROWESS), drotrecogin alfa (activated) reduced the absolute risk of 28-day all-cause mortality by 6.1% [adjusted relative risk reduction (RRR) = 19.4%;p = 0.005].[1] The overall mortality rates in the placebo and drotrecogin alfa (activated) groups were 30.8% and 24.7%, respectively. The consistency of the RRR associated with drotrecogin alfa (activated) was assessed across subgroups of severe sepsis patients defined by baseline markers of disease severity.
METHODS. Patients with severe sepsis (N = 1690) were randomly assigned to receive either placebo or drotrecogin alfa (activated) at a dose of 24 mcg/kg/hr for 96 hours. Subgroups were defined by baseline status of clinical and biochemical markers of disease severity which included pre-infusion APACHE II score, number of organ dysfunctions (OD), severity of OD (based on SOFA scores), need for vasopressor support, need for mechanical ventilation (mech vent), and markers of coagulopathy [Protein C (PC) and antithrombin (AT) deficiency] and inflammation (IL-6). The consistency of the effects of treatment on the relative risk (RR) of death in these subgroups was assessed by determining whether the 95% RR confidence interval (CI) for each subgroup included the observed RR for the entire population.
RESULTS. RRRs consistent with that of the overall trial population were observed across all subgroups. The point estimate of the RRR of the entire population was contained within the 95% CI of each subgroup with the exception of the patients in the 1st IL-6 quartile (n = 408;RRR = 53%). Point estimates of the RRR favored the drotrecogin alfa (activated) patients for all subgroups except for patients within the 1st APACHE II quartile (score 3 to 19;n = 433). In this subgroup, a non-statistically significant difference in mortality rate was observed in the drotrecogin alfa (activated) group compared to the placebo group (15.1% vs. 12.1%;p = 0.36). Mortality reductions with drotrecogin alfa (activated) were observed for patients not requiring mech vent (n = 415;RRR = 23.0%), not requiring vasopressor support (n = 446;RRR = 29.0%), without cardiovascular OD at entry (n = 476; RRR = 13.9%), without respiratory OD at entry (n = 418;RRR = 22.7%), with IL-6 levels < 1000 pg/ml (n = 1017;RRR = 20.2%), with normal PC levels (n = 195;RRR = 41.7%), and with normal AT levels (n = 285;RRR = 24.6%). For patients within the 1st APACHE II quartile with 2 or fewer organ failures (n = 322), administration of drotrecogin alfa (activated) was associated with a 19.9% RRR.
CONCLUSION. Reductions in mortality were observed in all subgroups defined by baseline markers of disease severity, with the exception of the 1st APACHE II quartile. Clinical interpretation of this latter finding is complicated by the relatively low event rate in this subgroup and the lack of its consistency with all other subgroups defined by clinical and biochemical measures of low disease severity. We conclude that the beneficial effect of drotrecogin alfa (activated) across subgroups defined by baseline markers of disease severity, as assessed by RRR, is consistent with that observed in the overall trial population.
REFERENCE. Bernard GR, Vincent JL, Laterre PF et al. NEJM 2001; 344: 699–709.

Oral Presentations
Metabolism and endocrinology – 423–427

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LUNG VERSUS SKELETAL MUSCLE AMINO ACID FLOW IN SEPTIC ARDS PATIENTS

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INTRODUCTION. Catabolic stress, as sepsis, is characterized by accelerated skeletal muscle amino acid release. The relative contributions of skeletal muscle and pulmonary tissue in maintaining amino acid homeostasis were studied in septic ARDS patients (according to the ESICM criteria).

METHODS. Six septic patients with ARDS were enrolled (gender: 4 m, 2 f; age: 63 ± 6 yrs; BSA: 1.95 ± 0.06 m2; PaO_2/FiO_2 < 200). We measured simultaneously arterial (A), mixed venous (Mv) and femoral venous (Fv) blood concentration of Glutamine (Gln), Alanine (Ala) and Phenylalanine (Phe) as well as lung and leg blood flow by thermodiluition and plethismography, respectively. We have calculated amino acid arteriovenous differences across muscle (A-Fv) and lung (Mv-A) as well as muscle and lung amino acid flow according to the Fick principle. Substrate flux in one leg was considered accounting for 1/4 of whole-body muscle metabolism. Data are presented as mean ± SEM.

RESULTS. (A-Fv)Gln and (A-Fv)Ala (-59.4 ± 18.8 and –62 ± 12.3 nmol/ml) were higher (p < 0.05) than (Mv-A)Gln and (Mv-A)Ala (-7.6 ± 10.4 and –7.6 ± 4.3 nmol/ml). (A-Fv)Phe and (Mv-A)Phe were not significantly different (-8.4 ± 12.8 vs –2.6 ± 4.6 nmol/ml). Lung amino acid flow (Gln –20.0 ± 36.9, Ala –23.1 ± 14.3, Phe –24.3 ± 19.1 μmol/min/m^2) were not significantly different from whole-body muscle amino acid flow (Gln –38.8 ± 12.9, Ala –46.3 ± 11.7, Phe –7.3 ± 2.8 μmol/min/m^2).

CONCLUSION. In septic ARDS patients both lung and muscle importantly contribute to maintaining amino acid homeostasis. Gln and Ala release from total skeletal muscle and lung are similar. In septic ARDS patients the lung exhibits a negative protein balance and provides glutamine and alanine to the whole body.

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EFFECT OF STEROIDS ON VASOPRESSOR NEED IN STABLE DISTRIBUTIVE SHOCK AND EVALUATION OF THE 1 μG CORTICOTROPIN TEST

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INTRODUCTION. Patients with distributive shock may suffer from a relative adrenocortical insufficiency, and treatment with substitutive doses of steroids can result in a reduction of vasopressor therapy. The interpretation of a standard 250 μg corticotropin stimulation test is difficult for cases of relative adrenal insufficiency in the critically ill, so that the rapid reduction in vasopressor need following steroid replacement is suggested to be the best clinical clue to the diagnosis*. Furthermore, the 250 μg corticotropin test has been reported to be rather insensitive to detect absolute adrenal insufficiency. We investigated the possibility that the haemodynamic response to corticosteroid substitution could be correlated to the serum cortisol response to 1 μg corticotropin stimulation, which has been suggested to be a superior test in the critically ill.

METHODS. 300 mg hydrocortisone was administered intravenously in continuous infusion to consecutive patients with distributive shock requiring at least 100 ng/kg/min noradrenaline to maintain MAP > 60 mmHg and in whom dose alterations not greater than 50 ng/kg/min had been necessary in the preceeding 24 hours. The vasopressor dose was recorded 24 hours later. Prior to corticosteroid supplementation, cortisol levels were measured at baseline and 30 and 60 minutes after administration of 1 μg corticotropin.

