BEST FREE PAPER SESSIONS

General and regional anaesthesia

1 High PEEP in the perioperative management of the morbidly obese
Erlandsson K, Odenstedt H, Olegård C, Söndergaard S, Lundin S, Stenqvist O
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Avoiding atelectasis and gas exchange impairment is important in peri-operative management of morbidly obese patients.

Aims: Titration of PEEP level to preserve end expiratory lung volume (EELV) without compromising circulation peroperatively.

Methods: 15 patients, BMI of 49 (37–62), scheduled for laparoscopic gastric bypass surgery were studied in 15° head up position. Patients were anaesthetised with propofol, fentanyl, rocuronium and ventilated with an oxygen/air mixture with FIO2 0.3. Electric Impedance Tomography (EIT) (Dräger/GOE MFD) was used for on-line monitoring of EELV changes. EIT was calibrated with N2-washout EELV measurements and stepwise increased tidal volumes. Cardiac index (CI) was measured with esophageal doppler (Cardio-Q), oxygen consumption with indirect calorimetry and shunt calculated using standard formulas.

Before optimising PEEP, 0.5 l of colloid was infused followed by another 0.5 l before surgery started. Measurements were taken during PEEP optimisation and during 30 minutes after the surgical procedure.

Results: The lowest PEEP with stable EIT baseline, i.e. stable EELV, was 15 ± 2 cmH2O. EELV increased significantly from 1.7 ± 0.4 before to 2.2 ± 0.51 (P < 0.001) after surgery. CI increased from 2.6 ± 0.51/min before to 3.1 ± 0.81/min after the surgical period (P < 0.01) and shunt flow remained stable, 14 ± 5% before and 12 ± 4% after the surgical period.

Conclusions: Optimising preload using colloids made it possible to titrate PEEP according to EIT measurements of lung volume changes. Adequate PEEP was 13–17 cmH2O, which was maintained after induction until extubation, when CPAP was instituted. With this regime EELV increased during the procedure, shunt flow was stable and CI increased.

2 The effects of PEEP upon subdural ICP and CPP during craniotomy
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Adult respiratory distress syndrome (ARDS) develops in up to 20% of patients with severe head injury. Positive end-expiratory pressure (PEEP) is often required to support oxygenation. It is well known that PEEP might increase intracranial pressure (ICP) in intensive care patients, but the effects of PEEP, however, has not been investigated during craniotomy.

Method: Subdural ICP, mean arterial blood pressure (MABP) and CPP were studied during application of 7 cmH2O PEEP in 14 patients with cerebral tumors and 3 patients with subarachnoidal hemorrhage. In 14 patients jugular bulb pressure (JBP) was measured simultaneously. The pressures were recorded one minute before and at 0, 1, 2, and 3 minutes after PEEP application. Controlled ventilation was applied in all patients. The maximal respiratory pressure was recorded.

Results: The maximum respiratory pressure increased from 16 to 23 cmH2O. During the recording period MABP decreased from 71.5 to 68.6 mm Hg (P = 0.002) subdural ICP increased significantly from 5.3 to 6.7 mm Hg (P < 0.001), CPP decreased from 66.5 to 61.9 mm Hg (P < 0.001), and JBP increased from 4.3 to 5.6 mm Hg (P = 0.002). The increase in ICP was not correlated to the ICP level before PEEP application (R = 0.108, P = 0.679). The linear regression for the relationship between increase in JBP (ΔJBP) and increase in ICP (ΔICP) was found to be significant (R = 0.821, P < 0.001).

Conclusion: During craniotomy PEEP of 7 cmH2O increases ICP and decreases MABP and CPP significantly. The increase in ICP is correlated to the increase in jugular bulb tension, but not to the level of ICP obtained just before PEEP application.

3 A comparative study between desflurane and sevoflurane in day-case varicose vein surgery using the laryngeal mask airway with spontaneous breathing
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Aim: The aim of the present study was to compare desflurane with sevoflurane during an intermediate day-case surgical procedure with special reference to quality of anaesthesia and recovery.

Method: We conducted a prospective randomised single-blinded study in 70 ASA I-II patients undergoing elective ambulatory varicose vein surgery. All patients were anaesthetised according to a standardised protocol including multi-modal analgesia and anti-emetic therapy; patients were randomised to receive either sevoflurane or desflurane as main anaesthetic while breathing spontaneously through a laryngeal mask airway (LMA). Fresh gas consisted of oxygen in air.

Results: No signs of stressful haemodynamics were observed during induction or surgery and there was no significant difference in incidence of airway irritation. Emergence was significantly faster in patients anaesthetised with desflurane. Recovery was uneventful in all patients and pain and PONV were infrequently seen and with similar profile/incidence in both groups. Patients satisfaction was overall high and without difference between groups.

Conclusion: Both agents, desflurane and sevoflurane, can be used as main anaesthetic during ambulatory anaesthesia with the laryngeal mask airway and without muscle relaxation, desflurane being associated with faster recovery, and a fully comparable postoperative course.

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4 Is thoracic epidural analgesia superior to conventional postoperative pain management after coronary bypass surgery?
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Aims: The aim of this study was to compare thoracic epidural analgesia (TEA) with conventional postoperative pain therapy (CPT) regarding extubation, VAS-scores, mobilization and lung function.

Methods: Consecutive randomised patients for first time coronary bypass surgery were included. The TEA group received TEA until the 3rd postoperative morning. Lung function was measured on the 1st, 3rd and 5th postoperative day. VAS-score and mobilization were registered.

Results: 152 patients were studied from which 71 received TEA. They were extubated and mobilized earlier than the CPT group and VAS-scores until the 1st postoperative morning were also lower. Subsequently we found no significant difference between the two groups regarding VAS-score and mobilization. In both groups postoperative lung functions decreased and did not reach preoperative values on the 5th day, without significant difference between the TEA and the CPT group.

Conclusion: The use of TEA allowed early extubation and mobilization. In the TEA group lower VAS-scores were found until the 3rd postoperative morning. Thereafter no differences between the two groups regarding VAS-score and mobilization were found. Despite the initial results, TEA did not prevent postoperative decrease in lung function.

5 The effect of patient position during performance of CSE anaesthesia for C-section
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Aims: The aim of the present study was to evaluate whether placing the patient of the sitting or lateral decubitus position during low-dose combined spinal-epidural anaesthesia would affect the occurrence of hypotension and the technical aspects of the block.

Methods: After prehydration with 1000 mL Ringer’s solution and 500 mL Hydroxyethylstarch 60 elective Caesarean section patients were randomly assigned to receive a spinal injection at the L3-L4 or L4-L5 interspace in the lateral decubitus or the sitting position. The injected combination consisted of 6.6 mg hyperbaric bupivacaine with sufentanil 3.3 μg. After securing the epidural catheter patients were turned to the supine position and a prophylactic dose of 5 mg ephedrine was given. Registered were the upper sensory level and motor block at incision and after wound closure, blood pressure at 2 min. intervals, ephedrine requirements, side-effects, Apgar scores and umbilical blood pH.

Results: Patients of the sitting group experienced less hypotension and required less ephedrine (P=0.012). Less problems with identifying the epidural space were noticed with this position (P=0.01). However more patients in this group required additional local anaesthetics by the epidural route (35% vs 3%, P=0.007). In the lateral group more patients had sensory blocks spreading more cephalad than T3 (P=0.014). There were no differences between both groups with respect to motor block at incision and at leaving the operating room, nausea/vomiting and pruritus. Apgar scores did not differ but umbilical artery pH values were significantly higher in patients of the sitting group (7.31±0.04 vs 7.26±0.03, P=0.02).

Conclusion: It was concluded that performing a CSE technique for Caesarean section in the sitting position was technically easier and caused less hypotension explained by less cephalad spread of the anaesthetic solution.

NO, APC and HES

6 Minor influence of endogenous nitric oxide on pulmonary perfusion distribution in prone sheep with PEEP ventilation
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Aims: PEEP increases pulmonary nitric oxide (NO) generation (Persson et al, Anesthesiology 1995;82:969). We examined the role of NO on lung blood flow distribution in prone sheep ventilated with 10 cmH2O PEEP.

Methods: Distribution of blood flow was measured in about 1000 lung regions per animal in 11 anesthetized sheep. Measurements were done with iv. injections of 15 μm radioactive microspheres at baseline, after inhibition of nitric oxide synthase (NOS) with L-NAME (25 mg/kg) and after reversal of NOS-inhibition with L-Arginine. Perfusion heterogeneity (coefficient of variation, CVvar) was partitioned into a gravitational (CVgrav) and an isogravitational (CVarogr) component (Melsom et al, Acta Physiol Scand 1997;159:199).

Results: The vertical distribution of perfusion remained unchanged by the interventions. Differences in measures of heterogeneity were not statistically significant (Table).

<table>
<thead>
<tr>
<th></th>
<th>No PEEP</th>
<th>PEEP 10 cmH2O</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (n=3)</td>
<td>I-NAME (n=3)</td>
</tr>
<tr>
<td>CVtotal</td>
<td>0.39±0.07</td>
<td>0.39±0.07</td>
</tr>
<tr>
<td>CVgrav</td>
<td>0.29±0.07</td>
<td>0.32±0.06</td>
</tr>
<tr>
<td>CVArogr</td>
<td>0.26±0.07</td>
<td>0.29±0.06</td>
</tr>
</tbody>
</table>

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Conclusion: Endogenous NO does not play a major role in distribution of blood flow in the healthy sheep lung ventilated with PEEP.

7 Nitric oxide regulates regional pulmonary perfusion

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Aims: Improved oxygenation has previously been shown in patients with acute lung injury when ventilated in prone position. Other investigations have shown that V/Qs were more uniform in prone than in supine position leading to a more efficient gas exchange while in the prone position compared with supine. We hypothesized that this was due to higher regional production of nitric oxide in dorsocaudal lung regions.

Methods: We measured nitric oxide synthase mRNA expression and nitric oxide production by citrulline assay in ventral and dorsal lung tissue from patients and pigs. In vitro responses of lung arteries from dorsocaudal and cranioventral regions of porcine lungs to different endothelium-dependent vasodilators were studied in vitro. In volunteers, regional lung perfusion in prone and supine positions was assessed by Single Photon Emission Computed Tomography using 99mTc macroaggregated albumin before and after inhibition of nitric oxide synthase by Nω-monomethyl-L-arginine infusion.

Results: Nitric oxide mRNA expression and nitric oxide production were significantly higher in dorsal compared with ventral human lung regions. Nitric oxide synthesis was higher also in dorsal porcine lung tissue. Acetylcholine, bradykinin and nitric oxide synthase by HES 200 when dosed repeatedly

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Background and aims: Repeated infusions of hydroxyethyl starch (HES) may result in marked plasma accumulation and change over time of the pharmacokinetic behaviour of HES. The aim of this trial was to study how a novel low molecular weight HES (HES 130/0.42/6.5) would compare with conventional HES 200 in this respect.

Methods: HES 130 and HES 200 (50 g HES within 4 h/day) were studied in a randomized sequence cross-over trial (2 periods of 5 consecutive days) on 9 healthy volunteers. HES plasma con
4 Intensive care outcome

concentration (also used for kinetic computations) and pharaco-
dynamic properties were measured.

<table>
<thead>
<tr>
<th>Result</th>
<th>Day</th>
<th>AUC$_{20}$</th>
<th>C$_{max}$</th>
<th>t$_{1/2}$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HES 130</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Day 1</td>
<td>28.4 ± 6.3</td>
<td>4.3 ± 0.7</td>
<td>3.8 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>Day 5</td>
<td>36.6 ± 8.3</td>
<td>4.4 ± 0.4</td>
<td>4.7 ± 0.4</td>
</tr>
<tr>
<td></td>
<td>Day 10</td>
<td>61.4 ± 6.2</td>
<td>6.1 ± 0.7</td>
<td>4.7 ± 0.7</td>
</tr>
<tr>
<td></td>
<td>Day 20</td>
<td>88.6 ± 6.2</td>
<td>6.9 ± 0.5</td>
<td>8.7 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>Day 30</td>
<td>88.6 ± 6.2</td>
<td>6.9 ± 0.5</td>
<td>17.4 ± 3.0</td>
</tr>
</tbody>
</table>

(1Means ± SD; 2area under concentration curve from 0–24h (mg/ml * h); 3maximal concentration (mg/ml); 4concentration at 20h after infusion end (mg/ml); 5elimination half-life (h); 6below quantification limit).

HES 130 and HES 200 showed significantly different time profiles of pharmacokinetic coefficients (P < 0.00000; ANOVA). Relative change of blood volume and colloid oncotic pressure were similar despite the marked increase of colloid concentration and half-life with HES 200.

Conclusions: Repeated administration of HES 130 does not lead to accumulation and shows better time-to-time reproducibility of the pharmacokinetic coefficients than HES 200. As the accumulation of HES 200 does not enhance its volume effect, avoidance of accumulation with HES 130 is deemed to improve reliability and safety of the colloid.

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### Intensive care outcome

#### 11 Prevalence of signs of critical conditions and emergency responses in hospital wards – the SOCCER study

Harrison G, Jacques T, Kilborn G, McLaws ML

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**Aims:** To estimate the prevalence of recordings of disturbed physiological variables in adult patients which may be appropriate ‘call criteria’ for Medical Emergency Teams (MET).

**Methods:** Cross-sectional survey of 3160 admissions in general wards in 5 hospitals in a 14 day period. Recordings of 26 potential early signs (ES) and 21 late signs (LS) of critical conditions were collected. These ES and LS were agreed a priori by a panel of senior ICU and Emergency clinicians. They included published MET call criteria.

**Results:** 54.7% of admissions had ≥1 recording of ES, & 16.0% had ≥1 LS. In rank order of recordings per 100 admissions, the top 10 ES were SpO$_2$ 90–95% (193.7), systolic blood pressure (SBP) 80–100 mmHg (85.2), pulse rate 40–49 or 121–140 bpm (32.0), SBP 181–240 mmHg (23.0), “Other” (22.1) (eg breathlessness, temperature >38°C), decreased urine output (15.5), BSL 16–23 mmol/L (14.6), complaint of chest pain (13.6), altered mentation (13.5). The most prevalent LS were SpO$_2$ < 90% (31.5), pulse rate <40 or >140/min (6.6), SBP < 80 mmHg (4.2), GCS ≤ 8 (3.8), unresponsiveness to verbal commands (2.4), failure to reverse variable <1 hour (2.0), respiratory rate <3 or >40/min (0.9) airway obstruction/stridor (0.9), urine output <200 mls/8 hours (0.7), PaO$_2$ < 50 mmHg (0.7). Signs were often recorded on multiple occasions.

**Conclusions:** There was a high incidence of recordings of disturbed physiological variables. Changes to hospital emergency response systems to include MET should be supported by training programs for nursing and junior medical staff on the management of early and late signs of critical conditions.

#### 12 Is risk adjustment for old age adequate in the APACHE II system?


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**Aims:** To examine risk adjustment with the APACHE II system within discrete age groups in the Swedish Intensive Care Registry.

**Methods:** Admissions (n = 20,403) to 28 ICUs during 2002 and 2003 were grouped according to age as in the APACHE II system (16–44, 45–54, 55–64, 65–74, 75 y and older) and outcome was plotted on an APACHE II risk-adjusted trend chart. Vital status at 30 days after admission was secured from a national database.

**Results:** Survival in the oldest age group was constantly lower than expected during the study period.

Conclusions: Risk adjustment for age, particularly old age, was poor in this large cohort of admissions to Swedish ICUs. This indicates a need for refitting the original risk model to current Swedish data.
13

Correlation between cortisol response in the short synacthen test and survival after admission to intensive care

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Aims: Recently, there has been renewed interest in corticosteroid therapy for patients with septic shock. While some studies have confirmed the usefulness of moderate doses of glucocorticoids during septic shock others have not. The study reported here audited the cortisol response of patients with septic shock and correlated them with outcome after admission to intensive care (ITU).

Methods: A short synacthen test was undertaken in patients with septic shock admitted to our ITU between April 2003 and December 2004. Nonresponders (cortisol rise less than 250 nmol l⁻¹) were commenced on hydrocortisone 100 mg/24 hours. Pearson’s correlation coefficient was used to determine any statistical relationship between clinical improvement and cortisol response in the short synacthen test.

Results: Of 524 patients admitted to ITU 127 (24.2%) underwent the short synacthen test. Responders and Nonresponders numbered 40 (31.5%) and 87 (68.5%) respectively. There was no statistical correlation (0.314, not significant) between cortisol response in the short synacthen test and improved outcome in patients with septic shock.

<table>
<thead>
<tr>
<th>Short synacthen test</th>
<th>Clinical improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responder</td>
<td>Yes 19</td>
</tr>
<tr>
<td></td>
<td>No 17</td>
</tr>
<tr>
<td>Nonresponder</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>38</td>
</tr>
</tbody>
</table>

Conclusions: Cortisol response in the short synacthen test and subsequent steroid replacement in nonresponders was not associated with improved survival in patients with septic shock. Furthermore, responders, 31.5% of patients, avoided unnecessary steroid intervention.

14

Continuous EEG predicts neurological outcome after cardiac arrest and induced hypothermia

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Aim: The purpose of our study was to correlate EEG-patterns to outcome after cardiac arrest and induced hypothermia.

Methods: Twenty-five consecutive patients with coma after cardiac arrest (GCS ≤6) were treated with mild induced hypothermia (33 ± 1°C) for 24 h. Cold fluids were used for induction and the CritiCool® (MTRI Inc) for maintaining hypothermia and for controlled rewarming (0.5°C/h). Patients were sedated and continuous EEG with trend-analyses (NervusMonitor®, Taugagreining Inc.) was monitored until spontaneous awakening or persistent coma/death. The monitoring was blinded to the ICU-physician and only clinically evident seizures were treated. The EEG-pattern at the time of normothermia was assessed blindly by a neurophysiologist and correlated to patient outcome.