RESULTS. Noradrenaline dose was significantly reduced by ^{3}50% (median 210 ng/kg/min [interquartile range 117–347] versus 50 [interquartile range 0–105]; p = 0.005, Wilcoxon signed ranks test) after 24 h in the first ten patients. According to the classical criteria, absolute adrenal insufficiency was diagnosed in two patients (cortisol levels after corticotropin stimulation remaining below 20 μg/dl) and relative adrenal insufficiency was suggested in three patients (cortisol levels rose < 10 μg/dl after stimulation). In the remaining five patients, 1 μg corticotropin stimulation led to increase of cortisol > 10 μg/dl with absolute levels > 20 μg/dl, suggesting adequate adrenal reserve.

CONCLUSION. Vasopressor need was significantly decreased in all our patients following corticosteroid supplementation, clinically suggesting adrenal insufficiency. However, the 1 μg corticotropin test could detect adrenal insufficiency (relative or absolute) in only half of the patients. In contrast to previously reported data, our results suggest a much higher incidence of absolute adrenal insufficiency in critically ill patients (20% versus 2–3%). Therefore, the 1 μg corticotropin test might be more sensitive in detecting absolute adrenal insufficiency in the critically ill with persistent vasopressor need.

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SELECTIVE INOS INHIBITION DECREASES IN VIVO NO PRODUCTION, BUT INCREASES MORTALITY DURING PORCINE ENDOTOXAEMIA

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INTRODUCTION. Inhibition of nitric oxide synthetase (NOS) during sepsis can adversely affect hepatosplanchnic function by inhibiting endogenous NOS production. Although inhibition of inducible (i)NOS would not have these effects, controversial results were found. One explanation for detrimental effects seen when using iNOS inhibitors is related to whether an endotoxic stimulus is present.

METHODS. Multi-catheterized female pigs (20–25 kg) received endotoxin (ET, 3 micog/kg/min) during 24 hours; 4 hours after start ET infusion aminoethyl-isothiourea (AE- ITU, 10 mg/kg/hour, n = 6) was started until 48 hours after start ET infusion. Control animals (n = 7) received saline only. NO production was assessed using the conversion of L-[15N2]Arginine to L-[15N]Citrulline. Splanchnic perfusion was measured using para- aminohippuric acid (PAH) dilution method and assessed with saline calibrated tonometry (Pmucosal-arterial CO_2). Oxygen delivery and extraction was determined for the whole body and splanchnic organs using thermodilution and PAH dilution methods, respectively combined with blood gas analysis.

RESULTS. AE-ITU induced a significant reduction in in vivo NO production (p < 0.001) A decreased Pm-aCO_2 in the AE-ITU treated pigs was seen from the start of the AE-ITU infusion (mean 1.75 ± 0.3 mmHg vs. 0.75 ± 0.4, p < 0.05 AE-ITU vs. placebo). Hepatic oxygen extraction ratio increased (0.5 ± 0.1 vs. 0.3 ± 0.1, p < 0.05) without increase in global oxygen delivery. However, after cessation of the endotoxin infusion, the iNOS inhibition decreased oxygen saturation in the hepatic vein (25 ± 7% vs. 48 ± 5, p = 0.001) coinciding with an increased hepatic oxygen extraction. This was associated with an increased mortality beyond 24 hours (57.1 vs. 100%, p = 0.04).

CONCLUSION. Inhibition of iNOS during hyperdynamic endotoxaemia is related to improved hepatosplanchnic perfusion and function. However, prolonged inhibition of NOS without endotoxin stimulus increases mortality.

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ANALYSIS OF ACID-BASE EQUILIBRIUM IN CRITICALLY ILL PATIENTS USING THE STEWART'S APPROACH

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INTRODUCTION. According to the Stewart's model, plasma pH depends on 3 different distinct variables which are: the SID (strong iron difference, which is the difference between the cations and anions strongly dissociated), the $PaCO_2$ and the weak acids (mostly albumin). Metabolic acid-base balance disorders (mABD) leading to HCO_3 variations (Δbicar) can be due to a SID variation (ΔSID) or to a change in albumin concentration (Δalb). On the other hand, a ΔSID can be associated to none Δbicar if there is a subsequent correcting Δalb. The aims of this study was to: 1.validate this model and find out the link between HCO-3 and the other features of SID: Na + , Cl-, lactate, other anions, $PaCO_2$, and albumin; and 2.determine the impact of each of these variables on mABD genesis.

METHODS. During a 2 months period, arterial blood samples were systematically examined to determine albumin levels on patients' arrival and then every morning for the remaining days. The following formulas have been used: SIDapparent = $(Na + + K + + 2Ca_2 + + 2Mg_2 +)$-Cl-. SID = HCO_3 + Pi- + Alb-. Pi- = phosph(0,309 ph-0,469), and Alb = albumine(0,123 ph-0,631). Strong anions other than Cl– and lactates (AxF-) have been calculated with the following formula: AxF- = SIDapparent – (SID + lactates + 9). The formula linking $[HCO_3]$ to each of the main distinct variables has been appreciated by multiple regression, allowing to calculate the part of each variable in the metabolic acid base balance. A $p < 0,01$ was considered as significant. The results are given in mean ± SD.

RESULTS. 381 blood samples have been performed in 78 patients. HCO_3 variability is explained in 97% ($r2 = 0,968$) by the changes in all the distinct variables. Albumin levels were constantly low (25,1 ± 5,1 g/l) leading to an increase in HCO3 of 2.2 ± 1.2 mmol/l, (range: –1 to + 6 mmol/l). There is a strong relationship between (ΔSID-Δbicar) and albumin levels ($r2 = 0,53$), confirming that Δalb can hide a ΔSID. In case of metabolic acidosis (Δbicar < -2, n = 128), high levels of AxF-, lactates and the hyponatremia account respectively for: 56, 22, and 11% of the Δbicar. In case of metabolic alcalosis (Δbicar > + 2, n = 101), hypochloremia and low levels of blood albumin account for 56 and 40% of the Δbicar.

CONCLUSION. The Stewart's model is efficient in our study. Low levels of blood albumin account for a metabolic alkalosis that can hide a change in the organic acids concentration. Accordingly, the SID is a more suitable parameter than the bicarbonate concentration to assess the mABD secondary to an increase of organic acids in intensive care patients.

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CARDIOPULMONARY BYPASS FOR CARDIAC SURGERY AFFECTS LACTATE METABOLISM

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INTRODUCTION. Disturbances of glucose and lactate metabolism have been repeatedly observed after bypass for cardiac surgery. Among several etiologies associated to explain these abnormalities, low splanchnic blood flow and liver hypoperfusion during the bypass may have a major implication. The purpose of this work was to investigate the role of bypass on lactate metabolism by an exogenous-lactate-challenge-test (ECLT, (1)).

METHODS. Three groups of patients undergoing cardiac coronary bypass were investigated: before surgery (n = 20, Pre-op), after surgery with bypass (n = 20, CPB-CAB) and after surgery without bypass (n = 20, MID-CAB). Lactate metabolism was investigated by ECLT: 2.5 mmol/kg BW of Na-lactate were infused during 15 min, plasma lactate concentration (L) was followed before and at T = 0, 5, 10, 15, 30, 60, 90 and 120 min after the end of the perfusion. Lactate clearance (LC) and endogenous lactate production (ELP) were calculated from basal lactate and from the area under the curve. A two-exponential fitting permitted the modeling of lactate decay (Kaleidagraph® Abelbeck Software, Reading, PA, USA) to calculate two half-lives (HL-1 and HL-2). Results are given as means ± sem, statistical comparisons (ANOVA followed by a PLSD test): * significant difference vs Pre-op and $ vs CBP-CAB, $p < 0.02$.

RESULTS. We failed to find significant difference concerning basal lactate and endogenous production among the 3 groups, none of the studied parameters of lactate metabolism differed between Pre-op and MID-CAB. Peak value, LC, HL-1 and HL-2 in CBP-CAB significantly differed from the 2 other groups (Pre-op and MID-CAB).

	Basal L mM	Peak L mM	L C mL/kg/min	ELP µmol/kg/min	HL-1 min	HL-2 min
Pre-op	1.5±0.3	8.6±0.3	9.4±1.0	15.0±1.8	17.2±2.4	74±12
CBP-CAB	1.8±0.2	12.4±1.2*	6.0±1.0*	12.1±1.9	10.6±1.3*	171±40*
MID-CAB	2.2±0.3	9.6±0.7$	9.6±0.8$	19.3±2.2	18.9±2.5$	48±3$

CONCLUSION. The bypass procedure rather than the disease or the surgical procedure seems to be responsible for the observed change in lactate metabolism. The decreased lactate clearance associated with the increased HL-2 suggest an impairment of lactate metabolism. The lack of difference in basal lactate in these patients indicates that despite the decreased lactate clearance, the metabolic capacity is sufficient for the metabolism of a normal rate of lactate production.

REFERENCE. Ann Surg 1999;229: 505–13.

Oral Presentations
Catheter-related infection – 428–432

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USEFULNESS OF QUANTITATIVE BLOOD CULTURES FOR DIAGNOSIS OF CATHETER-RELATED BLOOD STREAM INFECTION

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INTRODUCTION. Catheter Related Blood Stream Infection (CRBSI)diagnosis should be made without removing the Central Venous Catheter (CVC)to avoid risks associated with reinsertion and to reduce costs. This prospective study assessed the usefulness of a differential quantitative blood culture technique (lysis centrifugation with Isolator) in the diagnosis of CRBSI without catheter removal in suspected septic episodes.
METHODS. During a period of 12 months (January-December 2000)in a general ICU, simultaneous central catheter blood and peripheral blood culures were obtained from patients with suspected CRBSI. The CVC remained in situ pending culture results. A colony count fivefold higher in blood drawn from the CVC than in blood through the peripheral vein was used as a cut-off value and the catheter was removed and its tip cultured semiquantitatively.
RESULTS. 118 catheters and associated blood samples from 88 patients were analyzed. CRBSI occurred in 26 patients. A Sensitivity of 87, a Specificity of 98, a Positive Predictive Value (PPV) of 94 and a Negative Predictive Value (NPV) of 94 were obtained (see Table).

Tip cultures	Negative	Positive	Total
Differential cultures			
Negative	78	5	83
Positive	2	33	35
Total	80	38	118

CONCLUSION. We confirmed the results of other authors: the differential quantitative blood cultures without catheter removal seems effective in the diagnosis of CRBSI in patients in Intensive Care Unit.

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ESTIMATION OF VENOUS CATHETER -INDUCED BACTEREMIA

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INTRODUCTION. The use of central venous catheters in I. C.Us is obligatory and unavoidable in most cases, but it can often cause serious complications related to the insertion point, to the techniques, the route of, and on the kind of the catheter. Even under optimal circumstances catheter associated bacteremias often occur. The confirmation of catheter-induced infection may be of vital importance in its early etiological treatment.

METHODS. In an ongoing study in our I. C. U., we evaluated a number of 125 cases of patients with suspicion of catheter-associated bacteremia. In all of these cases catheters were removed after quantitative assessment of the skin (Maki et al.) at the insertion point, the tip of the catheter and blood sample from a peripheral vein was send for cultivation.

RESULTS. Out of the 125 cases, of febrile I. C. U. patients who had catheterized central veins, according to the location (site of insertion), in 21 cases the catheters were inserted in jugular veins (group A), 79 were subclavian (group B) and 25 were inserted in the femoral veins (group C). In group A, 7 patients presented with colonized skin at the insertion point, in 3 cases the catheter tip was found to be colonized and in only 4 cases we had a colonized blood culture. In-group B the skin colonization was limited to 14 patients, the catheter tip was colonized in 7, and 19 patients had colonized blood culture. In-group C we had 12 cases with colonization of the skin at the insertion point, 4 colonized catheter tips and 4 positive blood cultures.

CONCLUSION. . In spite of the limited results until now we can assume that quantitative and semi quantitative analysis of the skin at the insertion point by it self is not an adequate fact contributing to the diagnosis of venous catheter associated bacteremia. We also suggest, by the above results, that the V. C. A. B. is 1) often enough, 2) it can only be diagnosed by catheter tip cultures and 3) the catheter tip contamination exists is almost the half of cases with contamination of the skin at the insertion point

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IMPACT ON THE OUTCOME OF CATHETER-RELATED BLOODSTREAM INFECTION DEPENDING ON THE PATHOGEN INVOLVED

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INTRODUCTION. Studies evaluating the impact of catheter-related blood-stream infection (CRBI) on the outcome have not differen- tiated episodes caused by coagulase negative Staphylococcus (CNS) from other pathogens. We set out to determine whether mortality attributable to CRBI caused by CNS is significan-tly lower than that for other pathogens.