Results: All 25 patients survived until at least day 2 after arrest and EEG-monitoring was successfully performed. Seventeen of 25 patients regained consciousness and could leave the ICU, while 8 of 25 patients died in the ICU without regaining consciousness. All patients who did not regain consciousness had a flat EEG, electrical status epilepticus or suppression burst EEG pattern at normothermia. All patients who regained consciousness had a continuous EEG at normothermia.

Conclusion: EEG is an easily applied method. This pilot study favours continuous EEG monitoring as means of early prediction – time of normothermia – of cerebral outcome after cardiac arrest.

Observational study on the incidence of low central venous oxygen saturation in emergency admissions in a multidisciplinary ICU

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Introduction: Early optimization of oxygen transport guided by central venous oxygen saturation (ScVO₂) can improve outcome in septic patients (1). The aim of this study was to characterize different groups of emergency admissions to a multidisciplinary intensive care unit (ICU) with respect to ScVO₂.

Methods: During three month, emergently admitted patients were screened for the presence of a central venous catheter. ScVO₂ was measured at arrival and after the first six hours in the ICU. Outcome parameters were length of stay in hospital (LOS) and 28 day mortality.

Results: 82 patients were included in the study. Overall mortality was 21%. LOS was 20 ± 16 days (mean ± SD). Patients with a ScVO₂ < 60% at admission (n = 18) had a 2-fold, albeit not significant increase in mortality (33% vs. 18%; P > 0.05). In these patients, ScVO₂ increased during the first six hours from 52 ± 5% to 63 ± 9% (P < 0.05). Changes in ScVO₂ during the first 6 hours were not predictive for LOS or mortality.

<table>
<thead>
<tr>
<th>n</th>
<th>ScVO₂ (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Admission</td>
<td>After 6 h</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>21</td>
<td>65 ± 10</td>
</tr>
<tr>
<td>Septic</td>
<td>15</td>
<td>68 ± 11</td>
</tr>
<tr>
<td>Brain</td>
<td>13</td>
<td>79 ± 10</td>
</tr>
<tr>
<td>Respiratory</td>
<td>8</td>
<td>59 ± 12</td>
</tr>
<tr>
<td>Other</td>
<td>25</td>
<td>74 ± 12</td>
</tr>
</tbody>
</table>

*P < 0.05 vs. cardio.+ respiratory

Conclusions: Admission ScVO₂ < 60% is associated with a high mortality in emergency ICU patients. Although standard ICU treatment was able to increase ScVO₂ in these patients, mortality remained high. Patients with sepsis had already a normal ScVO₂ at admission, which was not further increased by standard ICU treatment.

Monitoring of fluid status

16 Right-ventricular end-diastolic volume and ejection fraction in the assessment of fluid response in early septic shock
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Introduction: Optimal intravascular fluid replacement is a fundamental component of intensive care treatment. Blood volume cannot be reliably assessed clinically, and there are no parameters which consistently predict the response to fluid administration. We assessed effects of volume challenges on right ventricular end-diastolic volume (EDV), ejection fraction (EF), stroke volume (SV) and central venous pressure (CVP) in patients with septic shock receiving volume challenges on clinical indication.

Methods: 10 patients admitted to the ICU with septic shock (age: 71 (45-78) years, SOFA score 13 (6-17), median, range) were monitored with a pulmonary artery catheter (PAC) with fast response thermistor. Colloid aliquots of 200 ml were administered over 10 minutes based on clinical indication. Hemodynamic and respiratory data were continuously recorded, and 2 min – mean values calculated before and after fluid administration. An increase of 2 mm Hg (CVP), and 10% (EDV, EF, SV), respectively, was considered significant.

Results: The treating physicians diagnosed 36 episodes of need for fluid administration (1–8/patient). Fluid administration was associated with an increase in CVP in 17 instances (47%), and an increase in SV in 4 (11%), in EDV in 3 (8%), and in EF in 2 (6%) instances, respectively.

Physiologic response  Proposed mechanism  Frequency of observations

EDV ↑; SV ↑  Correction of hypovolemia  1 (3%)
EDV ↑; SV →  Over-filling  2 (6%)
EDV →; SV ↑  Increased contractility  3 (8%)
EDV →; SV →  Vasodilatation  30 (83%)

Conclusions: In early septic shock, fluid administration seems to support vasodilatation. Interestingly, the traditional sign of a positive response to fluid – an increase in stroke volume – was hardly ever recorded, despite increasing CVP in half of the measurements. We propose that fast thermistor PAC can be used to assess both the underlying pathophysiology and the response to treatment in such conditions.

17 Effect of mechanical ventilation on inferior vena cava diameter in paediatric patients
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Aim: Echocardiographic measurement of the diameter of the inferior vena cava (DIVC) may be used to monitor perioperative volume status. This study was undertaken to investigate the effect of mechanical ventilation on diameter of the inferior vena cava (DIVC) variability and if this has any correlation to body weight.

Methods: The study was performed with ethical approval and parental informed consent. External echocardiography was used to assess DIVC in consecutive paediatric patients during sevoflurane anaesthesia. To visualize the inferior vena cava a two-dimensional echographic sector was used in sub-xiphoidal long axis view. The variation (ΔDIVC) was calculated as percent of the diameter.

Results: 36 patients aged 8 months to 16 years with an average weight of 31.5 kg (range 7.8–66.3) are included in this abstract. There was no correlation between body weight and ΔDIVC (r = 0.048). In spontaneously breathing patients (n = 20), IVC collapsed at inspiration. ΔDIVC was −12.7 ± 13.3%. In mechanically ventilated patients (n = 16), IVC expanded at inflation. ΔDIVC was 9.8 ± 14.1% (P < 0.001).

Conclusion: ΔDIVC has previously proven useful as a simple and non-invasive method to detect fluid responsiveness in mechanically ventilated adult patients1. ΔDIVC had no correlation to body weight. These results suggest this method is suitable to use in paediatric patients for assessing hypovolemia.

Reference
1. Intensive Care Medicine 2004;30:1740–1746

18 A new kinetic approach for estimating extravascular retention (“Third spacing”) of crystalloid fluid during surgery and anaesthesia
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Aims: We introduce a kinetic approach to study extravascular retention of fluid without involving radioactive tracers. Studies in sheep show that isoflurane might be associated with excessive third-space losses.

Methods: 30 patients undergoing thyroid surgery lasting for 134 ± 32 min received 25 ml/kg of acetated Ringer’s solution over 30 min. Anaesthesia was randomized to be based on either isoflurane or propofol. The distribution and elimination of infused fluid was estimated using volume kinetics based on the fractional dilution of haemoglobin over 150 min. This calculation accounted for the amount of fluid present in a system of exchange between a functional central (v1) and a peripheral (v2) body fluid space. Eliminated fluid that did not appear as urine was considered to have been “lost” from the kinetic system, either by evaporation, bleeding or sequestration within the body (“third spacing”).

Results: Plasma dilution increased by approximately 30% during infusion in both groups and thereafter remained half as high. The analysis showed that excess fluid volumes present in v1 and v2 over time were virtually identical in the isoflurane and propofol groups. The rate of water loss by evaporation, surgical plasma loss, and the extravascular retention averaged 2.0 ml/min (isoflurane) and 2.2 ml/min (propofol).

Conclusion: Thyroid surgery under general anaesthesia is associated with a fluid loss of 300 ml in addition to urinary excretion
Monitoring of fluid status

20

Initial high levels of TAU in ventricular cerebrospinal fluid correlate to one-year outcome after severe traumatic brain injury

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Aim: Traumatic brain injury (TBI) is a major cause of morbidity and mortality in young persons. There is lacking clinically available biomarkers important for the treatment & prognosis of TBI-patients. Tau proteins are micro-tubular binding proteins mainly found in neurons. We investigated if Tau levels in ventricular CSF (vCSF), during the initial post-traumatic days, correlated to one-year outcome after severe TBI.

Methods: Patients (n = 40) with severe TBI, (Glasgow coma scale (GCS), <8), were included. Tau in vCSF was collected from an inserted ventricular catheter & measured from day 0, (day of trauma), through day 11, using sandwich ELISA techniques. The results were correlated to one-year outcome measured by Glasgow outcome scale (GOS). Patients (n = 20) with normal pressure hydrocephalus (NPH) served as controls.

Results:
1. A correlation (P < 0.01) was found between initial vCSF-Tau levels & GOS at one-year.
2. Above a cutoff of 2126 pg/ml on day 2–3 in vCSF-Tau, the sensitivity to discriminate between dead and alive after one year was 100% and the specificity was 81%.
3. The sensitivity & specificity to discriminate between bad (GOS 1-3) & good outcome (GOS 4-5) was 83% & 69%, respectively, if vCSF-Tau was >702 pg/ml.
4. Patients with GOS 1 (dead) had higher vCSF-Tau levels on days 2–3, (P < 0.001) compared to both surviving patients (GOS 2-5) & NPH controls.

Conclusions: These results suggest that vCSF-Tau may be an important early marker for predicting long-term outcome of TBI patients. Furthermore, the results indicate that Tau may play a role in the pathophysiology of TBI.
ORAL FREE PAPER SESSIONS

Neurointensive care

21 How is cerebral perfusion pressure measured in Scandinavia?
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Aims: Cerebral perfusion pressure is an important parameter in neurointensive care patients. Cerebral perfusion pressure (CPP) equals mean arterial pressure (MAP) minus intracranial pressure (ICP). Since active treatment is often used to reach the target CPP recommended in the literature, it is important that CPP is measured in a reproducible way. The aim of this study was to find out how CPP is measured in neurointensive care departments in Norway, Sweden and Denmark.

Method: 5 Norwegian, 5 Swedish and 5 Danish neurointensive care departments answered a questionnaire regarding method for ICP-measurement, reference points for pressure calibration and positioning of the patient. Using a laser vater, the vertical height of all the reference points used was measured in 20 healthy volunteers. Results from the measurements and the questionnaire were used to calculate CPP-differences that can be attributed to differences in routines only.

Results: 8 of the 16 departments used parenchymal transducers, while 8 used ventriculostomy and external pressure transducer as first choice for ICP measurement. When an external ICP-transducer was used, the reference point was foramen Monroi (temple) in 8 of 13 depts, the forehead in 2/13, meatus acusticus externus in 2/13 and the ventral horn in 1/13. The reference point for MAP was foramen Monroi in 3/16, medio-acusticus externus in 2/13 and the ventral horn in 1/13. Differences in measurement routines would account for CPP difference between 16 and 28 mm Hg in the volunteers.

Conclusion: Standardisation of method for CPP measurement is needed.

22 Oxygenation and cerebral perfusion pressure improved in the prone position
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Aims: To analyse the effect of prone position on intracranial pressure (ICP), cerebral perfusion pressure (CPP) and systemic oxygenation in patients treated in neurosurgical ICU.

Methods: Eight patients with traumatic brain injury or subarachnoid haemorrhage, and acute respiratory failure were included. They were treated with sand bags on the chest, and in the prone posture. The weight of the sand bags was 10% of the patient’s body weight. A Stryker frame was used to turn patients prone.

Results: A significant improvement in PaO₂ was observed in the prone position, from 12.6 ± 1.4 kPa in supine to 15.7 ± 3.2 kPa in prone (P < 0.02). Both intracranial pressure and mean arterial pressure increased in the prone position, from 12 ± 6 to 15 ± 4 mmHg (P < 0.03), and from 78 ± 8 to 88 ± 8 mmHg (P < 0.005), respectively. The arterial pressure rose to a higher extent than intracranial pressure, resulting in improved cerebral perfusion pressure (from 66 ± 7 to 73 ± 8 mmHg, P < 0.03) in the prone position. Treatment using sand bags did not influence ICP and did not have any positive respiratory effect.

Conclusions: The prone position can be used to improve the oxygenation as well as cerebral perfusion pressure in patients with traumatic brain injury or subarachnoid haemorrhage. However, this method should be cautiously used within neurosurgical intensive care.

23 High quality resuscitation improves outcome in patients with severe traumatic brain injury (TBI)
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Background: Pre-hospital advanced life support is cost-intensive but could prevent or reduce secondary brain damage and thereby improve long-term outcome.

Aims: To test the hypothesis that patients with on-scene resuscitation by a high quality helicopter-based emergency team (HT) after severe TBI have a better one-year outcome assessed by Glasgow Outcome Scale (GOS) compared to patients with a paramedic-based (PT) resuscitation.

Methods: Analysis of 763 of a total of 1502 consecutive patients with TBI admitted to the Surgical Intensive Care Unit of a level I trauma centre. Inclusion criteria: native pre-treatment Glasgow Coma Scale (GCS) ≤ 8. Excluded: GCS > 8 (643); age < 6 years (64); incomplete data sets (32). Sampling period: 1984–2002.

Statistics: Mann-Whitney-Test, two-tailed. P < 0.05 considered as significant.

Results:

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Agea</th>
<th>ISSb</th>
<th>Admission timea</th>
<th>GCSb</th>
<th>GOSb</th>
</tr>
</thead>
<tbody>
<tr>
<td>HT</td>
<td>243</td>
<td>38.9 ± 18</td>
<td>32.4 ± 10</td>
<td>288 ± 100 min</td>
<td>5.2 ± 1</td>
<td>2.7 ± 1.6</td>
</tr>
<tr>
<td>PT</td>
<td>520</td>
<td>32.4 ± 20</td>
<td>30.5 ± 9</td>
<td>167 ± 29 min</td>
<td>5.3 ± 1</td>
<td>2.12 ± 1.7</td>
</tr>
</tbody>
</table>

Data presented as mean ± SD; *P < 0.05, ‡P = 0.08, #P = 0.29

Conclusions: Our data suggest that on-scene resuscitation by a HT improves GOS on year after severe TBI. Limitations: Long data collection period; age difference. Age has a high impact on outcome. Patients in the HT group were younger but had a higher Injury Severity Score (ISS).
24

Prediction of evolution to encephalic death (ED) in spontaneous intracerebral haemorrhage at admission to ICU

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Aims: to assess the risk of encephalic death in patients admitted to ICU presenting a spontaneous intracerebral haemorrhage analyzing volume and location of the haemorrhage.

Methods: we retrospectively analyze Glasgow (GCS) at admission, location and volume of the haematoma evaluating computerized tomography (CT) in 78 patients with the method A×B×C/2 described by Kothari. Patients are classified in two groups: group I for GCS less or equal to 8 and volume of the haematoma (lobar, basal ganglia, cerebellum or brain stem) higher than 65, 50, 20 and 5 cc. Group II include the rest. Statistical analysis of the volume is done by ANOVA test, location by Fisher’s exact test and GCS by Chi-square method.

Results: 25 out of 78 progress to brain death. 22 present lobar haemorrhage, 36 of basal ganglia, 12 of the cerebellum and 8 of brain stem. 31 belong to group I and 22 present ED. Only 3 patients of the group II progress to ED. Patients with a GCS less or equal than 8 have higher risk of evolution to ED (P<0.0001), Odds ratio 46.6 (95% confidence limits 5.83–373.38). Probability of brain death with this method has a sensibility of 88% and a specificity of 83%. Among lobar haematomas with volume > 65 cc the probability of brain death is 75% and specificity 64.3%. In basal ganglia haemorrhages with volume > 50 cc sensibility is 90.9% and specificity 92%. In haematomas of the cerebellum (volume > 20 cc) and brain stem (volume > 5 cc) sensibility is 100%. Brain death occurs the first five days of stay.

Conclusions: volume of haemorrhage measured by CT scan at admission, together with the GCS are very good and easy prognostic indicators of evolution of spontaneous intracerebral haemorrhage to brain death.

25

Organ donations in Iceland 1992–2002

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Aims: To acquire information of organ donations and organ waiting lists in Iceland 1992–2002, the beginning of an organ procurement system

Methods: Records of all patients treated at the ICU at Landspitali University Hospital in Fossvogur 1992–2002 were studied. Information of organ donations at other units and number on organ waiting lists was attained. Results are shown as medians (25th, 75th percentile).

Results: 527 patients died at the ward 1992–2002 (48 (45;52) annually). Of them 68 (13%) were declared deceased because of brain death. Permission for organ procurement was requested from 464 patients of the group II progress to ED. Patients with a GCS less or equal than 65, 50, 20 and 5 cc. Group II include the rest. Statistical analysis of the volume is done by ANOVA test, location by Fisher’s exact test and GCS by Chi-square method.

Results: 25 out of 78 progress to brain death. 22 present lobar haemorrhage, 36 of basal ganglia, 12 of the cerebellum and 8 of brain stem. 31 belong to group I and 22 present ED. Only 3 patients of the group II progress to ED. Patients with a GCS less or equal than 8 have higher risk of evolution to ED (P<0.0001), Odds ratio 46.6 (95% confidence limits 5.83–373.38). Probability of brain death with this method has a sensibility of 88% and a specificity of 83%. Among lobar haematomas with volume > 65 cc the probability of brain death is 75% and specificity 64.3%. In basal ganglia haemorrhages with volume > 50 cc sensibility is 90.9% and specificity 92%. In haematomas of the cerebellum (volume > 20 cc) and brain stem (volume > 5 cc) sensibility is 100%. Brain death occurs the first five days of stay.

Conclusions: volume of haemorrhage measured by CT scan at admission, together with the GCS are very good and easy prognostic indicators of evolution of spontaneous intracerebral haemorrhage to brain death.

26

The importance of magnetic resonance imaging in acute cerebellitis

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Aim: Acute cerebellitis is a rare condition often characterized by cerebellar dysfunction with rapid onset. Acute cerebellitis is postulated to result from viral and/or autoimmune etiologies. We report a case of acute fulminant cerebellitis and stress the importance of MRI.