METHODS. From January 1996 to March 2001, 1412 patients were admi-tted to a 8-bed unit of a large urban Hospital with tea-ching accreditation. CRBI was defined as isolation of the same strain in blood cultures and in the semi quantitative culture of a catheter tip (yielding > 15 colonies). Only ICU-acquired (> 48 h) episodes were considered. Isolation of a pathogen in catheter tip without concomitant positive blood culture were not included. Severity of illness at the admission to the ICU was evaluated by APACHE II score and the expected mortality was also calculated. The systemic response to the CRBI and the appropriateness of empirical antibiotherapy were also noted. Patients were followed up until death or hospital discharge. Standardized mortality ratio (SMR) was calculated as the ratio between hospital mortality and expected mortality, with the corresponding 95 % confidence interval.

RESULTS. In this period forty-nine episodes of CRBI were diagnosed. Twenty-five episodes were due to CNS (Group I) and 24 to other microorganisms (Group II): *Acinetobacter baumanii* (5), *Candida albicans* (5), methicilin- resistant *Staphy-lococcus aureus* (5), methicilin-sensitive *Staphylococcus aureus* (2), *Klebsiella pneumoniae* (3), *E. coli* (1), *Streptococcus viridans* (1), *Enterococcus spp* (1), polymicrobial (1). Age, APACHE II score, and expected mortality at admi- ssion did not differ between these two groups. Systemic response was severe sepsis or septic shock in 8 % of the cases in Group I and in 58 % in Group II ($p < 0.001$). Empiric antimicrobial therapy was appropriate in 44 % in Group I and in 75 % in Group II ($p = 0.02$). Hospital mortality was higher than expected mortality in Group I (36 % vs. 23 %) and in Group II (62 % vs. 29 %). SMR in Group I was 1.56 (95 % CI 1.51 – 1.61) and 2.1 (2.02 – 2.18) in Group II.

CONCLUSION. Mortality related to ICU-acquired CRBI is increased both in CNS and no-CNS episodes.

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PREDICTIVE RISK FACTORS FOR COLONIZATION AND INFECTION OF CENTRAL VENOUS CATHETERS

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INTRODUCTION. As the use of central venous catheters (CVC) is associated with colonization (CVC-c: CVC-tip culture positive for a micro-organism) and/or infection (CVC-i: CVC-tip and blood culture both positive for same micro-organism), we undertook a 6-month observational audit on our medical-surgical 22-bedded ICU to evaluate main risk factors for CVC-c and CVC-i.
METHODS. Demographic data, 1 st 24 hour APACHE II score, risk factors (e. g. diabetes, renal failure, liver failure, neutropenia,) and the presence, number and type of CVC were collected on all 713 patients admitted. For each removed/changed CVC, the tip was cultured with the Maki roll semi-quantitative technique. If systemic infection was clinically suspected, aerobic and anaerobic blood cultures were taken and incubated for 5 days (Bactec 9240, Becton Dickinson, USA). SPSS software was used for statistical analyses with p values < 0.05 considered significant.
RESULTS. 857 CVC (730 triple-lumen, 100 double-lumen, 23 pulmonary artery catheters) were inserted for a total of 4131 line-days. 43 CVC-c and 40 CVC-i were recorded in 39 and 35 patients, respectively. A Multinomial Logistic Regression model was performed using CVC-c and CVC-i as the dependent variables, and the risk factors shown below as independent variables. CVC total indwelling days, number of CVC, renal failure and MRSA carriage were independent predictive factors of CVC-i and CVC-c (see Table). Logistic regression analysis was performed in the 74 CVC-c patients using CVC-i as the dependent variable and the above risk factors as independent variables to assess which were responsible for causing line-related bacteraemia. The total indwelling time of the CVC(s) was an independent predictive factor of CVC-i: OR: 4.7 (95 % CI 1.8–19.1)($p = 0.0319$).

Risk Factors	CVC-c/no CVC-c/i Odd Ratios (95 % CI)	CVC-i/no CVC-c/i Odd Ratios (95 % CI)
CVC indwelling days	1.11 (1.04–1.19)	1.18 (1.1–1.26)
Number of lines	0.15 (0.04–0.6)	0.42 (0.07–2.7)
Liver failure	0.29 (0.07–41)	0.37 (0.08–1.7)
Renal failure	7.36 (1.32–41)	19.07 (1.81–201)
Neutropenia	6.05 (0.54–67)	0.64 (0.03–12.3)
Immunodeficiency	0.07 (0.01–0.49)	0.41 (0.02–7.44)
Surgery < 1 week prior	2.91 (1.06–8)	2.19 (0.67–7.2)
MRSA carriage	0.31 (0.12–0.79)	0.25 (0.09–0.7)

CONCLUSION. The number and indwelling duration of CVC are independent predictive factors of colonisation and line-related bacteraemia.
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CENTRAL VENOUS CATHETER-RELATED BACTERAEMIA: EPIDEMIOLOGY, SEVERITY OF ILLNESS AND THERAPY

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INTRODUCTION. Central venous catheters (CVC) are essential for the critically ill patient clinical management to facilitate the infusion of pharmacotherapies, resuscitative and maintenance fluids. However, their use may be complicated by their colonisation (CVC-c: culture of CVC-tip positive for a microrganism) or infection (CVC-i: CVC-tip and blood culture, positive for same microrganism)(1,2). We conducted a 6 month prospective audit to determine CVC-c and CVC-i prevalence in our ICU.
METHODS. The presence, number and type of CVC were collected on all patients admitted to our ICU over a 6 month period. The Maki roll plate semi-quantitative technique was used for CVC tip culture. All patients with CVC-c and CVC-i, were identified by daily prospective surveillance of all positive cultures. For all positive results, Gram stain, identification, together with ACCP/SCCM sepsis criteria and therapy for CVC-i, were noted. Standard media, methods and techniques were used for microrganism isolation and identification. SPSS (SPSS Inc., Chicago, USA) software was used for statistical analyses. P values < 0.05 were considered significant.
RESULTS. 857 CVC (of which, 730 conventional, 100 dialysis and 23 Swan-Ganz catheters) were inserted in 713 patients for a total of 4131 line-days. Forty-three CVC-c and 40 CVC-i occurred respectively in 39 patients and in 35 patients with a rate of infection of 9.6 for 1000 line-days were recorded. The single CVC indwelling median time was higher in patient with CVC-i (10, IQR 6–11) and CVC-c (8, IQR 6–10) than in patient without any infectious complication (2, IQR 1–4) ($p = 0.000$-ANOVA). Coagulase-negative Staphylococci caused a CVC-i in 12 cases out of 45 CVC-c, while Staphylococcus aureus in 11 out of 36, Klebsiella spp. in 8 out of 16, Enterobacter spp. in 4 out of 9 and Candida albicans in 3 out of 8. The probability of developing CVC-i is increasing in relation to the CVC indwelling time. (32 % after 7 days, tripled after 14, 100 % after 3 weeks). Septic shock was recorded in 21 (53 %) of cases of CVC-i. No antibiotic therapy (Rx) was given for all CVC-c, but CVC was removed or changed. Thirty (75 %) CVC-i were treated with 5 (IQR 5–6) day mono-(Rx) median course, 7 (18 %) with 7 (IQR 8–10) day median course of combination-(Rx). In 2 patient only the CVC removal was performed and 1 patient died before starting (Rx).
CONCLUSION. Bacterial CVC-c, an essential prerequisite for CVC-i, can be treated by the only CVC-removal. CVC-i, related to the CVC indwelling time, is mostly complicated by a high severity of illness and need to be treated by an appropriate and adequate (Rx), together with the CVC removal.
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Oral Presentations
Airway management – 433–437

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INFLUENCE OF THE HUMIDIFICATION DEVICE ON THE WORK OF BREATHING (WOB) DURING NON-INVASIVE VENTILATION (NIV)

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INTRODUCTION. In intubated patients, it has been shown that WOB is greater with heat and moisture exchangers (HME) than with heated humidifiers (HH). The aim of this study was to evaluate the influence of the humidification device on WOB during NIV.

METHODS. HME and HH were compared in patients undergoing NIV for hypercapnic acute respiratory failure. Each patient was randomly ventilated for 20 min with HH and HME, with PEEP (P) and at ZEEP (Z). At the end of each period, the arterial blood gases, WOB and pressure-time product (PTP) were measured.

RESULTS. 9 patients were studied. Results are shown in the table.

	RR	V_E (l/min)	pH	$PaCO_2$ (mmHg)	PaO_2 (mmHg)	WOBeso (J/min)	PTPeso (cmH_2O*s/min)
HME-Z	29 ± 11	16 ± 4.5	7.37 ± 0.04	59 ± 9	74 ± 14	16.2 ± 7.9	195 ± 115
HME-P	30 ± 11	12.8 ± 5.6	7.38 ± 0.04	59 ± 10	74 ± 13	9.6 ± 7.7*	146 ± 91*
HH-Z	27 ± 7	12.8 ± 4.3	7.39 ± 0.04*	57 ± 10*	74 ± 6	9.3 ± 5.6*	135 ± 77*
HH-P	28 ± 8	13 ± 3.5	7.39 ± 0.04*	56 ± 10*	73 ± 11	8 ± 4*	115 ± 71*

*$p < 0.05$ compared with HME-Z

CONCLUSION. During NIV, WOB is greater with HME than with HH. This effect may be related to HME's deadspace responsible for an increase in capnia. With PEEP, this is less pronounced probably because of deadspace "wash-out" due to higher expiratory leaks. HME should not be used during NIV especially in hypercapnic patients.

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INFLUENCE OF HEAT AND MOISTURE EXCHANGERS ON DEAD SPACE AND GAS EXCHANGE IN PATIENTS WITH RESPIRATORY DISTRESS

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INTRODUCTION. The use of cascade humidifier (CH) instead of heat and moisture exchangers (HMEs) represent a decrease in dead space. The aim of this study is to cuantify the decrease of dead space (VD) and analyze the effect on arterial blood gases (ABG).

METHODS. Nine consecutive intubated and mecanically ventilated patients with respiratory distres syndrome and under pharmacological coma were studied during the following phases: 1/Basal: HME and ventilatory parameters adjusted by the responsible physician.2/ CH instead of HME without changes in the previous ventilatory parameters.3/ CH with reduction of Vt so as to reach a $PaCO_2$ equal to basal phase. Determinations of dead space (Vd), Vd/Vt (Douglas bag and Bohr's equation), plateau pressure (PP) and ABG were performed after approximately 60 minutes of stabilization. Respiratory rate (rr), FiO_2, I:E ratio and PEEP were unchanged throughout the study. HMEs used were all the same (Edith Flex, Datex Ohmeda, Sweden). Statistical analysis: ANOVA.

RESULTS. See table 1 (expressed as mean ± SD). Mean FiO_2 was 0.88 ± 0.15, rr 21 ± 5, PEEP 12 ± 2.

	Phase 1	Phase 2	Phase 3	P
Vt (ml)	543 ± 96	543 ± 96	450 ± 102	0.090
Vd(ml)	386 ± 47	349 ± 53	288 ± 41	0.001
Vd/Vt(%)	72 ± 10	65 ± 11	65 ± 10	0.239
Ph	7.30 ± 0.08	7.36 ± 0.08	7.29 ± 0.10	0.190
PaO_2(mmHg)	137 ± 80	140 ± 77	122 ± 80	0.878
$PaCO_2$(mmHg)	54 ± 7	45 ± 7	53 ± 7	0.015
Pp(cmH_2O)	33 ± 5	32 ± 4	26 ± 3	0.002
Compliance(ml/cmH_2O)	27 ± 8	28 ± 6	33 ± 7	0.156

CONCLUSION. The use of CH instead of HME induce a statistically signifcative decrease in Vd and $PaCO_2$. The reduction of Vt to reach a basal $PaCO_2$ represent an adicional reduction in Vd.

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COMPLICATIONS OF ENDOTRACHEAL SUCTIONING (ES) DURING MECHANICAL VENTILATION: INCIDENCE AND RISK FACTORS

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INTRODUCTION. Periodic ES is necessary to avoid accumulation of secretions and endotracheal tube occlusion in mechanically ventilated patients. The aim of this study was to evaluate the incidence and the risk factors of complications due to ES.

METHODS. During a 3 month period, all ES procedures were recorded and complications were reported for each patient. Pertinent ventilatory settings (FiO_2 and PEEP) and medical treatment (anticoagulant therapy) were collected.

RESULTS. 79 patients and 4117 ES were evaluated. Complications were reported in 12 % of all ES and in 57 % of the patients: desaturation 5 % (35 patients), hemorrhagic secretions 4 % (23 patients), haemodynamic changes 2 % and heart rate modifications 1 %. In the group of patients showing episodes of desaturation, FiO_2 (72 % vs 58 %, $p < 0.01$) and PEEP (7 vs 3 cmH_2O, $p < 0.001$) were greater than in the group with no episodes of desaturation. Length of mechanical ventilation (17 vs 6 days, $p < 0.001$) and of ICU stay (24 vs 11 days, $p < 0.001$) were also greater. A logistic regression found PEEP as the only independent risk factor for desaturation (ORa, 1.5; IC95 %, 1.17–1.86; $p < 0.01$). Patients showing hemorrhagic secretions during ES had a length of mechanical ventilation (16 vs 9 days, $p < 0.001$) and of ICU stay (21 vs 15 days, $p < 0.05$) greater than patients who did not. Episodes of hemorrhagic secretions were not linked to anticoagulant therapy.