Methods and results: A 4-year-old boy presented in our hospital, after an episode of tonic-clonic convolution. History revealed fever, 38–39°C, and an upper respiratory tract infection of two days’ duration. Upon arrival he underwent emergency intubation. After stabilization, physical examination revealed fixed and dilated pupils. Emergency CT scan showed marked obstructive hydrocephalus; the fourth ventricle was not visualized with suspicion of a posterior fossa mass. An external ventricular drain was immediately placed. He was ventilated and received Mannitol and Dexamethasone for brain edema and Valproic acid as anti-epileptic treatment. Although the CSF, obtained from the ventricular drain was unremarkable, he was empirically treated with Acyclovir and Cefotaxim. The same day MRI scan was performed and demonstrated a swollen cerebellum, with no other abnormality detected. The patient deteriorated rapidly died after 3 days. A diagnosis of acute cerebellitis was made based on the MRI findings. PCR confirmed the presence of Coxsackie A7 in the CSF.

Conclusion: Neuro-imaging plays an important role in the diagnostic work-up of patients with neurological symptoms. In the acute setting, a CT scan is indicated mainly to exclude evidence of raised intracranial pressure. MRI is the modality of choice to demonstrate cerebellar pathology, which may remain undetected on CT scan.

27

Glutamate concentration in the brain is not altered by an iv glutamine infusion in head trauma patients

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Aims: Intravenous glutamine supplementation to long staying multiple organ failure ICU patients decreases mortality. In head trauma patients concerns about the interstitial free glutamate concentration in the brain was studied. Here the effect of iv glutamine supplementation to head trauma patients upon interstitial free glutamate concentration in the brain was studied.

Methods: Head trauma patients in the neurosurgical ICU (n = 15) were studied. Patients were blindly randomised to receive glutamine and placebo in a cross-over design during two consecutive 24h periods. A glutamine infusion, 0.33 g/kg/20 h was
Neuroanaesthesia

28 Operating theatre time utilization in neurosurgery

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Aim: Operating theatre utilization is an important issue in all institutions. The aim of present analysis was to examine patient flow and time utilization of operating theatres on the department of Neurosurgery, Aarhus University Hospital.

Methods: Data on patient flow on 172 neurosurgical procedures were analyzed. The data were broken down into transit, preparation (induction of anaesthesia, preparation for surgery), surgery and recovery.

Results: The mean procedure time was 196 minutes, broken down into relevant parts, the time for transit, anaesthesia induction, preparation for surgery, surgery and recovery were 12, 24, 32, 104 and 27 minutes respectively. Actual operating time was 53% of the time theaters were in use. The patient population was divided into prone and supine procedures. Preparation for surgery was 5 minutes longer (29 vs. 34 minutes) when patients had surgery in supine position. Additionally data was broken down into different groups; craniotomies (n = 28), supine spine (n = 68), prone spine (n = 42), hydrocephalus surgery (n = 12) and miscellaneous (n = 22). Time for transit (10–15 minutes) and anesthetic induction (22–25 minutes) were equal in the groups. Surgical preparation was longer in craniotomy cases (44 minutes) than the other groups (28, 26, 35 and 36 minutes respectively). Actual operation time ranged from 56 to 153 minutes (hydrocephalus surgery – craniotomy), this corresponded to 57% and 59% of the actual theater time. Recovery in theater and transport to the recovery room ranged from 26 to 30 minutes in the groups.

Conclusion: The analysis can be used in optimization of patient flow and work related procedures in a neurosurgical-operating unit.

29 Cranioectomy for cerebral aneurysm surgery. Intracerebral pressure and cerebral perfusion pressure related to hunt and hess grade

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Aim: To determine the correlation between intraoperative ICP, CPP, and Hunt and Hess (H&H) grade in patients with cerebral aneurysm during anesthesia with propofol/fentanyl.

Methods: Ninety-eight nimodipine-treated patients were included. H&H grade was determined within one hour of anesthesia in un-intubated/non-sedated patients. Perioperative ICP and CPP were measured. Dural tension before opening of dura and the degree of brain swelling after opening of dura were assessed by the surgeon.

Results: No significant differences were found in the demographic data, PaCO2, PaO2, rectal temperature, mean arterial blood pressure or hemoglobin. ICP and number of patients with cerebral swelling increased progressively with increasing H&H grade (Table 1).

Conclusion: Patients with unruptured cerebral aneurysms and Hunt and Hess grade 1, anesthetized with propofol/fentanyl, have a low ICP and brain swelling rarely occurs after opening of dura. In Hunt and Hess grade 2 and 3, ICP and brain swelling are progressively increased.

30 Halothane as background anesthesia in studies investigating the neuroregenerative potency of the brain after neuronal damage


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Aim: The present study tested the suitability of halothane as a background anesthetic in studies investigating neurogenesis.

Methods: 24 fasted rats were randomly assigned to an ischemic and a non-ischemic group and were anesthetized, intubated, and ventilated. Anesthesia was maintained with 0.8% halothane in O2/air and fentanyl. In animals rendered ischemic (n = 12) bilateral carotid artery occlusion plus hemorrhagic hypotension to a MAP of 40 mmHg was performed for 10 minutes. In sham operated animals (n = 12) no ischemia was induced. Pericentral temperature, arterial blood gases and pH were maintained constant. 12 untreated rats were investigated as naive controls. In all rats bromodeoxyuridine (BrdU, a marker for newly generated cells) was administrated i.p. for seven days after ischemia/
randomization. After 28 days the brains were removed and hippocampal damage was evaluated using HE. Immunofluorescence double staining (BrDU and NeuN) was performed to label newborn neurons in the dentate gyrus.

**Results:** After cerebral ischemia eosinophilic neurons were observed in the hippocampus, while no histopathologic damage was found in sham operated or naïve animals. 28 days after ischemia/randomization in ischemic animals 5180, in sham operated rats 1760, and in naïve control animals 2150 new neurons were counted in the dentate gyrus.

**Conclusions:** 0.8% halothane and fentanyl produced adequate analgesia and hypnosis as indicated by lack of movement, physiological systemic hemodynamic variables, and EEG. Although halothane is supposed to be neuroprotective, neuronal damage occurred in halothane anesthetized animals after cerebral ischemia. The physiologic rate of neurogeneration in the dentate gyrus was about 2150 neurons in seven days. Two hours of halothane-anesthesia did not affect neurogenesis compared to naïve animals. After cerebral ischemia halothane allowed a 3-fold increase of newborn neurons. Therefore, low concentrations of halothane combined with fentanyl represents adequate background anesthesia in studies investigating adult neuronal stem cells after cerebral ischemia in ethical and neurogenic terms.

31

**The effect of low dose dexmedetomidine on internal carotid artery blood flow**

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**Aims:** To evaluate the effect of low dose dexmedetomidine (Dex) on internal carotid artery blood flow in patients.

**Methods:** 30 adults were randomly divided into 2 equal groups, one given a loading dose of Dex 0.4 μg/kg i.v. in 5 min then intravenous infusion of Dex 0.4 μg/kg/h over 30 min, the other saline. MAP, HR, SpO2, and end-tidal PCO2 & BIS were recorded as were diameter, blood flow velocity, blood flow of common carotid artery (CCA) and internal carotid artery (ICC).

**Results:** The blood flow velocity, blood flow of CCA showed an initial increase (P < 0.05) then returned to normal in 15 min. The blood flow velocity and blood flow of the ICC decreased by 17% – 21% (P = 0.05 – 0.01) at 15 and 25 min compared to baseline. MAP and HR decreased 15.2% and 19.8% respectively (P < 0.05); no respiratory depression was observed.

**Conclusions:** Low dose dexmedetomidine (0.4 μg/kg loading dose followed by 0.4 μg/kg/h continuous infusion) decreased the blood flow of the internal carotid artery.

32

**Comparative study of the ICP-reducing effect of hyperventilation, 10 degree reverse Trendelenburg position, mannitol, indomethacin or drainage during craniotomy for supratentorial tumours**

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Department of Anaesthesiology, Århus University Hospital, Denmark

**Aims:** The effect of low dose dexmedetomidine on internal carotid artery blood flow in patients.

**Methods:** From our database concerning subdural measurement we collected consecutive data from 65 patients. The inclusion criteria were: subdural ICP > 10 mmHg, combined with increased tension of dura. The following ICP-reducing managements were analysed: 5 min of hyperventilation (n = 15), 10 degree rTp (n = 15), mannitol treatment 0.5–1.0 g/kg (n = 15), drainage 17 ± 9 ml (n = 11), and indomethacin 0.5 mg/kg (n = 9). The changes in ICP (ΔICP) and CPP (ΔCPP) were calculated. The effect of mannitol was recorded 5 min after mannitol infusion, and the effects of rTp, drainage or indomethacin after one minute.

**Results:** No significant inter-group difference as regards demographic, neuroradiological findings or maintenance dose of anaesthesia was disclosed. Likewise, no significant differences in CPP or ICP before treatment were found. The ICP-decreasing effects of drainage, rTp, mannitol treatment or indomethacin were superior to hyperventilation, and drainage was superior to all other treatments. Compared with rTp and hyperventilation a significant improvement in CPP was observed with mannitol, indomethacin and drainage.

**Conclusion:** The ICP-reducing effect of drainage is superior to other treatment modalities. No differences were disclosed between rTp, mannitol treatment or indomethacin, but these modalities were superior to hyperventilation.

33

**Subdural ICP during craniotomy in patients without space-occupying lesions**

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**Aims:** At high ICP opening of dura is followed by brain swelling through the opening of dura. In patients with space-occupying lesion cerebral swelling rarely occurs at ICP < 5 mm Hg. On the other hand, at ICP > 13 mm Hg cerebral swelling occurs with high probability (1). Until now, no studies of ICP in patients without space-occupying cerebral lesions are available during craniotomy.

**Method:** In 30 patients with either unruptured cerebral aneurysm (n = 19) or trigeminal neuralgia (n = 11) ICP was measured during craniotomy before opening of dura. The patients were anaesthetized with propofol/fentanyl. Simultaneously, jugular bulb pressure (JBP) was measured in 11 patients. The degree of dural tension and cerebral swelling after opening of dura were also estimated.

**Results:** The median subdural ICP was 5 mm Hg (range 0–11). Dural tension was estimated as normal in 27 patients, and increased in 3 patients. In only one patient swelling of the brain occurred after opening of dura. ICP was not correlated to PaCO2, cerebral perfusion pressure or propofol maintenance dose, but significant correlations were found between weight of the patients and ICP (ICP = -0.12 + 0.083 × weight, P = 0.039, n = 30), and jugular bulb pressure and ICP (ICP = 1.30 + 0.882 × JBP; P = 0.001, n = 11).

**Conclusion:** In patients without space-occupying cerebral lesions, anaesthetized with propofol/fentanyl median ICP is 5 mm Hg. Cerebral swelling after opening of dura rarely occurs. ICP correlates with weight of the patients and jugular bulb pressure.

**Reference**

34 Spinal subdural pressure during surgery for spinal tumor and tethered cord

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Aim: To our knowledge studies of CSF pressure during spinal surgery have never been performed. In the present study subdural CSF pressure (CSFP) was measured before opening of dura in prone-positioned patients with spinal tumor or tethered cord.

Method: In six patients with spinal tumor and four patients with tethered cord the surgeon inserted a 12G needle through the dura and CSFP was measured with transducer technique. Mean arterial blood pressure (MABP) was measured as well. In 4 patients with tumor CSFP was measured caudally and cranially to the tumor. The effects of 5 min hyperventilation, 2 min 10 cm PEEP, and 10° reverse Trendelenburg (10-rTp) position upon CSFP were analysed.

Results: In neutral position the median (range) of CSFP was 9.0 mm Hg (4–17) and 8.0 mm Hg (0–10) in patients with tumor and tethered cord, respectively. In four patients the regional difference between caudal and cranial CSFP was 11, 7, 6 and 5 mm Hg. Hyperventilation reduced CSFP in 3 of 5 patients with tumor and 2 of 3 patients with tethered cord. The decrease in CSFP averaged 3.2 and 1.0 mm Hg, respectively. In the other patients CSFP was unchanged or increased ≤1 mm Hg. 10 cm PEEP increased CSFP in 4 of 6 tumor patients by 2.6 mm Hg, and in 1 of 4 patients with tethered cord. The effects of 10-rTp will be presented.

Conclusion: Spinal CSFP can be measured accurately during operation. Both hyperventilation and PEEP application changed CSFP. Regional difference in CSFP was found in patients with spinal tumors.

35 Comparative studies of immediate postoperative cerebral hyperaemia in patients subjected to either propofol/fentanyl or propofol/remifentanil anesthesia for supratentorial cerebral tumor

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Aims: In this prospective pilot study, the immediate postoperative values of flow velocity and arterio-venous oxygen difference (AVDO2) in patients subjected to either propofol/fentanyl (P/F) or propofol/remifentanil (P/R) anesthesia were compared.

Methods: From our database concerning subdural ICP measurement we collected consecutive data from patients subjected to supratentorial tumor surgery in P/F (n = 12), or P/R anesthesia (n = 14). The following parameters were obtained: Flow velocity (FV) over the middle cerebral artery and mean arterial blood pressure (MABP) immediately before anesthesia, during anesthesia, during spontaneous respiration immediately before extubation and 5 min after extubation. PaCO2 and AVDO2 were measured during anesthesia, on spontaneous respiration before extubation and 5 min after extubation.

Results: The demographic data did not show any inter-group difference. Cerebral perfusion pressure (CPP) and propofol maintenance dose were lower during anesthesia in the remifentanil group. Compared with preanesthetic levels of FV, significant percentage increases in FV and decreases in AVDO2 were observed during spontaneous respiration and five minutes after extubation in P/F anesthetized patients, but not during P/R.

No significant differences between groups were disclosed as regards demographic data, neuroradiological data, histopathological diagnose, PaCO2, temperature, SATv, AVDO2 or ICP. Before hyperventilation ICP averaged 6.8 mm Hg and 6.5 mm Hg, and during hyperventilation 5.1 mm Hg and 4.6 mm Hg in P/F and P/R anesthetized patients, respectively (P > 0.05). Both before and after hyperventilation CPP was significantly higher in the P/F group (mean values 80 mm Hg contra 70 mm Hg before, and 82 mm Hg contra 70 mm Hg after).

Conclusion: Postoperative cerebral hyperaemia is more pronounced in propofol/fentanyl anesthetized patients compared with patients anesthetized with remifentanil/propofol.

36 A comparative study of ICP and CPP in patients with cerebral tumours, anaesthetized with propofol/fentanyl or propofol/remifentanil

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Aims: To study subdural ICP and cerebral perfusion pressure (CPP) during craniotomy in patients with cerebral tumours anesthetized with either propofol/fentanyl (P/F) or propofol/remifentanil (P/R).

Methods: Subdural ICP, mean arterial blood pressure (MABP), CPP, PaCO2, jugular venous saturation (SATv), and AVDO2 were measured during anesthesia, on spontaneous respiration before opening of dura in supine-positioned patients with supratentorial tumours.

Results: No significant differences between groups were disclosed as regards demographic data, neuroradiological data, histopathological diagnose, PaCO2, temperature, SATv, AVDO2 or ICP. Before hyperventilation ICP averaged 6.8 mm Hg and 6.5 mm Hg, and during hyperventilation 5.1 mm Hg and 4.6 mm Hg in P/F and P/R anesthetized patients, respectively (P > 0.05). Both before and after hyperventilation CPP was significantly higher in the P/F group (mean values 80 mm Hg contra 70 mm Hg before, and 82 mm Hg contra 70 mm Hg after).

Conclusion: During craniotomy for supratentorial tumours subdural ICP does not differ significantly between propofol/fentanyl and propofol/remifentanil anaesthetized patients. Cerebral perfusion pressure, however, is significantly higher in propofol/fentanyl anaesthetized patients.
Regional anaesthesia

37 Cardiac output changes during onset of spinal anaesthesia in elderly patients
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Aims: To describe the changes in cardiac output (CO) during onset of spinal anaesthesia in elderly patients using the radial artery pressure curve.

Methods: Twenty-eight elderly (≥60 years) patients scheduled for elective plastic or orthopaedic lower limb surgery under spinal anaesthesia were included. CO was measured using a pulse wave algorithm derived from the radial artery pressure curve (LiDCO/PulseCO™). This method is based on a calibration where an intravenous injection of lithium chloride is given. Data collection ended when the patients were ready for surgery or if ephedrine was given.

Results: Data collection was terminated after a mean time of 16 min. At that time point, 12 patients had sensory loss at T7 or higher (the high block group – HBG) and 16 had a spread to T8 or lower (the low block group – LBG). In the HBG, CO had decreased 1.2 L/min vs. 0.1 L/min in the LBG (P = 0.02). Initially, however, CO increased to a maximum value after a mean of 7 min. This increase was 1.4 L/min in the HBG vs. 0.9 L/min in the LBG (P = 0.03), and occurred when MAP had decreased 14 mmHg on average. At termination of data collection, MAP had decreased 41 vs. 26 mmHg (P = 0.03) and a total of 18 patients had hypotension, defined as a 25% decrease in MAP.

Conclusions: Using a method with high time resolution, we were able to detect important changes in cardiac output during onset of spinal anaesthesia with a significant decrease only if sensory block reached T7 or higher. Interestingly, cardiac output increased initially concomitantly with the initial decrease in arterial blood pressure in these patients.

38 Is combined spinal epidural anaesthesia safe for Caesarean section?
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Aims: The debate on the most appropriate regional technique for Caesarean section has progressed from epidural versus spinal anaesthesia to combined spinal epidural (CSE) anaesthesia in the 21st century. Concerns have arisen on the necessity for and potential higher complication rates of the latter method. This audit was conducted to provide evidence of technical difficulties, complications and failure rates of this increasingly popular technique in this patient population.

Methods: Retrospective analysis was conducted on data collected prospectively over an eight-year period in a teaching hospital in the United Kingdom.

Results: A total of 1863 patients due for Caesarean section under CSA in all pts except one (aneurysm of the popliteal artery, prone position). Haemodynamics were remarkably stable. In two cases of revision due to haematoma, spinal anaesthesia was administered successfully through the spinal catheter. No anaesthesia-related complications occurred.