CONCLUSION. Almost 60 % of patients experience complicated ES. Desaturation, a potentially life-threatening complication, occur in patients needing high levels of PEEP. In these patients, means to prevent the occurrence of this complication are needed.

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MONITORING OF NEGATIVE PRESSURES DURING ASPIRATION WITH OPEN AND CLOSED SYSTEMS IN ANESTHETISED PIGS

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INTRODUCTION. Suction in the ET-tube induces physiological changes that might be due to negative pressures in the trachea. In a recently published in vitro study, it was found that suction created extreme negative pressure in a lung model. We therefore monitored the trachea pressures during aspiration in healthy pigs.

METHODS. Pigs were studied during pressure controlled ventilation. The V_T was 14 ml/kg, PEEP 3 cmH_2O. The pigs were anaesthetised with Ketamin, Fentanyl and Pavulon in a continues-infusion. An ET-tube 6.0 mmID and suction catheters no. 12 FR and no. 14 Fr were used. A comparision of closed system versus open system during suction was done. The pressure sensitive element of the PressureWire™ System (Radi Medical System, Uppsala, Sweden) was position at the end, but outside, the ET-tub. Suction flow measurements (4040 C TSI Inc, USA) were performed in a bench model.

RESULTS. During aspiration we found a statistical significant lower pressure when using the no. 12 Fr catheter in an open suction system than with a closed system, see Table (mean ± -SEM). There was no difference between the negative pressures resulting from aspiration with the no. 14 Fr catheter, however remarkably low. When the flow was measured it was found that the peak flow at the tip of the suction catheter no. 14 Fr was 40 % higher than for no. 12 Fr, and the steady flow was 16 % higher.

	Open system	Closed system
Catheter no.		
no. 12 Fr (n = 6)	–11±1 cmH_2O *	–5±1 cmH_2O
no. 14 Fr (n = 5)	–52±12 cmH_2O	–70±14 cmH_2O

Student's T-test * = $p < 0.001$

CONCLUSION. This study confirms the previous study done in vitro. Suction in the ET-tube causes negative pressures in the lungs that can contribute to gas exchange impairment due to collapse of lung tissue. Using a thinner catheter the negative pressures became much lower due to the decrease in flow. Less negative pressure could then be less harmful to the lungs, but one obvious question that follows is how effective aspiration with a small catheter is.

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CLOSED SYSTEM SUCTIONING HAS LITTLE SUCTIONING EFFECT AND LITTLE SIDE-EFFECTS

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INTRODUCTION. The protective properties of closed system suctioning (CSS) has been questioned(1). The ventilatory and circulatory effects of closed vs. open suctioning in a lavaged lung model as well as the effectiveness of suctioning were studied.
METHODS. Six pigs were anaesthetised and intubated with endotracheal tube (ETT) no 7 supplied with a tracheal pressure catheter and connected to a Servo 900C ventilator. Gas exchange was evaluated using pulse-oximetry and a pulmonary artery catheter for SvO_2 monitoring. Broncho-alveolar lavage with 12 ± 2 L saline produced surfactant depletion. Open and closed suctioning with 12 and 14 Fr catheters at a vacuum level of –20 kPa was studied during pressure controlled ventilation (PCV). Suctioning was applied for 5, 10 and 20 seconds. Parameters were registered at base line, 1 min and 5 min after suctioning (Table 1). In a second stage we applied 10 ml of gel below the tube and performed open and closed suctioning with 12 Fr catheters during either PCV, CPAP 0 or CPAP 10 cmH_2O with vacuum levels –20 kPa and –40 kPa. The amount of gel removed was measured by weighing the systems before and after suctioning (Table 2).
RESULTS.

	Open system baseline	Open system 1 min	Closed system baseline	Closed system 1 min
SvO_2 %	55 ± 6	40 ± 11*	54 ± 9	50 ± 10*
SpO_2 %	93 ± 4	58 ± 10*	93 ± 2	83 ± 8* #
Crs mL/cmH_2O	18 ± 2	13 ± 2*	19 ± 2	17 ± 4
Ptrach cmH_2O	24 ± 4	–5 ± 5*	24 ± 2	4 ± 6* #

Table 1: Aspiration 10 s during PCV with a 12 Fr catheter, –20 kPa, (n = 6). * $p < 0,05$, 1 min vs. Baseline. # ANOVA significantly different vs. Open system.

	Open system	Closed system	Closed system	Closed system
Ventilatormode	PCV	CPAP 10	CPAP 0	CPAP 10
Vacuumlev (kPa)	–20	–20	–20	–40
Sucked gel (g)	1,25 (0,8–1,6)	0,3 (0–1,0)	0,98 (0,1–1,7)	0,28 (0–0,8)

Table 2: Aspiration 10 s with 12 Fr catheter after gel deposition, (n = 6). Mean values and (range).

CONCLUSION. Closed system suctioning with small catheters and a low vacuum level has less negative side-effects than open suctioning but seems to be less effective in removing secretions. A certain amount of alveolar collapse must be allowed to make the suctioning manoeuvre effective. It is important to develop a suctioning-technique that minimises the negative side-effects of CSS and optimise the interaction between suctioning system and ventilator.
REFERENCE. Warning! Suctioning. Stenqvist et al. Acta Anaesthesiol. Scand. 2001 Feb; 45(2): 167–72

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INFLUENCE OF AGE OF RED CELLS ON HAEMOGLOBIN INCREMENT AFTER TRANSFUSION TO CRITICALLY ILL PATIENTS WITHOUT CLINICALLY APPARENT BLEEDING

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INTRODUCTION. Despite evidence that anaemia is well tolerated by most critically ill patients [1], red cell transfusion remains a common intervention to increase haemoglobin concentration (Hb). Stored red cells undergo changes that may alter cell survival after transfusion, but there are no data relating the age of transfused cells to subsequent changes in Hb in the critically ill.
METHODS. As part of an audit of transfusion practice in our ICU daily data were prospectively collected regarding transfusion, indications for transfusion, the number of red cells transfused, age of the units, and daily Hb. The total data set consisted of 1146 patient days in 176 patients (data complete for 93 % of total patient days). There were 159 transfusion episodes (a day on which 1 or more red cell units were prescribed) for anaemia without clinically apparent bleeding (80 % total transfusion episodes). From these data we extracted transfusion episodes for which the age of red cell units transfused varied by no more than 5 days, and no further transfusion occurred during the following 48 hours. These data were arbitrarily divided by mean red cell age into 3 groups: age 4–13 days, 13.1–22 days, 22.1–31 days.
RESULTS. 68 transfusion episodes fulfilled the set criteria. The mean (SD) increment for the whole group was 6.2 (4.4)g/L on the day after transfusion and 3.4 (3.0)g/L 2 days after transfusion. Overall there was no correlation between age of red cells and Hb change (r = 0.09). There were no significant differences between the 3 groups (table 1).