Conclusions: Advantages of CSE included good haemodynamic control, ease to top-up, and ease to provide a new spinal block for revision surgery. As disadvantages we count the large number of technical problems, which, fortunately, did not seem to cause any permanent harm, and the relatively frequent need for additional analgesia.

39 Evaluation of a spinal catheter (28G) anaesthesia technique in arterial bypass surgery of the lower extremities
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Aims: To evaluate the feasibility of continuous spinal anaesthesia (CSA) in arterial bypass surgery of the lower extremities.

Methods: Forty-one patients (pts) (51-98 received CSA through a 28G spinal catheter (CoSPAN®, Kendall) at interspace L2-3 or L3-4. Initially, 1 ml of ropivacaine 7.5 mg/ml was given, followed by increments of 0.5 ml, as needed, until sensory block reached Th10. CVP was controlled (±3 cmH2O). During surgery the patients received heparin i.v.

Results: The identification of the intrathecal space did not succeed in one patient, and two or more punctures were needed in 7 pts. A bloody tap occurred in 2 pts. Mild paraesthesia during puncture or catheter advancement was observed in 10 pts. Catheter adapter problems during anaesthesia (tightlyness of seal) were encountered in 3 pts. Mean dose of ropivacaine was 28.8 mg (24.2 mg during the first hour). Thirteen pts felt mild pain during the incision and received supplemental analgesia. Surgery (mean 170 min, range 66-327 min) could be completed under CSA in all pts except one (aneurysm of the popliteal artery, prone position). Haemodynamics were remarkably stable. In two cases of revision due to haematoma, spinal anaesthesia was administered successfully through the spinal catheter. No anaesthesia-related complications occurred.

Conclusions: The overall failure rate for the CSE technique for Caesarean section is about 1%, with failures being higher for non elective section compared to elective section. The requirement for intra-operative epidural top up is infrequent however this is balanced by the serious complication rate being very low.

40 Can changes in skin resistance be used to test the sympathetic block of a thoracic epidural block?
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When testing an epidural block, ice testing and prick testing are used to determine the extent of the block. To be able to test
Regional anaesthesia

41 Decreased bleeding during radical prostatectomy using hypotensive epidural analgesia compared to normotensive general anaesthesia

Dall R1, Jensen TM2, Jensen JG3, Pedersen KV1, Juelsgaard P1, Wernberg M1

1Department of Anaesthesiology, 2Department of Urology, Aarhus University Hospital, Denmark

Aims: To investigate if radical prostatectomy was associated with less bleeding when performed in hypotensive epidural analgesia (HEA) compared to normotensive general anaesthesia with epidural analgesia intended to cover only the surgical incision (GA).

Methods: Forty patients with prostate cancer were randomised to either HEA (n = 19) or GA (n = 21).

Results: The total bleeding (ml) was significantly less in the HEA group (1093 ± 164 (HEA) vs. 1590 ± 209 (GA); P < 0.003). MAP and CVP (mmHg) were lower in the HEA group (MAP 47 ± 1.1 vs. 65 ± 1.7 (MAP) and CVP 2 ± 0.6 vs. 13 ± 0.8 (CVP); both P < 0.005). Conclusion: We found decreased bleeding associated with HEA during radical prostatectomy. Furthermore, the surgeons expressed that the decreased bleeding associated with HEA positively influenced the possibility for nerve-sparing surgery.

42 Simultaneous bilateral infraclavicular blocks with reduced doses of lidocaine using ultrasound guidance (case report)

Sandhu N, Maharlouie B, Patel B, Erkulwater E

New York University School of Medicine, New York, NY, USA

Aims: Simultaneous bilateral infraclavicular blocks (BIFCB) are rarely performed for fear of local anesthetic toxicity, and when indicated they are given 30 minutes apart to separate two peaks of absorption. Ultrasonography allows to observe the spread of anesthetic; hence, precise placement perineural anesthetic permits reducing its dose. (1,2). Three patients with simultaneous BIFCB blocks are described.

Methods: All patients were appropriately sedated with midazolam and fentanyl followed by BIFCB using 20 ml of anesthetic solution (lidocaine, 2%, with 1:200 000 adrenaline and 1:10 ml of sodium bicarbonate) on each side guided by ultrasound (Sonosite 180, probe 4–7 MHz). A 22G needle was brought close to each of the three cords and 4–6 ml of local anesthetic was deposited around each. A 19G catheter was placed under axillary and posterior cord to prolong anesthesia and for post operative pain control.

Case 1: A 71 year old man (80 kg, 5′11″ ASAPS IIIIE), with a history of hypertension, stroke, residual right hemiparesis and non-Hodgkin’s lymphoma of neck & mediastinum had incision and drainage of abscesses of left arm and right hand using simultaneous BIFCB.

Case 2: A 42 year old male (79 kg, 5′6″, ASA I) had completion amputation of multiple fingers of both hands under BIFCB.

Case 3: A 16 year old boy (56 kg, 5′4″, ASA I) had open reduction and plating of right arm fracture and repair of lacerations of left arm under BIFCB.

Results: all patients had dense sensory motor block of all nerves of upper extremities. In two patients catheters were used for post op analgesia, and in one for repeating block for a second surgery. Conclusions: Ultrasound guidance allows safe administration of BIFCB by accurate delivery of anesthetic.

Reference

43 Suprascapular nerve block for postoperative pain control after arthroscopic shoulder surgery

Achabahian A, Kim J

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Aims: To compare a combination of a long-acting suprascapular nerve block and a short-acting interscalene block, versus an intermediate-acting interscalene block, in patients undergoing shoulder arthroscopic acromioplasty and/or rotator cuff repair.

Methods: Forty patients undergoing shoulder arthroscopic acromioplasty and/or rotator cuff repair were randomized to one of two groups. Patients in the SSIS group received a combination of a long-acting suprascapular nerve block (using bupivacaine) with a short-acting interscalene block (using mepivacaine), while patients in the IAIS group received an intermediate-acting interscalene block (using a mixture of bupivacaine and mepivacaine). Postoperative pain was assessed using a VAS scale every 4 hours for the first 48 hours. Pain medication use and patient satisfaction were also recorded, as well
as the time to return of motor and sensory function of the upper extremity.

Results: While pain scores were slightly higher in the SSIS group at 4 and 8 hours, they were thereafter consistently lower than in the IAIS group. Analgescic consumption and patient satisfaction were not significantly different. Motor and sensory function of the upper extremity returned significantly earlier in the SSIS group (9.0 ± 6.8 vs. 19.4 ± 12.0 hours).

Conclusions: A combination of a long-acting suprascapular nerve block with a short-acting interscalene block provides better pain control beyond the first few hours, with earlier return of motor and sensory function, than an intermediate-acting interscalene block.

44 The efficacy of “Periconal Anesthesia” in time consuming vitreoretinal operations
Agah M, Ahranjani R
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Aims: We prospectively evaluated the efficacy of periconal anesthesia (peribulbar, periorcular) in time consuming vitreoretinal operations.

Methods: we prospectively studied 72 patients who were operated for vitrectomy and retinal reattachment surgery with periconal anesthesia. The local anesthesia mixture consisted of 4 ml 2% lidocaine, 4 ml 0.75% bupivacaine and 150 units of hyalurinidase. With a sharp, fine 27G × 20 needle. LA mixture was injected from 2 sides, first inferotemporal and second superonasal of the orbital rim. The adequacy of the periconal anesthesia was evaluated preoperatively on basis of globe akinesia and anesthesia based on four grades (IV, III operable and I, II inadequate for surgery). The cooperation of the patients on injection and during surgery were classified to three grades (E = Excellent, S = Satisfactory and P = Poor). We evaluated onset and duration of anesthesia and akinesia and complications.

Results: 44 women, 28 men ages from 39 to 84 (mean = 66.16 years). The operation time was 55–240 minutes (mean = 113.78). Considering anesthesia and akinesia 71 patients were in group III and IV. Considering the operation, 71 patients (99%) were cooperating sufficiently in the beginning of the surgery; IOP was without any change during operation because there was no pain and strain. The surgeon’s satisfaction was incredibly more than retrobulbar. There was no complication due to insufficient anesthesia.

Conclusions: Our results show that periconal anesthesia can be effectively used for time consuming vitreoretinal operations. It has low rate of complications and is very well tolerated by the patients and may be preferred for local anesthesia especially in scleral bucking procedures in patients with high myopia.

Cardiopulmonary resuscitation

45 Outcome after cardiac arrest and induced hypothermia
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Aims: The purpose of our study was to prospectively collect and evaluate data from comatose cardiac arrest patients, treated with induced hypothermia.

Methods: Patients in coma after cardiac arrest (GCS ≤ 6) were treated with mild induced hypothermia (33°C ± 1°C) for 24 h. Cold fluids (2–3 liters NaCl) were used for induction and the CritiCool® (MTRE Inc) for maintaining hypothermia and for controlled rewarming (0.5°C/h). Patients were sedated during treatment and muscle relaxants were given intermittently. The cerebral performance category scale (CPC) was used to determine outcome, where CPC 1 and 2 represent a good outcome and 3–5 a bad outcome.

Results: Median time from arrest to CPR was 6 min and from arrest to ROSC 17 min. Hospital outcome in 130 consecutively treated patients showed a good outcome in 61 patients (47%) and a bad outcome in 69 patients (53%). Sixty percent of patients with an initial rhythm of VT/VF and 15% with an initial rhythm of asystole/PEA had a good outcome. Median time in the ICU was 97 h.

Conclusion: Our results compare favorably with historical controls supporting the published studies. Also, patients who survive do so with a good cerebral performance, whereas most patients with a bad outcome die.

46 The Northern Hypothermia Registry

Northern Hypothermia Network Steering Group

Aims: Two independent studies have shown that early treatment with induced hypothermia protects from neurological sequelae and death after out-of-hospital cardiac arrest. An advisory statement from the International Liaison Committee on Resuscitation (ILCOR) supports the importance of therapeutic hypothermia. We believe that it is imperative to implement these new recommendations into clinical practice under strict control of treatment safety and outcome. The Northern Hypothermia Registry is a database on the Internet designed to enable evaluation of all patients treated with intensive care after cardiac arrest.

Methods: Data concerning patient and cardiac arrest characteristics are collected in the Utstein-style. Data on hypothermia treatment, safety aspects, clinical investigations, laboratory values and general intensive care parameters are collected. Outcome is documented as neurological score at ICU and hospital discharge. Outcome at six months is registered separately and linked to the original data.

Results: Denmark, Iceland, The Netherlands, Norway and Sweden are represented in the Registry and 31 centres have signed up for participation. The on-line registration has been open since October 2004. Today 185 patients are registered. Data from these patients are currently under statistical evaluation and will be presented at the meeting.

Conclusions: The Northern Hypothermia Registry will provide an easy and powerful way of evaluating the safety and outcome aspects of a new and promising treatment strategy after cardiac arrest.
arrest and to strengthen treatment inclusion criteria. Furthermore it will generate ideas on where to focus future clinical trials in the field of therapeutic hypothermia.

47 Somatosensory and brain stem auditory evoked potentials in cardiac arrest patients treated with therapeutic hypothermia
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Aims: To study the short-latency median nerve somatosensory evoked potentials (SEP) and brain stem auditory evoked potentials (BAEP) in comatose cardiac arrest patients treated with therapeutic hypothermia and to evaluate their prognostic value in outcome prediction.

Methods: 60 consecutive comatose patients (age 18–75) resuscitated from out-of-hospital ventricular fibrillation cardiac arrest were randomly assigned to the hypothermia group of 33 ± 1°C (N = 30) or normothermia (37 ± 1°C, N = 30) for 24 hours as part of the Hypothermia After Cardiac Arrest (HACA) trial. All patients were sedated with midazolam and fentanyl and relaxed with pancuronium. SEPs and BAEPs were recorded 24 hours after cardiac arrest. The clinical outcome was assessed six months after cardiac arrest.

Results: All wave latencies for both SEP and BAEP were significantly prolonged in the hypothermia group. Bilaterally absent cortical N20 waves in SEP recordings predicted permanent coma with a specificity of 100% in both treatment arms. BAEP recordings did not correlate with the outcome in either treatment group.

Conclusions: Our results suggest that the prognostic ability of median nerve short-latency SEPs is not affected by the use of therapeutic hypothermia. BAEPs had no additional value in outcome prediction.

48 Do patients with documented clinically abnormal observations prior to in-hospital cardiac arrest have a worse outcome than those without?
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Aims: Patients suffering in-hospital cardiac arrest (IHCA) often have documented abnormal clinical observations prior to the arrest. The aim of this study was to assess whether these patients have a less favourable outcome following IHCA.

Methods: A multiple logistic regression analysis of prospectively collected Ustein style resuscitation data and retrospectively collected hospital chart data from 1993 to 2002. Patients were defined as having abnormal clinical observations if they had one of the following documented eight hours before the arrest: systolic arterial blood pressure below 90 or over 200, pulse rate below 40 or over 140 beats per minute or oxygen saturation below 90. Pre-arrest variables included were: age, gender and functional status, reason for hospital admission, days in the hospital before the arrest, witnessed or unwitnessed arrest, arrest occurring outside regular working hours, monitored or not monitored ward and initial rhythm.

Results: Three-hundred-and twenty-one patients were included in the study. Survival to hospital discharge of patients with clinically abnormal observations was 9% and 18% among those without (P < 0.05). Independent pre-arrest predictors of mortality were age exceeding 72 years (odds ratio [OR] 2.2 confidence interval [CI] 1.05–4.6), un-witnessed arrest (OR 13.8, CI 1.8–108.8), initial rhythm other than ventricular fibrillation or ventricular tachycardia (OR 7.1, CI 3.3–15.4), and the presence of documented clinical abnormal observations prior to the arrest (OR 3.5, CI 1.5–8.4).

Conclusions: Patients with documented clinically abnormal observations before IHCA have a worse outcome than those without. Efforts should be made to identify these patients in time, thereby possibly avoiding the arrest.

Reference

49 Teaching CPR to laypersons in 24 minutes using the MiniAnne® resuscitation-manikin
Ibye DL, Rasmussen LS, Lippert FK
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Background: Only one in four witnessed out-of-hospital cardiac arrest in Denmark receive bystander CPR. This is probably due to a lower level of CPR education in the population. Several methods could be used to improve this situation.

Aims: To test whether a 24 minutes DVD-based self-training CPR-course using a simple, take-home resuscitation manikin is as efficient as a six hours course traditionally used for teaching CPR to laypersons.

Methods: We included 240 laypersons (age 21–55) with no previous CPR-training (<5 y). They were allocated into two groups where 44 persons attended the six hours course (6H), while 196 used Laerdal MiniAnne Manikin (MAM), trained for 24 minutes and took home the manikin for subsequent self-training. After three months skill-retention was assessed with the Laerdal Resuscitainer manikin and the Laerdal PC Skill reporting System 2.0 in a 5 minutes test.

Results: Assessment of breathing was performed significantly more often in the 6H-group (91% vs. 72%), whereas in the MAM-group average inflation volume and chest compression depth were significantly higher (642 mL vs. 538 mL and 45 mm vs. 39 mm, respectively). Hands-off time tended to be lower in the MAM-group (188 vs. 202 sec., P = 0.05). In both groups we identified a high proportion of incorrect hand-position during compressions (>80%).

Conclusions: Practical CPR-skills seem to be more easily retained with a high degree of self-training while other aspects seem to be remembered better when attending an instructor-based course. It is remarkable that so many use incorrect hand-position during compressions.

50 Methylene blue added to a hypertonic-hyperoncotic solution increases survival in experimental cardiac arrest
Miclescu A, Wiklund L
Uppsala University Hospital, Sweden

Aims: Methylene blue (MB), a free radical scavenger that inhibits the production and actions of nitric oxide may counteract nitric-oxide excessive vasodilatation which occurs during cardiac arrest.

Method: An experimental pig model of extended cardiac arrest (12 min cardiac arrest and 8 min CPR) has been employed to assess the addition/no addition of methylene blue to the previ-
Monitoring 17

Methods: In 52 pts after CA, in the age 62 ± 13 years clinical state and concentration of NTpBNP just after CA and in 2 consecutive days at 8:00 am was assessed. The comparison of this data in 24 pts, survived after CA and discharged from the intensive care unit (ICU), and 28 pts after CA who died in ICU, was performed.

A referee group of 22 pts, aged 60 ± 11, with stable coronary artery disease (CAD), was emerged.

Results: A markable increase of concentration of NTpBNP in pts after CA, multiplicate times higher than in pts with CAD, was observed. In pts after CA, died in hospital, compared to pts after CA, survived, markable higher concentrations of NTpBNP were found in first 2 days after CA. There was a better prognosis for pts with NTpBNP below 50 000 pmol/l (P < 0.01) just after CA and below 100 000 pmol/l (P < 0.01) in 2nd day after CA. In logistic regression analysis the prognostic value of presence of early spontaneous ventilation, no tachycardia during first two days after CA and the concentration of NTpBNP below 50 000 pmol/l was similar to that assessed by the GCS, SAPS II, MODS II and APACHE II.

Conclusions: (1) The concentration of NTpBNP in early stage after CA is of prognostic value in pts after CA. (2) In pts after CA lower concentrations of NTpBNP, early spontaneous ventilation and no tachycardia during list two days after CA make a cluster of syndromes of prognostic value similar to the prognostic values of common scales used in critical care.

52

Long-term subjective and objective impact of BIS monitoring on the conduction of relaxant sevoflurane-N2O anesthesia

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LänsiJukkhuset, Kalmar and The Karolinska Institute, Stockholm, Sweden

Aims: To investigate if increasing experience with BIS-monitoring objectively and subjectively alters the conduction of anesthesia.

Methods: 1709 prospective cases with BIS monitoring were anesthetized by 30 experienced CRNAs. After a one-year period without monitoring data was collected from 320 prospective cases handled by 8 of the CRNAs. Each CRNA did 10 cases with “blindly” recorded BIS followed by 10 “open” cases, and after another 20 “open” cases (no data collection), 20 new patients were randomized to “blind” (n = 10) or “open” BIS (n = 10). Recorded data included BIS parameters (mean, >60, 40–60, <40 during maintenance (MA); mean, >60 during induction (IND)), age corrected MAC
tox
eq
max equivalents (MACeto%), and VAS rated BIS utility.

Results: Among the first 1709 patients BIS > 60MA decreased by 35% to 13 ± 8% (P < 0.05) with increasing experience, and this remained in the subsequent 160 “blind” and 160 “open” cases. Compared with the first part, time with BIS > 60MA in these following “blind” and “open” cases was 4.7 (4 ± 14%; P < 0.04) and 2.7 (2 ± 9%; P < 0.01) times longer, respectively. Time at BIS 40–60MA has increased by 29% to 40 ± 31% (P < 0.03) and 39% to 43 ± 31% (P < 0.005), respectively. No significant differences were found between “blind” and “open” cases. Over the entire study, the CRNA rated BIS utility increased by 68% to 74 ± 14 mm (100 mm scale) in the last 160 “open” cases (P < 0.0001), albeit only weakly related to the BIS data.

Conclusions: Experience from, on average, 128 BIS monitored cases was associated with markedly increased user approval, but only modest objective changes in the conduction of anesthesia. Previous experience including assumptions on appropriate gas delivery and hemodynamics may account significantly although BIS monitoring is available and desired.

53

EEG Spectral Entropy RE-SE-difference during induction phase and skin incision in propofol or sevoflurane anaesthesia

Aho AJ, Yli-Hankala A

Tampere University Hospital, Tampere, Finland

Aims: EEG Spectral Entropy consists of two parameters: State Entropy (SE) and Response Entropy (RE). It is assumed that RE-SE-difference (D) may indicate inadequate anaesthesia or...
Methods: Thirteen yearling sheep were anesthetized and underwent thoracotomy and left (n = 7, LPE group) or right (n = 6, RPE group) pneumonectomy. After determining EVLWIG and EVLWITDD (PICCOplus and COLD-Z021, respectively, Pulsion Medical Systems), lungs were harvested separately for EVLWIG. To evaluate the relationships between EVLWITDD, EVLWIG and EVLWITDD, we used linear regression and Bland-Altman analysis. P < 0.05 was regarded statistically significant.

Results: After PE, EVLWIG, and EVLWITDD decreased by 30% and 40% in the LPE group and by 34% and 54% in the RPE group, respectively (P < 0.05). EVLWIG derived from both lungs correlated significantly with EVLWIG, EVLWITDD (r² = 0.61) and EVLWITDD (r² = 0.38) measured at the baseline. EVLWI of residual lung correlated with the last measurement of EVLWITDD (r² = 0.33) and EVLWIG (r² = 0.68). In summary, r² values were 0.85 for EVLWIG vs. EVLWITDD and 0.81 for EVLWIG vs. EVLWIG, respectively (n = 26, P < 0.05). After PE, the mean bias ± SD was 2.19 ± 1.61 ml/kg between EVLWIG and EVLWITDD and 0.24 ± 1.22 ml/kg between EVLWIG and EVLWITDD (P < 0.05).

Conclusions: After lung volume reduction, EVLWITDD and EVLWIG correlated closely with EVLWIG. In spite of moderate overestimation compared with postmortem EVLWI, both thermodiagnotic methods might become useful monitoring tools in major lung surgery allowing unlimited number of measurements perioperatively.

56 Trans-pharyngeal ultrasound guided internal jugular vein cannulation

Bivlacqua S, Romagnoli S, Gelsomino S, Ciappi F, Ridolfi N, Sorbara C
Department of Anesthesia and Cardiac Surgery Intensive Care, Careggi Hospital, Florence, Italy

Aims: To describe the technique of Trans-pharyngeal ultrasonography, to guide cannulation of the internal jugular vein.

Methods: The short axis view of the neck vascular bundle is achieved through the transpharyngeal positioning of the transesophageal echocardiography probe. The probe is inserted 12-20 cm from the jaw and rotated laterally 15-20 degrees throughout the pharyngeal lateral wall. When the proper position of the probe is achieved, it can be left stable on the trolley. The needle is introduced into the vein under real time ultrasound vision. During the last 2 years, we selected 75 cardiac patients in whom jugular vein cannulation would be difficult or at risk (previous carotid surgery, coagulopathies, predicted difficult anatomy) and who were elected to be monitored with the transesophageal echocardiography.

Results: Ultrasound guided cannulation was successful from the first attempt in all the patients without any immediate complications.

Conclusions: Further studies are needed to assess the reliability of this method for routine use, as well as its proper indications and to compare it with conventional ultrasonography.

55 Extravascular lung water after pneumonectomy

Kuzkov V, Kuklin V, Suberov E, Kirov M, Waerhaug K, Johnsen S, Myrmel T, Bjertnaes L
Medical Faculty, University of Tromsø, Tromsø, Norway

Aims: We compared extravascular lung water index, determined with the transpulmonary single thermodilution (EVLWITDD) and the thermo-dye dilution (EVLWITDD), with post mortem gravimetry (EVLWIG) before and after pneumonectomy (PE).

Methods: Thirteen yearling sheep were anesthetized and underwent thoracotomy and left (n = 7, LPE group) or right (n = 6, RPE group) pneumonectomy. After determining EVLWIG and EVLWITDD (PICCOplus and COLD-Z021, respectively, Pulsion Medical Systems), lungs were harvested separately for EVLWIG. To evaluate the relationships between EVLWITDD, EVLWIG and EVLWITDD, we used linear regression and Bland-Altman analysis. P < 0.05 was regarded statistically significant.

Results: After PE, EVLWIG, and EVLWITDD decreased by 30% and 40% in the LPE group and by 34% and 54% in the RPE group, respectively (P < 0.05). EVLWIG derived from both lungs correlated significantly with EVLWIG, EVLWITDD (r² = 0.61) and EVLWITDD (r² = 0.38) measured at the baseline. EVLWI of residual lung correlated with the last measurement of EVLWITDD (r² = 0.33) and EVLWIG (r² = 0.68). In summary, r² values were 0.85 for EVLWIG vs. EVLWITDD and 0.81 for EVLWIG vs. EVLWIG, respectively (n = 26, P < 0.05). After PE, the mean bias ± SD was 2.19 ± 1.61 ml/kg between EVLWIG and EVLWITDD and 0.24 ± 1.22 ml/kg between EVLWIG and EVLWITDD (P < 0.05).

Conclusions: After lung volume reduction, EVLWITDD and EVLWIG correlated closely with EVLWIG. In spite of moderate overestimation compared with postmortem EVLWI, both thermodiagnotic methods might become useful monitoring tools in major lung surgery allowing unlimited number of measurements perioperatively.

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Results: Ultrasound guided cannulation was successful from the first attempt in all the patients without any immediate complications.

Conclusions: Further studies are needed to assess the reliability of this method for routine use, as well as its proper indications and to compare it with conventional ultrasonography.
Detection of breaths by photoplethysmography is independent of age and sex

Nilsson L, Goscinski T, Kalman S, Lindberg L-G, Johansson A
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Aims: The non-invasive optical technique photoplethysmography (PPG) can beside its common use in pulse oximetry be used to monitor respiratory rate. Circulatory and respiratory physiology differs between the sexes and changes with age. We compared the concordance between a respiratory reference and the respiratory synchronous variation in the PPG (PPGr) between men and women and between young and old men.

Methods: We studied three groups of 16 healthy volunteers each; young males (YM), old males (OM) and young females (YF). Reflection mode PPGr from the forearm was collected together with end-tidal CO₂ during ten minutes of normal breathing. We analyzed the concordance of the signals with squared coherence analysis, spanning from 0 (no association) to 1 (maximal association).

Results: Coherence values were high and there was no significant difference between the groups (P = 0.67).

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<td>Median (quartile range)</td>
<td>0.93 (0.25)</td>
<td>0.92 (0.14)</td>
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Conclusions: We used coherence values as an index of signal quality. An easily detected respiratory signal is of importance if the PPG technique is to be clinically useful. We have earlier shown that PPGr doesn’t change with awake state or anesthesia, or with spontaneous respiration or positive pressure ventilation. It is of clinical importance that PPGr quality also is independent of sex and age.

Time relation between respiratory signals can be analysed by automated algorithms

Nilsson L, Goscinski T, Kalman S, Lindberg L-G, Johansson A
Linköping University Hospital, Linköping, Sweden

Aims: The analysis of physiological signals often includes an investigation of concordance and time difference between the studied variations. We investigated the respiratory synchronous variation derived from the optical non-invasive technique photoplethysmography (PPGr) and its relation to a respiratory reference. No golden standard exists for this type of analysis. We compared visual analysis to the automated cross-correlation and squared coherence analysis.

Methods: Data was recorded for ten minutes of normal breathing from 48 healthy volunteers. Reflection mode PPGr from the forearm was collected together with end-tidal CO₂. One and the same analyzer, unaware of the results from the automated analyses, performed visual detection of breaths in both signals. Squared coherence analysed the spectral densities at the respiratory frequency, whereas the cross-correlation took the full spectra of the signals into account.

Results: The correlation between the three methods was high, r = 0.93. Between the automated methods the correlation was 0.98, between the visual and cross-correlation method 0.92 and between the visual and coherence method 0.87.

Conclusions: Visual analysis of respiratory signals is time consuming. The automated methods performed equally well and we suggest that they are more appropriate as they can be more easily applied for longer periods of time. Which automated method to use needs to be further studied during clinical circumstances with irregular breathing and artefacts.

Photoplethysmography for central and obstructive apnea detection

Goscinski T, Nilsson L, Kalman S, Lindberg L-G, Johansson A
Linköping University Hospital, Linköping, Sweden

Aims: The non-invasive optical technique photoplethysmography (PPG) can beside its common use in pulse oximetry also be monitoring respiratory rate. To be clinically interesting, PPG must be able to detect apnea as well as respiratory rate. Earlier studies have indicated that central apnea can be detected by PPG. We compared the amplitudes of the respiratory synchronous part of the PPG signals (PPGr), registered before, during and after simulated central as well as obstructive apnea in healthy volunteers.

Methods: Reflection mode PPG signals detected on the forearm and end-tidal CO₂ from a facemask open to ambient air were collected in 48 healthy subjects during the simulation of central and obstructive apnea. In the analysis, the different breathing periods were defined visually in the end-tidal CO₂ curve, and automated calculation of average PPGr amplitudes was done. The pre-apneic amplitudes were normalized to the value of 1.

Results: Due to a hidden calibration error, only 11 and 14 PPG measurements were analyzed during central and obstructive apnea, respectively. Amplitudes during central apnea were significantly lower compared with amplitudes before and after apnea. Amplitudes during obstructive apnea were significantly lower compared with amplitudes after obstructive apnea.

Conclusions: PPG can be used for identifying periods of central and maybe also obstructive apnea in healthy volunteers. The method may with further development become clinically useful as a monitor of spontaneous breathing, especially if combined with pulse oximetry in the same sensor.

The difference between PaCO₂ and ETCO₂ in laparoscopy assisted vaginal hysterectomy – comparing the thin and obese woman

Lee YK, Joe SK, Han SM, Yang HS
Asan Medical Center, Seoul, Korea

Aims: Laparoscopic surgery is widely used because it provides less postoperative pulmonary complications and more patient’s satisfaction. It promotes earlier recovery and reduce hospital stay. But it cause the CO₂ production increase because the operation field is aided by CO₂ pneumoperitoneum and by using electro-cautery. We measured the difference between PaCO₂ and ETCO₂ in laparoscopic assisted vaginal hysterectomy. We also investigate the obesity (by body mass index) influences the results or not.

Methods: Forty five patients (22 patients were obese, 23 patients were non obese) were enrolled this study. We measured the blood pressure, heart rate, ETCO₂ and PaCO₂ before and after establishment of CO₂ pneumoperitoneum and reverse Trendelenburg position and also after removing CO₂, returning to supine position. We adjusted the vol % of sevoflurane, tidal volume, respiratory rate and intraabdominal pressure regularly. And we studied the change of the capnogram, O₂ saturation and airway pressure.

Results: There was significant difference between PaCO₂ and ETCO₂. PaCO₂ increased more than ETCO₂ in obese. The
Blood transfusion, bleeding and fluids

frequency to adjust the tidal volume and respiratory rate to
set on the ETCO₂ to less than 45 mmHg was higher than in
obese.

Conclusions: The obese has tendency to CO₂ retention
during laparoscopic surgery, so we must pay attention to the
changes unless it cause many untoward side effects by CO₂
retention.

61 Persisting influence on respiratory and central
circulatory variables after a single intravenous
dose of CO₂ in pigs
Fors D, Jersenius U, Arvidsson D, Rubertsson S
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Aim: Laparoscopic liver resection is a relatively new surgical pro-
cedure. Pneumoperitoneum and liver dissection is recognized as
a risk factor for carbon dioxide embolism to the pulmonary cir-
culation. The embolisation could be difficult to detect and could
theoretically increase perioperative morbidity. The aim of this
study was to evaluate the cardiopulmonary effects in a pig
model during a time period of 4 hours after an experimental CO₂
embolisation.

Methods: Eleven piglets were anesthetized. Nine of them were
embolised with a single i.v. injection of 0.4 ml/kg CO₂ while two
served as controls. Extensive respiratory and cardiovascular
variables were monitored during four hours after embolisation
including pulmonary artery pressures, cardiac output and on-
line arterial blood gases monitoring.

Results: The embolised pigs had an increase in ventilatory dead
space, pulmonary vascular resistance and pulmonary artery
pressure and decrease in cardiac output that remained through-
out the observed time of four hours. Mean artery pressure and
heart rate were unchanged. An early sign of embolisation was a
rapid fall in endtidal CO₂ (EtCO₂) and PO₂ and a raise in PCO₂.

Conclusion: Persisting negative changes in cardiopulmonary
physiology remained for at least four hours after a single intra-
venous injection in spite of CO₂ being a highly soluble gas that
quickly would dissolve. This is a prolonged time influence of
CO₂ embolisation than previously described. Therefore, exten-
se monitoring could be recommended in early detection of an
embolisation in order to possibly limit morbidity in patients
undergoing laparoscopic liver surgery.

Blood transfusion management in critically ill
patients: have we met best practice goals?
Neutel E, Lopes Z, Mexedo C, Mogo R, Amil M, Camacho A
Intensive Care Unit and Immunohemotherapy Department at General
Hospital of Santo António, Oporto, Portugal

Context: Blood transfusions are highly prevalent among ICU
patients. Patient prognosis may be influenced by the transfusion
practice, therefore transfusion risk as well its benefit must be
considered. This decision may be highly variable, so it must be
based on the previously established guidelines. A consensus of
transfusion practice was established in the HGSA, in 1996 and
updated in 2001. The implementation of a hemovigilance pro-
gramme and evaluation of the application of clinical guidelines
appliance was also defined.

Objective: Document current clinical practice of blood compo-
nents uses in our ICU. Determine concordance with previously
established guidelines. Examine the relationship of blood trans-
fusion to clinical outcomes.

Methods: Studied population includes all adult patients admitted
to ICU, from November 15th 2002 to December 31st of 2004. Seven
hundred and twenty critically ill patients were included.
The subjects were characterised in relation to: admission diagnosis;
patient condition (SAPS II); length of stay in ICU and mortality.
The concordance with previously established guidelines was
analysed in each transfusion event. For statistical analysis
we used: mean ± SD, Student’s t-test*, Chi-square tests**, Mann-whitney***.

Results:

<table>
<thead>
<tr>
<th></th>
<th>Transfused N = 362</th>
<th>Not transfused N = 347</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU length of stay, mean (min-max)</td>
<td>11 (1–53)</td>
<td>3 (1–45)</td>
<td>&lt;0.036***</td>
</tr>
<tr>
<td>SAPSII mean (standard deviation)</td>
<td>39 (14)</td>
<td>35 (13)</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>Mortality n (%)</td>
<td>103 (29)</td>
<td>75 (22)</td>
<td>0.028***</td>
</tr>
</tbody>
</table>

The prevalence of transfusions was 51%. Patients who were
transfused had a longer stay, a higher SAPS score and a higher
mortality rate; compared with those not transfused. When we
analysed transfusion events, respecting red blood cell, platelet
and plasma, the concordance with HGSA established guidelines
was greater then 90%. The transfusion of albumin had a concor-
dance of 52.6%.

Conclusions: Transfusion practice in our unit improved over time.
Transfused group had worse clinical outcome.

63 Optimising efficacy of preoperative autologous
blood donation by adapting it to the
physiological principles of erythropoiesis
Singbartl G
Institute AIT – ENDO-Klinik Hamburg GmbH, Hamburg, Germany

Aims: Preoperative autologous blood donation (PABD) is con-
sidered an established autologous blood conservation measure.
To make it as efficacious (increase in RBC-mass/+RBC) as pos-
sible, it is important to know those parameters, that determine
efficacy of PABD.

Methods: Part 1: After IBR-approval, prospective analysis w/
respect to +RBC of 704 consecutive major orthopaedic surgery
pats participating in a routinely offered PABD-program. Global
statistical analysis by multiple univariate analysis of variances,
correlation analysis, multiple linear regression analysis; descriptive statistical analysis by t- / U-test, ANOVA, w/ Scheffé-test; P < 0.05 w/ Bonferroni-correction when appropriate. Part II: Prospective preference study after IBR-approval of two different PABD-concepts: 2 separately collected units [2SCU; n = 60] on 2 PABD vs. collecting 2 units on 1 PABD [1DD; n = 100] in 160 consecutive major orthopaedic surgery pats. Stat. analysis by t- / U-test; P < 0.05.

Results: Part I: Only 2 clinical parameters determined efficacy (+RBC) of PABD: 1) time-interval between PABD and surgery (T – S), that correlated positively w/ +RBC; 2) 2nd hct, that correlated negatively w/+RBC. To optimise +RBC, both a T – S of at least 4 weeks after (last) PABD was necessary together with an individually accepted anemic hct-level after PABD to push erythropoiesis efficaciously (1 PABD: +RBC = 147 ± 85 ml; 2 PABD: +RBC = 297 ± 79 ml). Part II: Under comparable conditions, pats. w/ 1DD regenerated more RBC than pats w/ 2SCU (261 ± 114 vs. 168 ± 133 ml; P < 0.05).