	Mean red cell Age 4–13 days (n = 23)	Mean red cell Age 13.1–22 days (n = 25)	Mean red cell Age 22.1–31 days (n = 20)
Age of red cells	8.9 (3.1)	17.8 (2.5)	27.7 (2.5)
Baseline Hb (g/L)	77.6 (9.9)	75.7 (6.1)	78.5 (8.1)
No. units transfused	2.0 (0.7)	1.96 (0.7)	1.95 (1.3)
Hb change day 1 (g/L)	5.8 (3.4)	6.5 (5.8)	6.8 (4.0)
Hb change day 2 (g/L)	2.9 (1.7)	3.3 (4.4)	4.0 (2.3)

Changes in haemoglobin concentration after transfusion with stored red cells of different ages. All values mean (SD). No significant differences between the groups.

CONCLUSION. We found no relation between the age of transfused red cells and changes in Hb on the 2 days following transfusion. Variances of the Hb changes were wide suggesting the interaction of many factors in addition to age of transfused cells. A larger study is needed to exclude an age of blood effect. The mean increase in Hb was smaller than expected irrespective of the age of red cells, and decreased significantly between the first and second post transfusion day. This may indicate reduced red cell survival in the critically ill.
REFERENCE. [1] Hebert PC et al. New Engl J Med 1999; 340: 409–17

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PLASMA INTERLEUKIN (IL)-8 LEVELS INCREASE FOLLOWING SINGLE UNIT RED BLOOD CELL TRANSFUSION IN SEPTIC PATIENTS

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INTRODUCTION. Evidence accumulates that transfusion of packed red blood cells (PRBC) may be harmful in critically ill patients through enhancing microvascular damage, by decreasing oxygen delivery and by the release of noxious cytokines. IL-8 is a potent chemo-attractant and primer of neutrophils and is therefore considered to play an important role in sepsis-induced organ failure. We investigated to what extent the IL-8 concentration in stored PRBC influences systemic IL-8 levels following transfusion in septic patients.

METHODS. Sepsis was defined according to ACCP/SCCM consensus guidelines. All patients received standard resuscitation treatment and were stable during the study period. PRBC stored at 4 °C for a maximum of 32 days were transfused at a Hb level < 8.5 g/dL using a 40 μm PALL blood transfusion filter. IL-8 was measured by chemo-illuminiscence immunoassay in a unit of PRBC and before, 1 and 2 hours after its transfusion in a septic patient. The lower limit of detection was 5 pg/mL.

RESULTS. 13 patients were consecutively enrolled. Male/female ratio was 9/4. Median age and APACHE II score were respectively 61 years (range 30–83) and 15 (range 10–39). Causes of sepsis were pneumonia (n = 11), urosepsis (n = 1) and cholecystitis (n = 1). The mean duration of PRBC storage was 24 ± 8 days. Compared to pretransfusion plasma levels (36.0 ± 7.8 pg/mL), IL-8 increased after transfusion (respectively 48.5 ± 10.8 pg/mL at 1 hour; p = 0.06 and 45.8 ± 7.7 pg/mL at 2 hours; p = 0.09; mean ± SEM, Willcoxon signed rank test). Il-8 levels in the blood concentrate were highly correlated with the change in patients' IL-8 levels 1 hour after transfusion (r 2 = 0,72; p = 0.006). IL-8 content in PRBC and storage time were not correlated. Eight patients survived till ICU discharge. Of the 5 non-survivors, 3 developed ARDS within 3 days after PRBC transfusion.

CONCLUSION. Transfusion of even a single unit of PRBC in clinical sepsis caused an acute and sustained increase in plasma IL-8 levels. This increase was directly correlated with the IL-8 concentration present in the stored blood. Given the potential impact of IL-8 on development of organ failure in septic conditions, these findings may have clinical importance.

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AGE OF STORED RED CELLS DOES NOT INFLUENCE INDICES OF OXYGENATION AFTER TRANSFUSION TO CRITICALLY ILL PATIENTS: RANDOMISED CONTROLLED TRIAL (RCT)

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INTRODUCTION. A previous unblinded observational study in the critically ill found a retrospective association between increasing age of transfused red cells and worsening gastric oxygenation assessed by gastric tonometry [1]. We carried out a prospective double-blind RCT that compared oxygenation indices in critically ill patients during and after red cell transfusion with leucodepleted red cells stored for either < 5 days or > 20 days.
METHODS. Stable critically ill patients with haemoglobin (Hb) < 9 g/dL and no clinically-evident bleeding were randomised to receive 2 units of leucodepleted red cells donated *either* < 5 days *or* > 20 - days from the date of study. The study was double-blind with randomisation done in the blood bank. Study end-points were gastric-arterial CO_2 gap and gastric intramucosal pH (pHi) measured by automated gas tonometry, whole blood lactate concentration, plasma pH, and base excess. The 2 red cell units were transfused according to a standardised protocol over 3 hours. Data were collected during baseline (2 hours, 5 data sets), transfusion (3 hours, 5 data sets), and post transfusion (5 hours, 5 data sets) periods. We explored differences between the groups over the study period using ANOVA and by comparing baseline to post transfusion period changes.
RESULTS. 22 patients were randomised (10 "fresh" red cells < 5 days old; 12 "stored" > 20 days old). Mean age of red cells in the groups was: "fresh" 2.3 (SD 0.4) days; "stored" 28.2 (SD 3.2) days. Mean increases in Hb concentrations were similar ["fresh" 1.5 (SD 0.8) vs "stored" 1.5 (SD 0.7)g/dL]. We found no statistically significant differences between the groups for any indices of global or regional oxygenation (table 1). There was a non-significant trend for worsening PCO_2 gap with the stored blood.