Conclusions: Adapting PABD to the physiological basics of erythropoiesis improves efficacy of PABD in a clinically relevant extent.

64
Preoperative autologous deposit vs. perioperative blood salvage: mathematical analysis of original patients data referring to efficacy

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Aims: Periop. blood salvage (PBS) and preop. autologous deposit (PAD) are considered established autologous transfusion alternatives. Mathem. analysis (MA) on comparing efficacy of these measures is still lacking.

Patients and methods: Prospect. analysis in 693 consecutive orthopaedic surgery pats participating in a PAD-program with 1 or 2 PAD. Calculation of increase in RBC (+RBC) due to PAD by the hct-method, and max. allowable blood loss (MABL) / RBC-loss until reaching hct min (18, 21, 24%). MA of MABL if no PAD was performed, but PBS exclusively, assuming a RBC-recovery-rate of 30% (PBS30). Re-transfusion of +RBC (due to either PAD or PBS30) and compensation of MABL, maintaining hct min constant despite ongoing blood-loss. Statistical analysis by t- / U-test, ANOVA; P < 0.05.

Results: +RBC due to PAD was 164 ± 11 ml enabling compensation of MABL (with hct min 18, 21, 24%) of 4.7 ± 1.1, 3.8 ± 0.9, or 3.1 ± 0.8 L; comparably, +RBC due to PBS30 was 431 ± 134, 346 ± 116, 273 ± 100 ml enabling compensation of MABL of 6.0 ± 1.6, 4.5 ± 1.3 or 3.4 ± 1.8 L, respectively. Pats with PAD superior to PBS (hct min 18, 21, 24%; 3.3%, 12%, 28.6%) were demonstrated with a longer time-interval between PAD and surgery (days) (hct min 18, 21, 24%; 40 ± 13 vs. 27 ± 11; 38 ± 10 vs. 26 ± 11; 35 ± 10 vs. 25 ± 10), and a lower hct before commencing PAD (hct min 18, 21, 24%; 35 ± 2 vs. 39 ± 3%; 36 ± 2 vs. 40 ± 3%; 37 ± 3 vs. 40 ± 3%) than pats with PBS.

Conclusions: PAD should be applied, only, if criteria for an efficacious stimulation of erythropoiesis are given to enable a sufficient +RBC. Otherwise PBS is the more efficacious autologous alternative for saving RBC and compensation of MABL.

65
‘Extreme’ acute normovolaemic haemodilution – better than nothing, even with a ‘normal’ minimal haematocrit level

Singbarl G
Institute AIT – ENDO-Klinik Hamburg GmbH, Hamburg, Germany

Aims: Acute normovolaemic haemodilution (ANH) is rated poorly efficacious in saving RBC (+RBC). Under special circumstances ‘extreme’ ANH (applying ANH until reaching hct min, then starting re-transfusion of ANH-U) might be necessary, even if a ‘normal’ hct min is mandatory. Efficacy can be best evaluated by math. modelling (MM) of original pats data w/ respect to 1st decisive lab-parameter limiting ANH; 2nd number of ANH-U collected until reaching hct min; 3rd Maximal allowable blood-loss (MABL); 4th gender-specific differences (m/f). ‘Extreme’ ANH-MM of original pats data is still lacking.

Methods: Prospective ANH-MM from 207 consecutive surgery pats eligible for ANH. Isovolemic exchange of blood vs. an artificial colloidal solution: applying ANH (500 ml per unit) until reaching first ANH-limiting parameter (hct min: 24, 21, 18%; platelets min: 100, 50 p. nl; fibrinogen min: 100 mg p. dl); RT of ANH-U plus administration of colloidal to maintain hct min despite ongoing blood-loss until all ANH-U had been retransfused (MABL). Statistical analysis by t-/U-test. Data are given as mean ±SD; statistical significance with P < 0.05.

Results: 1st hct min is the decisive ANH-limiting parameter. 2nd Depending on hct min (24 vs. 18%) between 6 and 9 (m) / 3 and 6 ANH-U (f) can be collected. 3rd Concerning hct min (24 vs. 18%) between 267 ± 83 and 502 ± 139 (m) / 136 ± 75 ml and 301 ± 100 ml of RBC (f), can be saved; compensating for MABL of between 3.7 ± 0.9 and 6.9 ± 1.2 L (m) / 1.9 ± 0.7 and 4.2 ± 1.0 L (f). 4th ANH is more efficacious in m than f.

Conclusions: ‘Extreme’ ANH is poorly efficacious in saving RBC, but can be effective in compensating for MABL even with a normal hct min.

66
Placenta percreta with bladder involvement and profound haemorrhage: two case reports

Katsanoulas C, Mouoli E, Kopatzidis H, Eftimiou A, Papazafiriou E, Gritsi-Gerogianni N
ICU, Hippokration General Hospital, Thessaloniki, Greece

Aims: Placenta percreta (P.p.) is a rare obstetric complication causing life-threatening haemorrhage. We present two cases of P.p. with bladder invasion leading to massive haemorrhage, treated in the ICU.

Case 1 presentation: A 37-year-old woman with a documented P.p. was admitted for elective caesarean and hysterectomy at the 36th gestational week. She sustained massive haemorrhage leading to DIC and profound shock (norepinephrine inf. up to 1.2 mcg/ kg/min). 12 h later, she was reoperated because of continuing bladder haemorrhage and shock. This was partially controlled by abdomen packing, 30 h later, she was again successfully operated for hypogastric arteries ligature. During the first 72 h, after the 1st operation, she was transfused 142 packed RBC and 353 4th ANH-U (f) can be collected. 3rd Concerning hct min (24 vs. 18%) between 267 ± 83 and 502 ± 139 (m) / 136 ± 75 ml and 301 ± 100 ml of RBC (f), can be saved; compensating for MABL of between 3.7 ± 0.9 and 6.9 ± 1.2 L (m) / 1.9 ± 0.7 and 4.2 ± 1.0 L (f).

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66
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Case 2 presentation: A 45-year-old woman with a 29th week, IVF, twin gestation was admitted for elective caesarean and hysterectomy because of a P.p. involving the bladder. After an 11days uneventful postoperative course, profound haematuria demanded massive transfusion. An urgent laparotomy revealed a remaining placental vessel penetrating the bladder wall. She
Infusion of hypertonic saline before elective laparotomy: Effects on cytokines and hormones

Kolsen-Petersen JA, Bendtzen K, Tonneesen E

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Aims: Infusion of hypertonic saline provides early hemodynamic benefits and may affect the immune system. It is unknown, how infusion of hypertonic saline in a clinically relevant dose affects plasma cytokines and stress hormones after surgery.

Methods: Sixty-two women scheduled for abdominal hysterectomy were randomized double-blindly to infusion of 4 ml/kg 7.5% NaCl (HS), 0.9% NaCl (NS4), both 4 ml/kg, or 0.9% NaCl 32 ml/kg (NS32) over 20 min. Blood was collected at baseline, 1, 4, and 24 hours after surgery (n = 34) for the determination of IL-1b, IL-6, IL-8, IL-10, IL-12, IL-1ra, and TNF-α. Serum cortisol and vasopressin were measured at these time points and 48 postoperatively. Epinephrine and nor-epinephrine (n = 26) were quantified at baseline, after infusion, 25 min after incision, 1, and 4 hours after surgery. Finally, C-reactive protein was measured at baseline, 24, and 48 hours after surgery.

Results: Surgery/anesthesia induced well-known changes in the measured cytokines and hormones. IL-8 showed an augmented increase 1 hour after surgery in the group treated with HS compared to the other groups (P < 0.01). The concentration of nor-epinephrine briefly increased after infusion of HS and NS32 but not NS4 (P > 0.05). Epinephrine was increased 25 min after incision in Group NS32 compared to the other groups (P < 0.05). No other differences were found between the groups.

Conclusion: Infusion of a clinically relevant dose of hypertonic saline before laparotomy may increase the concentration of circulating IL-8 postoperatively but appeared to have limited effect on the hormonal stress-response.

Hypertonic saline infusion does not change neutrophil oxidative burst or expression of endothelial adhesion molecules after surgery

Kolsen-Petersen JA, Rasmussen TB, Krogh J, Hokland M, Tonneesen E

Aarhus University Hospital and Aarhus University, Aarhus, Denmark

Aims: Previous studies found hypertonicity to affect neutrophils as not bioequivalent. Compared with HES 130/0.4/9:1, HES 130/0.42/6:1 proved as not bioequivalent. With HES 130/0.42/6:1 showed a smaller AUC0–24h and a faster clearance from the circulation. Despite this, its hemodilution effect was not inferior. The lower circulatory load with HES 130/0.42/6:1 is deemed to improve the safety profile of the respective colloid.

Methods: Fifteen women scheduled for open abdominal hysterectomy were randomized double-blindly to infusion of 4 ml/kg 7.5% NaCl, 4 ml/kg 0.9% NaCl, or 32 ml/kg 0.9% NaCl over 20 min. Blood was collected at baseline, after infusion, 1, 4, and 24 hours postoperatively for the determination of leukocyte and differential count, neutrophil membrane expression of endothelial adhesion molecules by flow cytometry, and O2- generation by superoxide dismutase-inhibitable reduction of cytochrome C. Groups were compared by two-way repeated measures analysis of variance after logarithmic transformation of the data.

Results: Surgery induced well-known changes in the number and distribution of white blood cells, reduced the expression of adhesion molecules, and halved the superoxide production unrelated to the toxicity or volume of the infused fluids.

Conclusions: Infusion of a clinically relevant dose of hypertonic saline has no detectable effect on the membrane expression of endothelial adhesion molecules or O2- generation in circulating neutrophils after elective abdominal hysterectomy.

HES 130/0.42/6:1 increases blood volume to the same extent but disappears faster from the circulation than HES 130/0.4/9:1

Lehmann G, Boll M, Hilgers R, Förster H, Burmeister M-A

Frankfurt University Hospital, Frankfurt, Main, Germany

Background and aims: In order to optimize the pharmacologic properties of hydroxvethyl starch (HES), low molecular and low substituted HES (“HES 130”) solutions have recently been developed. This trial aimed to investigate the bioequivalence of 2 novel HES 130 solutions showing different molar substitutions (0.4 vs. 0.42) and C2: C6-ratios (9 : 1 vs. 6 : 1).

Methods: HES 130/0.4/9:1 and 130/0.42/6:1 were studied in 7 volunteers using a randomized cross-over design. After top load administration of 50 g HES in 30 min, HES serum concentration was measured (for computation of model-independent pharmacokinetics), and relative blood volume change (based on hemoglobin concentration) was calculated.

Results:

<table>
<thead>
<tr>
<th></th>
<th>HES 130/0.4/9:1</th>
<th>HES 130/0.42/6:1</th>
</tr>
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<tbody>
<tr>
<td>AUC0–24h (mg/ml*h)</td>
<td>58.32 ± 9.23</td>
<td>45.97 ± 8.97*</td>
</tr>
<tr>
<td>Cmax (mg/ml)</td>
<td>9.86 ± 0.58</td>
<td>10.10 ± 1.20</td>
</tr>
<tr>
<td>t1/2 (h)</td>
<td>5.27 ± 0.43</td>
<td>4.61 ± 1.03</td>
</tr>
<tr>
<td>Cltot (l/h)</td>
<td>0.81 ± 0.34</td>
<td>1.14 ± 0.40*</td>
</tr>
</tbody>
</table>

*Mean ± SD; area under concentration curve of HES; maximal HES concentration; elimination half-life; total clearance; denotes P < 0.05 (Friedman’s test plus paired sign test). 30 min after infusion end, relative blood volume increased up to 20.2 ± 7.5% with HES 130/0.4/9:1 and 24.9 ± 9.6% with HES 130/0.42/6:1 and returned to baseline within 12 h. Conclusion: HES 130/0.4/9:1 and HES 130/0.42/6:1 proved as not bioequivalent. Compared with HES 130/0.4/9:1, HES 130/0.42/6:1 showed a smaller AUC0–24h and a faster clearance from the circulation. Despite this, its hemodilution effect was not inferior. The lower circulatory load with HES 130/0.42/6:1 is deemed to improve the safety profile of the respective colloid.
Aspects of general anaesthesia

70
Anaesthesia in very old emergency surgery patients
Kontinen N, Rosenberg PH
Helsinki University Central Hospital, Helsinki, Finland

Aims: Deteriorated organ function and reduced stress response in the elderly may cause postoperative morbidity. We analyzed management of anaesthesia and outcome in patients who were >100 years old when undergoing emergency surgery in our hospital in the years 1990–2004.

Methods: From the hospital data bank 12 patients (10 female/2 male) were identified who had undergone altogether 14 procedures in either general (GA) or spinal anaesthesia (SA).

Results: Median age was 101 (range 100–102). Eight patients underwent surgery for hip fracture, two for ischaemic leg, one for haematoma evacuation from the leg with later skin-grafting, and one for peritonitis. SA was used in 11 of the 14 cases, 6 as continuous and 5 as single-shot spinal anaesthesia (SSA). Direct arterial BP monitoring was used in 8 patients and CVP only in one. In the SA group, BP fell markedly in 6 patients, 4 of whom received SSA. In 2 of the 3 GA patients BP fell markedly after induction. Haemodynamics was managed with i.v. fluids, i.v. ephedrine, phenylephrine or noradrenaline. All but two SA patients received sedative drugs in the theatre. Six patients were disoriented postoperatively. Three patients died within two weeks (pneumonia, cerebral infarction, MI). Nine patients returned home and 5 lived more or less in their preoperative mental and physical state at least for a year.

Conclusions: Independently of the anesthetic method marked BP drops occurred and inotropic drugs were needed. We assume that better haemodynamic stability could have been obtained by monitoring CVP. Disorientation could probably have been avoided by reducing the doses of opioids and sedatives. Overall these very old patients tolerated emergency surgery quite well and most of them were discharged home.

71
Perioperative cortisol secretion is related to postoperative cognitive dysfunction
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Aims: The pattern of cortisol secretion is influenced by surgery. As cortisol can adversely affect neuronal function, this could be an important factor in the development of postoperative cognitive dysfunction (POCD).

Methods: We included 187 patients aged over 60 years undergoing major non-cardiac surgery with general or regional anaesthesia. Saliva cortisol levels were measured preoperatively and at 1 day, 7 days, and 3 months postoperatively in the morning (8 am) and in the afternoon (4 pm) using salivettes. Cognitive function was assessed preoperatively, on day 7, and at 3 months using four neuropsychological tests. POCD was defined as a combined Z score >1.96.

Results: After surgery, the cortisol concentration increased significantly. POCD was detected in 18.8% at 1 week and in 15.2% after 3 months. The preoperative ratio between the am and pm cortisol (am/pm ratio) concentration was 2.8 and 2.7 in patients with POCD at 1 week vs. those without POCD. The am/pm ratio decreased significantly postoperatively to 1.9 and 1.6 at one week, respectively (P = 0.02 for both). In an analysis considering all am/pm ratios, it was found that the persistent flattening in am/pm ratio was significantly related to POCD at 1 week.

Conclusions: The pattern of diurnal variation in cortisol level significantly related to postoperative cognitive dysfunction. Thus, circadian rhythm disturbance or metabolic endocrine stress could be an important mechanism in the development of cognitive dysfunction after major surgery.

72
Knowledge of and experience with difficult airway management among Danish nurse anaesthetists
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1Department of Anaesthesia, Roskilde County Hospital, Denmark, 2Department of Anaesthesia, Copenhagen University Hospital Glostrup, Denmark

Aims: In clinical practice in Denmark nurse anaesthetists play a key role. We aimed at assessing Danish nurse anaesthetists’ knowledge of and experience with difficult airway management, as well as their knowledge of Danish Difficult Airway Registry.

Methods: 27 nurse anaesthetists from different hospitals, with an average of 12.4 years of experience, filled in a survey about difficult airway management.

Results: None of the participants had all correct answers to the four multiple-choice questions about knowledge of difficult airway management as described in ‘ASA guidelines’. There was no correlation between the number of years in service as nurse anaesthetist and the number of correct answers. Three thirds of the participants had knowledge of Danish Difficult Airway Registry, but none had provided anaesthesia to a patient from the Registry.

Conclusions: Even experienced nurse anaesthetists demonstrate limited knowledge of systematic, guideline-controlled management of the difficult airway. The Danish Difficult Airway Registry is becoming quite well known among Danish nurse anaesthetists despite the fact that it is rather new. The study indicates that there is need and room for improvement of knowledge of difficult airway management among Danish nurse anaesthetists.

73
Causes of case cancellations on day of surgery: a system problem
1Norwegian University of Science and Technology, Trondheim, Norway, 2St Olav’s Hospital, Trondheim, Norway, 3Massachusetts General Hospital, Boston, USA

Aims: To quantitatively study root causes of cancellations.

Methods: We collected case cancellation data from hospital databases at Massachusetts General Hospital (MGH) (one year of data) and St. Olav’s Hospital (SOH) (for 2003 and 2004). At SOH, detailed root causes of 41 cancellations were collected over an eight day period (spring 2005).

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Aspects of general anaesthesia

Results: At SOH, 13.27% (1711) of cases in 2003 and 12.2% (1946) of cases in 2004 were cancelled. At MGH, 16.52% (6281) of cases were cancelled between 1/5/2003 and 30/4/2004. The most frequent reported cause at SOH was ‘Other Patient Illness’ (15.9% of all cancellations in 2003 and 15.01 in 2004). It was the fourth largest reported cause at MGH (13.12%). ‘Other’ was most frequent at MGH (21.43%), as compared to second (15.49%) in 2003 and fourth (10.53%) in 2004 at SOH. A striking pattern was that several dominant causes of cancellations were similar at the two hospitals in spite of different health care systems.

Conclusions: Cancellations seem to be a major problem and of similar magnitude at both hospitals. Our results indicate that cancellations are a system problem with both general and hospital specific causes. The routinely gathered data on causes of cancellation at the two institutions is not sufficient to tackle the fundamental system problems that lead to cancellations. Moreover, 10.5-21.4% of reported instances are recorded as “Other”, further limiting the usefulness of the recorded data. We are currently collecting data to substantiate a background for handling the problem of cancelling patients from the operating program.

An evaluation of cancellation in two independent surgery departments of the University Hospital LSH

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1Department of Anaesthesia and Intensive Care Medicine, 2Department of General Surgery, 3Department of Orthopedics, Landspitali University Hospital, Reykjavik, Iceland

Aims: Case cancellations on the day of surgery result in wasted operating room time, increased cost and increased stress for the patients. We examined the frequency and causes of cancellations on the day of surgery in two independent surgical departments at our hospital and the possible effect of outpatient preoperative (anaesthetic) evaluation (OPE) on the rate of cancellations.

Methods: Operating room records of two surgical departments at the Landspitali University Hospital (LSH) were examined retrospectively over a period of four years between January 2001 and December 2004. The number and causes of cancellations of elective cases on the day of surgery were analyzed. The two surgical departments are in separate buildings and one of them, Hringbraut (H) has an established OPE – clinic since the year 2000 while at the other, Fossvagur (F) patients are evaluated after submission to the surgical ward. All surgical specialties were presented except gynaecology and obstetrics.

Results: During this period of four years 1343 cases out of 12574 (10.68%) were cancelled at F. and 721 out of 13053 (5.52%) at H. The most common cause at F. was of administrative nature (2.32%) “no bed”. This cause accounted for 0.94% of cases at H. Other common causes were “unexpected illness of patient” F. 1.63%/H. 1.40% and other medical reasons 1.55% of cases at F. and 0.76% at H. At F. “other and unexplained” accounted for 1.39% of cases, but 0.29% at H. By grouping together three causes of cancellations (medical causes/patients personal reasons/no need for operation) which should usually be cleared in the OPE clinic 394 cases (3.15%) were cancelled at F. and 166 cases (1.27%) at H. (P < 0.05).

Conclusions: Elective surgery cancellations are a significant problem at LSH. While multifactorial in etiology, administrative problems and medical reasons are important factors. Preoperative anaesthetic evaluation at an outpatient clinic reduces patient related cancellations significantly.

The intraoperative use of a novel warm-air mattress for surgery in the lithotomy position

Gannédal P, Søldén E, Karlsson A

Karolinska University Hospital, Stockholm, Sweden

Aims: To elucidate the changes in core body temperature (CT) with an intra-operative warm-air mattress designed for the lithotomy position.

Methods: After ethical approval and informed consent, 12 patients (ASA 1–III), scheduled for major recto-abdominal surgery were included. The mattress was placed under the entire back of the patient and the warming started before the induction of general anaesthesia. Baseline and postoperative CT was measured awake as tympanic temperature (TT). Intraoperative CT was measured in the oesophagus (ET). Skin temperature (ST) was measured on the back. The mattress temperature was adjusted to reach the aimed CT of ≥36.5°C. The skin was inspected for burns or decubital sores postoperatively and the next day. Data are presented as median and range.

Results: The initial TT awake was 37.2 (36.1–37.5)°C. The lowest TT (35.9°C, 35.3–36.6) was found after 75 (25–135) minutes. Ten patients reached the aimed CT within 75 (0–240) minutes while two patients only reached 36.3°C. TT at the end of the warming was 37.2 (36.6–38.6)°C. At 2 hours postop the TT was 37.0 (36.4–38.4)°C. The highest ST was 40.3 (38.4–41.5)°C. Estimated bleeding was 475 (150–4600) ml. No signs of burns or decubital sores were found.

Conclusions: Cutaneous warming with this mattress was an effective means of preventing intraoperative hypothermia during prolonged abdominal surgery. No device-related adverse effects were observed. It also gives access to the patient without interrupted warming.

Efficiency of peroperative forced warm air depending on duration of surgery

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Aim: Use of forced warm air is the most efficient method to avoid intraoperative hypothermia. We intended to look at the efficiency of this method with respect to actual operating time.

Methods: 20 ASA II–III patients for major abdominal surgery were allocated into two groups of 10. One group (C) had cotton blankets covering the upper thorax and arms, insulating hat and stockings. The treatment group (S) had an upper body forced air blanket as well, set at 38°C from the start of surgery to the end of anaesthesia. Room temperature was 21°C and fluids warmed to 37°C. All patients had general anaesthesia and continuous epidural analgesia. Temperature was measured with an intraoperative esophageal (E) and a digital ear (DE) probe. Everything else equal, extubation was performed in theatre if the patients’ temperature was >35.5°C.

Results: The groups were demographically comparable. Operating times were 188 ± 26 (C) / 217 ± 32 (S) min (n.s.). There were no significant differences in fluids administered. After an initial (30 min) decline of 0.3°C (C) and 0.4°C (S) the C group continued a steady decline in temperature to 34.4 ± 0.2°C on arrival in PACU. The S-group differed significantly from the controls from 90 min after start of surgery and throughout the study period. On arrival in PACU the S-group had an average temperature of 36.2 ± 0.2°C (P < 0.05). Accordingly extubation in theatre was performed significantly more frequent in the S-group (6/10 (S) vs 1/10 (C).

Conclusion: The intraoperative use of forced warm air is efficient for maintaining normothermia in abdominal surgery for surgical times of more than 90 minutes.

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Intensive care

Is discharge from ICU at night an adverse event?

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Aims: To examine relationships between ICU capacity, discharge at night (10 PM – 7 AM) and mortality within 7 days after discharge from ICU.

Methods: Discharge times for 27 987 patients that were discharged alive from 29 Swedish ICUs during 2002-2003 were analysed. Vital status was secured from a national database. ICU-bed capacity (per 100 000) and staffing (per ICU-bed) during 2002 was taken from a national questionnaire. Logistic regression was used to calculate odds ratios for crude and age-adjusted mortality. Non-parametric correlation was used to examine relationships between discharge at night and ICU capacity.

Results: The proportion of ICU-survivors that were discharged at night varied between ICUs from 1.3 to 10.6% (mean 5.9%). Death within 7 days after discharge varied 10-fold (1.9–19.2, mean 8.3%). Mortality after discharge at night was increased compared to discharge during daytime (10.2% vs. 8.1%, P < 0.01). The crude odds ratio was 1.28 (95% CI: 1.09–1.51; age-adjusted OR: 1.31, 95% CI: 1.11–1.54). Median ICU-bed density and staffing was 6.7 beds/100 000 and 6 nurses + nurse assistants per bed, respectively. There was no correlation between discharge at night and normalized ICU-bed capacity or staffing when admissions during 2002 were analysed (P = 1.0 and P = 0.08, respectively).

Conclusions: Discharge from ICU at night is associated with higher age-adjusted mortality, but with no relationship to ICU-bed capacity or staffing. Unplanned discharge from ICU at night should be considered as an adverse event.

Planning ICU-bed capacity with detailed mathematical models validated by actual data

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Aims: To explore the use of appropriate detailed mathematical models for planning ICU-bed capacity in order to avoid the poor method of estimation of capacity through the use of average length of stay and a target bed occupancy level.

Methods: A classification of ICU patients was developed to yield groups of patients with relatively homogenous lengths of stay. Arrival patterns of the patients by month, day of the week, and hours during a day were also derived. These results, and the appropriate information about the ICUs, were used in detailed mathematical models and a comparison of the model predictions given below in brackets with actual data showed that a good validation of the models had been achieved.

Results:

<table>
<thead>
<tr>
<th>ICU</th>
<th>ICU A</th>
<th>ICU B</th>
<th>ICU C</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICU-beds</td>
<td>7</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>Admissions</td>
<td>705 (704)</td>
<td>505 (508)</td>
<td>816 (818)</td>
</tr>
<tr>
<td>Transfers</td>
<td>0% (0.1%)</td>
<td>2.4% (2.3%)</td>
<td>No data (0.9%)</td>
</tr>
<tr>
<td>Bed Occupancy</td>
<td>38% (39%)</td>
<td>72% (72%)</td>
<td>65% (66.9%)</td>
</tr>
</tbody>
</table>

Table. Actual data and model predictions in brackets

Conclusions: Validated models for ICU-bed capacity have been achieved. These can now be used to evaluate a variety of scenarios. Examples are: changes in the number of beds, changes in the number and case-mix of the patients, and changes in the lengths of stay.

Acute renal failure in the ICU

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Acute renal failure (ARF) is an organ dysfunction (OD) commonly seen in ICU patients. For acute respiratory failure the number of concomitant OD influence mortality more than respiratory failure alone (Flaatten et al 2003). This investigation was performed in order to investigate survival after ARF with different degrees of concomitant organ failure.

Methods: The study was performed from 2000–2004 in a single 10 bed academic ICU. All adult patients had the sequential organ failure assessment (SOFA) scored in six vital organ systems on a daily basis. Severe organ dysfunction was defined as SOFA score of 3 or 4. Patients having severe ARF were extracted from the ICU database, and grouped according to the presence of other concomitant severe organ dysfunction (pulmonary, circulatory, CNS, liver and coagulation) or no such failure. Patients were followed for 90 days.

Results: There were 2166 admissions, and totally 432 admissions (19.6%) had severe ARF. Severe ARF was present at admission in 252. See table for more details.

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Age mean</th>
<th>SOFA max mean</th>
<th>Mortality %</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ICU</td>
</tr>
<tr>
<td>All ARF</td>
<td>432</td>
<td>52.4</td>
<td>12.1</td>
<td>41.4</td>
</tr>
<tr>
<td>ARF alone</td>
<td>36</td>
<td>36.6</td>
<td>5.7</td>
<td>0</td>
</tr>
<tr>
<td>ARF + 1OF</td>
<td>112</td>
<td>46.6</td>
<td>8.8</td>
<td>17.9</td>
</tr>
<tr>
<td>ARF + 2OF</td>
<td>142</td>
<td>59.2</td>
<td>12.1</td>
<td>43</td>
</tr>
<tr>
<td>ARF + 3OF</td>
<td>114</td>
<td>56.1</td>
<td>15.6</td>
<td>68.4</td>
</tr>
<tr>
<td>ARF + 4/SOF</td>
<td>28</td>
<td>51.6</td>
<td>19.5</td>
<td>71.4</td>
</tr>
</tbody>
</table>

Conclusion: Severe ARF is a frequent organ dysfunction in the ICU. The outcome of ARF is more dependent on the number of other OD.
Methods: Studies were carried out for 24 months on 508 randomly selected patients (surgical and non-surgical) in a 12-bed clinical Intensive Care Unit. For 6 months (134 patients), no SGOMs were used and for 18 months, SGOMs were applied to 374 patients. Besides, in both groups other prophylactic actions like position changes, skin care were applied. The following data were recorded: patients’ type (surgical, non-surgical, his condition, pressure sore risk (PSR) scored by Waterlow and Braden scores, time of PS occurrence, PS localization and severity, hospitalization time. Statistics used: Chi squared and Mann-Whitney tests.

Results: Patients of both surgical and non-surgical groups were characterized by high PSR. Waterlow’s median was 23 and Braden’s 11 points. Hospitalization time in ICU without SGOMs was 14.5 days, with SGOMs 12.2 days (p < 0.215). Statistically no significant differences in bio-medical parameters were found. The use of SGOMs decreased PSs development by about 10% in non-surgical patients and by 19% in surgical patients.

Conclusions: SGOMs application seems to be particularly useful in patients after emergency surgery and in the reduction of PSs development on sacral bone.

81 Parameters for propofol use in the adult intensive care unit: use of guidelines and education to improve compliance

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Aims: When sedation is administered properly by continuous intravenous (IV) infusion in the ICU it can enhance patient safety and comfort and lower cost of care. Evidence suggests that implementation of protocols, guidelines, or pathways will improve clinical and economic outcomes. Our goal was to show that guidelines, standing orders, and intensive educational programs would alter caregiver practice and improve adherence to parameters for use of continuous IV infusion of propofol.

Methods: The three parameters selected by intensivists and pharmacists as goals to guide propofol use for sedation in intubated ICU patients are:
#1 = 100% of patients who receive propofol will receive a concomitant analgesic medication;
#2 = 75% will have propofol administered for 72 hours duration;
#3 = 95% will have propofol administered at <100 mcg/kg/minute.
These parameters were included in a sedation guideline with standing orders and in an educational process. Implementation required collaboration by nurses, pharmacists, and physicians.

Results: Evaluation of the effect of static gel-overlay mattresses

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University of Medical Sciences, Department of Anaesthesiological Nursing and Intensive Care, Poznań, Poland

Aims: Evaluation of the effect of static gel-overlay mattresses (SGOMs) in prophylaxis of pressure sores (PSSs) in critically ill patients.

Methods: Studies were carried out for 24 months on 508 randomly selected patients (surgical and non-surgical) in a 12-bed clinical Intensive Care Unit. For 6 months (134 patients), no SGOMs were used and for 18 months, SGOMs were applied to 374 patients. Besides, in both groups other prophylactic actions like position changes, skin care were applied. The following data were recorded: patients’ type (surgical, non-surgical, his condition, pressure sore risk (PSR) scored by Waterlow and Braden scores, time of PS occurrence, PS localization and severity, hospitalization time. Statistics used: Chi squared and Mann-Whitney tests.

Results: Patients of both surgical and non-surgical groups were characterized by high PSR. Waterlow’s median was 23 and Braden’s 11 points. Hospitalization time in ICU without SGOMs was 14.5 days, with SGOMs 12.2 days (p < 0.215). Statistically no significant differences in bio-medical parameters were found. The use of SGOMs decreased PSs development by about 10% in non-surgical patients and by 19% in surgical patients.

Conclusions: SGOMs application seems to be particularly useful in patients after emergency surgery and in the reduction of PSs development on sacral bone.

82 The photo-diary as an aid for relatives of patients dying in the ICU

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Aims: To examine how relatives of patients dying in the ICU looked upon the photo-diary, which we use as an aid to help patients cope with their experiences during critical illness (Bäckman et al, Intensive Care Med 2001; 27:426).

Methods: Photo-diaries were written for long-stay patients during their time in the ICU and used to help follow up in the post-ICU clinic. Relatives of patients that died during their ICU stay (n = 26) were also invited to a follow-up at which they were given the diaries. Mean (range) age of the deceased was 65 (39–82) years and length of ICU stay was 20.5 (2–56) days. APACHE II probability of death was 46 (17–92%). A set of questions was mailed after 6 months to the relatives to examine the value of the diary. Another researcher not involved in the project analysed and graded the responses.

Results: Most relatives affirmed that the diary had been of use when coming to terms with their loss. Their comments about the value of the diary were graded as of no value (n = 1), some value (1), valuable (10), very valuable (10) or extremely valuable (2). All diaries appeared easy to understand and had been read multiple times (n = 14; >10 times, n = 12). The diary seemed to be of value for relatives also during their loved ones’ stay in the ICU. Pictures were appreciated by almost everyone, and most diaries (n = 21) had been shown to friends and relatives.

Conclusions: The ICU photo-diary may be a useful aid for bereaved relatives trying to cope with loss of their loved ones. Many relatives read and wrote in the diary during the patient’s stay in the ICU. This appeared to further increase the value of the diary.

83 Effect of enteral nutrition (EN) versus glucose-(GLU) or lipid-based (LIP) parenteral nutrition (PN) on tight glycaemic control

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Aims: To study the effect of EN vs PN, and GLU- vs LIP-based PN on achievement of tight glycaemic control.

Methods: Patients expected to stay in ICU for >48 h were treated to maintain blood glucose between 4.4 & 6.1 mmol/L. EN, PN or EN+PN was commenced within 48 h of admission. For 3 months, PN patients were given a continuous infusion of dextrose 75% + amino-acids, with lipid (Intralipid 20%, 500 mL) administered twice weekly (GLU). For a further 3 months a continuous infusion of dextrose/amino acids & lipid (ClinOleic
20%) was administered (LIP). PN was isocaloric & isonitrogenous. The same EN formulation (Isocal) was used throughout.

Results: Patient groups did not differ in age, sex or Apache II score. Patients receiving PN had a longer ICU length of stay compared with the entire population or those receiving EN. 10.588 blood glucose samples were recorded.

Conclusions: PN, compared to EN, was associated with improved achievement of tight glycaemic control. LIP PN, compared with GLU PN was associated with less biochemical hypoglycaemia.

Amino acid and insulin infusion attenuates the hepatic glucose production after 3 days fast
Gjedsted J, Mengel A, Schmitz O, Møller N, Tønnesen E
Dept of Anaesthesia, Aarhus University Hospital, Aarhus, Denmark

Aims: This study was undertaken to investigate the hepatic handling of Amino acids (AA) after 72 hours of fasting.

Methods: N = 10, male healthy volunteers was investigated 12 hours fasting (post absorptive (PA)) and fasting (72 h). At t = 0 a 180 min. basal period were started, at t = 180 a 180 min. hyperinsulinemic euglycemic clamp was performed with concomitant AA infusion. Glucose tracer (3-3H) glucose was started at t = 0.

Discussion: The metabolic stress of fasting affects insulin sensitivity in a complex manner – on one side elevated levels of FFA and decreased GIR/M-value signify insulin resistance in fat and muscle tissue.

Trauma patients in the ICU: predictors of survival
Ulvik A, Flaatten H
Haukeland University Hospital, Bergen, Norway

Aims: Injury is a leading cause of death in young adults. This study examines the association of age, severe traumatic brain injury (TBI), Injury Severity Score (ISS), Sequential Organ Failure Assessment (SOFA) score and Simplified Acute Physiology Score (SAPS) II regarding 90 days mortality of trauma patients treated in the ICU.