	"fresh" red cell group (n = 10) baseline-post transfusion	"stored" red cell group (n = 12) baseline-post transfusion
Gastric-arterial CO_2 gap (kPa)	0.41 [1.37,-5.51]	–0.37 [1.19,-2.22]
pHi	–0.02 [0.22,-0.08]	0.02 [0.14,-0.04]
Whole blood lactate (mmol/L)	–0.10 [1.25,-0.35]	–0.03 [0.82,-2.01]
Base Deficit (mmol/L)	0.70 [2.81,-0.20]	0.71 [2.64,-0.95]
Arterial pH	0.00 [0.03,-0.04]	0.00 [0.03,-0.03]

Changes in indices of oxygenation from baseline (mean of 5 values) to post transfusion (mean of 5 values) periods for the "fresh" (< 5 days from donation) and "stored" (> 20 days from donation) red cell groups. All changes median [maximum, minimum]. No significant differences between groups.

CONCLUSION. In stable anaemic critically ill patients we found no clinically or statistically significant differences in indices of global or regional oxygenation between patients transfused with 2 units of leucodepleted red cells stored either for < 5 days or > 20 days. This contrasted with a retrospectively observed correlation in patients with septic shock [1].
REFERENCE. [1] Marik PE, Sibbald WJ. JAMA 1993; 269: 3024–3029

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ANAEMIA AND BLOOD TRANSFUSION IN CRITICAL CARE (ABC) SURVEY: ORGAN FUNCTION AND MORTALITY IN TRANSFUSED PATIENTS

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INTRODUCTION. Anaemia is a common problem in critically ill patients admitted to intensive care units (ICUs). The impact of anaemia in ICU patients on morbidity and mortality is poorly defined. Anaemia is typically treated with blood transfusions to help maintain adequate oxygen delivery. This study was designed to assess the incidence of anaemia and the use of transfusions in critically ill patients throughout Western Europe.
METHODS. This prospective, observational survey collected anaemia and blood transfusion data on 3534 patients from 146 ICUs. Data on organ function were also collected using the Sequential Organ Failure Assessment (SOFA) score. For all admissions in participating ICUs during a 2-week period, data were collected daily for a maximum of 28 days or until hospital discharge, transfer, or death.
RESULTS. The mean admitting haemoglobin (Hb) was 11.3 ± 2.3 g/dL with 63 % having an admitting Hb less than 12 g/dL and 29 % with less than 10 g/dL. The transfusion rate during the ICU period was 37.0 % and was 12.7 % during the post-ICU period; the overall transfusion rate over the 28-day period was 41.6 %. Incidence of transfusion increased with age, ICU LOS, and organ dysfunction. Haemoglobin levels for transfused patients were consistently lower than for nontransfused patients upon ICU admission (10.1 g/dL versus 12.2 g/dL) and throughout the follow-up period. The last reported Hb was lower in transfused patients (10.5 g/dL versus 11.6 g/dL) despite receiving transfusion therapy. At every level of admitting organ function, nontransfused patients showed a greater improvement in organ function than transfused patients. ICU mortality was 13.5 % and 28-day overall mortality was 20.2 %. The overall mortality rate was significantly higher for transfused patients (29.0 %) than for non-transfused patients (14.9 %). Mortality differed significantly by Hb group for patients who were transfused with mortality rates increasing as Hb decreased. Transfused patients had higher mortality rates at every admitting Hb level when compared to nontransfused patients. However, mortality did not differ by Hb in nontransfused patients. Mortality increased as organ dysfunction increased in both transfused and nontransfused patients, however, mortality was higher in transfused patients at all levels of organ dysfunction with the exception of those with the most severe organ failure (those with SOFA > 7, for whom mortality rates were similar).
CONCLUSION. This survey provides evidence of the association between transfusions and age, ICU LOS, organ dysfunction, and mortality. Transfusions should be used cautiously and sparingly, and alternatives should be further evaluated.
REFERENCE. Hebert, PC, et al.: Does transfusion practice affect mortality in critically ill patients? American Journal of Respiratory and Critical Care Medicine 1997; 155: 1618–1623.

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THE IMPACT OF CHANGING THE LOCAL TRANSFUSION STRATEGY BETWEEN 1990 AND 2000, ON OUTCOME AFTER INTENSIVE CARE ADMISSION

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INTRODUCTION. Recent randomised controlled trials performed in ICU patients showed that a transfusion strategy implementing a transfusion trigger of 7.0 g/dl was at least as effective as a liberal transfusion strategy with a transfusion trigger of 10 g/dl, although it remains unclear if high risk cardiac patients with unstable angina and acute myocardial infarction might benefit from higher Hbg levels (1,2). We evaluated, therefore, the change of our institutional transfusion policy, which implied in 1999 a transfusion trigger of 8.5 g/dl, with our older policy, using a transfusion trigger of 10.0 to 10.5 g/dl.
METHODS. Data of all consecutive ICU patients treated during a period of 6 months in a medical- surgical- adult ICU of a university hospital were included. Group A comprised of 144 patients between January and June 1990, while Group B involved 351 patients between January and June 1999. Retrospective analysis of prospectively collected data included 35 variables related to patient characteristics, transfusion, oxygen-delivery parameters and outcome. Statistical analysis was with analysis of variance and Chi2.
RESULTS. Although the patient groups were different in size (n = 144 vs. n = 351), they were comparable, as far as their severity of illness scores (APACHE II) at admission is concerned. However, although the patients' age was significantly higher in group B compared to group A, the length of stay (LOS) and the mortality rate were significantly lower in this group compared to group A respectively (table 1). FFP and albumin administration, however, were not signifficantly different between groups. Table 1 displays the univariate analysis of baseline- and outcome characteristics of patient groups studied.

	Liberal transfusion policy (1990)	Restrictive transfusion policy (1999)	p value
APACHE II	19.9±8.4	21.1±7.7	ns
30-day Mortality (%)	42.2 %	32.8 %	< 0.01
Age (yr)	46.4±22.9	53.0±21.3	< 0.01
Hct – at admission (%)	37.2±6.8	34.9±6.3	< 0.01
Hct – at discharge (%)	34.3±6.5	30.8±3.3	< 0.000
RBC transfusion (u)	2.1±4.1	0.9±1.4	< 0.000
Length of Stay (days)	7.9±9.0	5.4±6.1	< 0.01

CONCLUSION. A restrictive transfusion strategy with a transfusion trigger of 8.5 g/dl is superior to a liberal transfusion strategy of 10.0 to 10.5 g/dl. Patients in the restrictive strategy group, although admitted in the ICU with a lower Hct compared to group A, were transfused with less RBC's. FFP and albumin administration, however, remained unchanged. Although other factors may contribute to the improvement in survival, the restrictive transfusion strategy had a positive impact on outcome and on LOS in the ICU.
REFERENCE. 1. Hebert,P.C. et al: NEJM 1999;340: 409–17 (2) Hebert,P.C. et al: CCM 2001;29: 442–4