Methods: This is a cohort study of all 328 severely traumatized patients (>18 years) admitted to a 10-bed general ICU in a university hospital from 1998–2003. Severe TBI was defined according to significant pathological findings on CT-scanning of the brain. Survival rates were found in the Norwegian Peoples Registry, while the other data were retrieved from the prospectively collected ICU database.

Results: Mean age of the 328 patients was 43.6 ± 19.7 years. Median ISS was 25 and 170 patients had severe TBI. A total of 265 patients survived more than 90 days. Multiple logistic regression analysis tested the association between chosen variables and 90 days mortality (see table).

Conclusions: Patient age and the results of SAPS II score and maximum SOFA score were associated to 90 days mortality while the results of ISS and the presence of severe TBI were not. Survival seems to be more dependent on the patient’s physiological response to the trauma than to the severity of the injury per se.
Cardiac anaesthesia

86 Outcome and functional autonomy and quality of life of elderly patients undergoing cardiac surgery
Berio I, Ghili L, Ridolfi N, Menini G, Sorbara C
Department of Anesthesia and Cardiac Surgery Intensive Care, Careggi Hospital, Florence, Italy

Aim: The purpose of this study was to examine outcome and functional autonomy and quality of life of elderly patients (≥80 y old) hospitalized for cardiac surgery.
Methods: Prospective cohort study of 65 patients ≥80 y admitted to a eight bed, surgical ICU in a 2000 bed, acute care hospital of Florence from January, 1st 2004 to June, 30th 2004 after cardiac surgery.
The severity at admission was estimated according to the Euroscore and SAPS II. All the patients underwent cardiac surgery before their ICU stay. Outcome measurements were made using telephone interviews with a questionnaire including evaluation of functional autonomy (SF-36) after 6 months of discharge from the ICU.
Results: The survival rate was 97% in the ICU, 94% in the Hospital. A total of 45 patients were alive and able to participate at the interview.
Conclusions: This study suggests the persistent high level of QoL with good hospital survival in elderly patients undergoing cardiac surgery.

87 Exercise testing indicates reduced ability to increase oxygen delivery on the first morning after coronary artery bypass surgery (CABG)
Skogvoll E, Kirkeby-Garstad I, Wisløff U, Stenseth R, Sellevold OFM
St. Olav's University Hospital, Trondheim, Norway

Aim: Does coronary bypass surgery affect O2 transport during exercise?
Methods: We studied 16 CABG patients with EF >50%. Mixed venous oxygen saturation (SvO2) was measured at rest, at 10 and 30 W bicycle exercise in bed before (day 0) and the first morning after the operation (day 1) using a pulmonary artery catheter. Oxygen consumption (VO2) was assessed by direct calorimetry. Analysis was with a linear mixed model.
Results: Mean age 60 ± 9 y, EF 69 ± 7%, SvO2 decreased by 1.1% pr. W on day 0 and by 1.5% pr. W on day 1 (P = 0.0003) and mean VO2 was reduced by 7.4% on day 1, VO2 increased (from rest to 30W) by 4.3 ± 1.9 ml kg⁻¹ min⁻¹ on day 0 and by 5.3 ± 2.6 ml kg⁻¹ min⁻¹ on day 1, a relative increase of 113 ± 58% and 118 ± 61%, respectively (NS).
Conclusions: The reduction in SvO2 during exercise was more pronounced after the operation, despite similar changes in VO2. The increase in oxygen extraction indicates reduced ability to compensate for the increased VO2 by increasing oxygen delivery.

88 Non invasive echocardiographic assessment of right atrial pressure in anaesthetised and mechanically ventilated patients
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Department of Anaesthesia* and of Cardiothoracic Surgery*, University Hospital of Basel, Basel, Switzerland

Aim: Transthoracic Doppler echocardiographic studies in awake patients have reported a correlation between right atrial pressure (RAP) and the ratio of the tricuspid peak early inflow velocity to early diastolic tricuspid annulus velocity measured by tissue Doppler imaging (E/Ea), allowing non invasive assessment of RAP. In this study, we tested whether the E/Ea ratio as recorded by transeosophageal echocardiography (TOE) allows for assessment of RAP in anaesthetised and mechanically ventilated patients.
Methods: Fifty patients undergoing elective coronary (CABG) surgery were studied after induction of general anaesthesia. RAP, mean airway pressure and the E/Ea ratio were obtained in the mechanically ventilated and hemodynamically stable patients prior to surgical incision. Correlations between mean RAP and E/Ea, and between RAP and airway pressure were assessed using linear regression.
Results: There was no correlation between RAP and the E/Ea ratio (see Figure) but a weak correlation between RAP and peak or mean airway pressures (r = 0.41, P = 0.004).
Conclusions: In anaesthetised and mechanically ventilated patients prior to CABG surgery, the E/Ea ratio as recorded by TOE did not allow for non-invasive assessment of RAP.

89

Low-dose recombinant activated factor VII in non-hemophiliac cardiac-surgery patients: a randomized case-control study
Romagnoli S, Bevilacqua S, Rossi A, Gelsomino S, Sorbara C
Department of Anesthesia and Cardiac Surgery Intensive Care, Careggi Hospital, Florence, Italy

Aims: to evaluate a low-dose rFVIIa in patients with intractable bleeding after cardiac surgery.

Methods: 20 patients at a single institution were randomly enrolled in the study from January 2004 to February 2005: at the end of a transfusional protocol, 10 patients were treated with 1.2 mg of rFVIIa (Group I) and 10 were controls (Group II).

Results: Median, 25th–75th 24-h blood loss percentiles were: 1685, 1590–1770 ml vs 3170, 2700–3850 ml in Group I and II, respectively (P = 0.0004). Median, 25th–75th of red blood cells (RBCs), fresh frozen plasma (FFP), and platelets (PLT) units transfused in Study Group and Controls were: 6, 4–8 U vs 21.5, 16.5–28 U, 0.0–4 U vs 7.5, 5–11 U, 0.0–4 U vs 9, 6–13 U, P = 0.001 (Fig. 1). In addition, a significantly improvement of PT (P = 0.01), INR (P = 0.006), aPTT (P = 0.01) and PLT count (P = 0.003) was detected in the Study Group vs Controls. Furthermore (Fig. 2), Group I-patients showed a lower ICU Length of Stay (LoS; \( \chi^2 = 15.9, P = 0.001 \)) and experienced a low surgical re-exploration rate (\( \chi^2 = 16.2, P < 0.001 \)).

Conclusions: In our experience, low-dose rFVIIa showed satisfactory results in cardiac patients with intractable bleeding. Further larger randomized series are necessary to confirm our findings.

90

Effect of albumin, gelatin and hydroxyethyl starch on coagulation after on-pump cardiac surgery
Niemi TT, Suojaranta-Ylinen R, Kukkonen S and Kuitunen AH
Department of Anaesthesia & Intensive Care Medicine, Helsinki University Hospital, Finland

Aim: To evaluate the effect of intravenous colloids on blood coagulation immediately after cardiac surgery.

Methods: 45 patients were randomised to receive 15 mL/kg of either albumin (ALB group), 4% sucrose-acelulated gelatin (GEL group) or 6% hydroxyethyl starch [MW 200 kDa/ degree of substitution 0.5 (HES group)] after primary and single on-pump cardiac surgery. The rate of colloid administration was based on clinical needs. Modified thromboelastometry (ROTEM®) using different activators [intrinsic ROTEM (InTEM); extrinsic ROTEM (ExTEM); fibrinogen ROTEM (fibrTEM), calcium (NaTEM)] was carried out at predetermined intervals.

Results and conclusions: Maximum clot firmness (MCF) and shear elastic modulus \( [G = 5000 \times MCF/(100 – MCF), \\text{dynes cm}^{-2}] \) was more decreased in GEL and HES groups than in ALB group immediately after completing the infusion (P < 0.01, Kruskal-Wallis analysis of variance). The effect was still seen two hours later and it was more pronounced in HES than in GEL group (fibrTEM, NaTEM). Clot formation time (CFT) (InTEM, ExTEM) was more prolonged immediately after HES than GEL (P < 0.001). After two hours CFT (ExTEM) had returned near the preinfusion level in GEL group but not in HES group (P < 0.05). Fibrinolytic activity was higher in HES than in GEL group two hours after the infusion as demonstrated by a decreased 60 min clot lysis index (P < 0.05). After on-pump cardiac surgery HES and gelatin impaired clot strength which may predispose patients to increased blood loss. As expected, the greatest impairment was seen after HES while albumin appeared to be the safest intravenous colloidal solution.

91

Single transpulmonary thermodilution during anesthesia in off-pump coronary artery bypass grafting
Kirov M, Kuzkov V, Lenkin A, Suborov E, Stastilin V, Borodin V, Chernov I, Shonbin A, Bjertnaes L
Northern State Medical University, City Hospital 1, Arkhangelsk, Russia, University of Tromsø, Tromse, Norway

Aim: To evaluate hemodynamic effects of midazolam, propofol, and isoflurane anesthesia by means of transpulmonary single thermodilution (STD) in patients subjected to off-pump coronary artery bypass grafting (OPCAB).

Methods: Twenty-two patients undergoing OPCAB were randomized to three groups receiving midazolam, propofol or isoflurane. During anesthesia, all patients received fentanyl and pipercuronium. After catheterization of the femoral artery, cardiac index (CI), cardiac function index (CFI), stroke volume index (SVI), stroke volume variations (SVV), global ejection fraction (GEF), left ventricular contractility index (dPmax), systemic vascular resistance index (SVRI), and other hemodynamic parameters were assessed by STD and pulse contour analysis (PiCCOplus, Pulsion Medical Systems). The measurements were performed after induction of anesthesia, during surgery, and at 2, 4, and 6 h postoperatively. The data were assessed using ANOVA followed by Scheffe’s test or test of contrasts when appropriate.

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Emergency medicine

Results: After revascularization, CI, CFI, and SVV increased in all groups in concert with a decline in SVRI (P < 0.05). In the midazolam group, SVI and GEF decreased perioperatively by 20–30% (P < 0.05). During surgery, propofol reduced GEF and dPmax by 10–15% (P < 0.05). These changes did not occur during isoflurane anesthesia.

Conclusions: In OPCAB, isoflurane provides better myocardial performance in comparison with midazolam and propofol, as evaluated by hemodynamic and volumetric data obtained with STD.

92
Five years of community-based prehospital thrombolysis (PHT) of STEMI-patients in North norway: significant time gained by training municipality ambulance personnel and primary doctors
Gilbert M, Sargård PB, Wang H
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Aims: To save time, lives and cardiac muscle, we organized an inter-active, decentralized community-based program for pre-hospital care of patients with acute chest pain. The aim was an earliest possible diagnosis, triage and administration of basic supportive care and thrombolysis in STEMI-patients, targeting rural populations in thinly populated areas.

Methods: Troms is a rural/urban subarctic county with 4.2 inhab/km². Average ground ambulance missions from districts to hospital are 120–190 km, or 137 minutes (median). Municipality ambulance personnel and primary doctors were trained for 2 days to triage, diagnose and give PHT when indicated in STEMI-patients. Each local unit had mobile 12-leads ECG with transmission to phone. ECGs and clinical data were sent to the on call hospital internists and Emergency Medical Dispatch Center operators in our hospital for optional discussions of treatment decisions.

Results: From 2000–2005, 1520 prehospital ECGs were transmitted, and 184 patients received PHT (75% men), 92.4% were discharged alive. Every 3rd PHT was given by ambulance personnel only, and protocol loyalty was similar between them and GPs. Median time factors: from symptom onset to start of chest pain to thrombolysis by training rural health workers to give PHT. More time can still be saved by improving logistics and reducing patients delays.

Conclusions: A median of almost 1.5 h was saved from start of chest pain to thrombolysis by training rural health workers to give PHT. More time can still be saved by improving logistics and reducing patients delays.

93
Incidence and cause of impaired consciousness among patients treated by a mobile emergency care unit in Denmark
Bach A, Christensen EF
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Aims: A mobile emergency care unit (MECU) staffed with an anesthesiologist is dispatched to seriously ill or injured patients according to predefined criteria among which “impaired consciousness” is one. In order to evaluate appropriate dispatch of the MECU, the aim of this study was to investigate the incidence and cause of impaired consciousness among patients to whom the MECU was dispatched.

Design: Descriptive study based on consecutively registered MECU data in 12 months. Data on demographics, tentative diagnosis and Glasgow Coma Scale (GCS) were retrieved. Tentative diagnoses were recorded according to International Classification of Diseases; version 10 (ICD-10). Impaired consciousness (IC) versus loss of consciousness (LOC) was defined as GCS < 15 and GCS < 9.

Results: The MECU attended 4752 patients. GCS was registered in 3835 patients; among these 1218 had IC of which 507 had LOC, giving incidence proportions of 31.8% and 13.2% of patients with recorded GCS. Most frequent diagnoses among patients with IC were: hypoglycaemia (n = 136, 49 with LOC), cardiac arrest (n = 118, 115 with LOC), stroke (n = 98, 27 with LOC), unattended death (n = 97, all with LOC), convulsions (n = 95, 24 with LOC), epilepsy (n = 72, 13 with LOC), alcohol intoxication (n = 71, 8 with LOC) and intracranial injury (n = 63, 19 with LOC).

Conclusions: Incidence of impaired consciousness was high and associated with diagnoses ranging from severe emergencies such as cardiac arrest and cerebrovascular diseases, all requiring the MECU, to less severe such as convulsions and alcohol intoxications. This indicates need for improved dispatch of the highly specialized MECU.

94
Comparison of airway management with the Intubating Laryngeal Mask®, Laryngeal Tube® and Cobra® by paramedical students in anaesthetized patients
Helsinki University Central Hospital, Helsinki, Finland

Aims: Alternative methods with shorter learning curves for inexperienced paramedical staff are needed as a substitute for endotracheal intubation (ETI).

Methods: The success of insertion, oxygenation and ventilation of the Intubating Laryngeal Mask (ILMA), the Laryngeal Tube (LT) and the Cobra (COB) in anaesthetized patients without use of muscle relaxant were compared. After informed consent 96 patients were monitored and anaesthetized for general surgery. After induction of anaesthesia, 32 paramedical students inserted ILMA, LT or COB in a random order. The number of insertion attempts, the time needed for insertion, and oxygenation and ventilation parameters were recorded. The students gave a subjective evaluation of the airway devices after the test.

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Respiratory intensive care

95
Helicopter transport of sick neonates
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Aims: The Norwegian Helicopter Emergency Medical Service (HEMS) employs anaesthesiologists and paramedics who are not formally trained in neonatology to provide stabilisation and transport of sick neonates. We describe neonatal transport by HEMS in central Norway and report the outcome.


Results: A total of 252 neonates were transported, indicating a prevalence of 0.90 per 100 newborn. Median response time was 30 min, on scene stabilisation time 38 min and transportation time 30 min. Median gestational age (GA) was 38 weeks and 4.8% of the neonates were <4100 g and/or <28 weeks. Main clinical problems were respiratory disease, asphyxia and malformations; 58 neonates (12%) died within one year. No deaths were transport-related. Tube- or ventilator problems were noted in 7 out of 66 transports of ventilated neonates. Other technical problems were few. Regarding ventilation, oxygenation and circulation, the clinical condition of most neonates improved during transport and the median temperature rose from 36.5°C to 37.0°C. Hypoglycaemia (<2 mmol/l) was documented in 19 missions after transport, among these 8 received glucose infusion. Four neonates might have profited from HEMS-delivered surfactant therapy.

Conclusions: HEMS in central Norway provides rapid medical assistance in a wide spectrum of neonatal problems, but more attention should be paid to proper ventilation and prevention of hypothermia and hypoglycaemia.

96
Emergency in-hospital anaesthesia assistance
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Aims: While anaesthesia and intensive care remain the core activity, anaesthesiologists and nurse anaesthetists are heavily involved in the management of in-hospital medical emergencies and trauma. We investigated the extent of this involvement provided by the department of Anaesthesiology at our 900-bed hospital in the year 2002.

Methods: Missions involving emergency medical assistance were identified through computer search of the department's database. We assessed medical aspects, place, time, and type of intervention.

Results: We identified a total of 646 missions, of which 501 occurred in the emergency department and 145 on the general wards. The majority (64%) occurred during call-hours (4 pm—8 am). We found that as many as 4 to 7 missions occurred on any single day 40 times (i.e. days) during the year; which is in accordance with a Poisson statistical model.

Trauma (50%) and cardiac arrest (20%) dominated the material. Other medical emergencies included seizures, cerebrovascular events, intoxication, respiratory arrest, cardiac arrhythmias, internal bleeding, pulmonary oedema and loss of consciousness.

Airway management was important, as 61 patients received bag-valve-mask ventilation and 164 were intubated and ventilated. In addition to measures during advanced cardiopulmonary resuscitation, circulatory support (i.e. volume infusion, blood transfusion and/or vasoactive drugs) was considered the primary treatment in 44 patients.

Conclusions: The department of Anaesthesiology daily provides comprehensive emergency medical assistance at other hospital departments. Staffing and activity planning – especially during call-hours – must consider the possibility of a sudden medical emergency.
98 A prospective study of non-invasive ventilation (NIV) in acute on chronic obstructive pulmonary disease (COPD) in the ICU
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Aim: To examine use of non-invasive ventilation in patients admitted due to an acute exacerbation of COPD.

Methods: A fixed dataset was collected over 18 months for consecutive admissions for acute COPD to 9 general ICUs serving a discrete region (population 980 000). Data on all ICU admissions were obtained from the Swedish Intensive Care Registry (www.icuregswe.org) and vital status was secured from a national database.

Results: 103 COPD patients (median 11 per unit, mean 1.7% of all ICU admissions) were diagnosed using clinical signs and spirometry (n = 56) or clinical signs only (n = 47). Mean (SD) age and APACHE II score were 70 (10) yrs and 21 (7) points, respectively. Breath rates at admission were 28 (8) bpm and arterial blood gases were pH 7.26 (0.11), PCO2 10.3 (3.0) kPa, PO2 8.5 (3.2) kPa, without significant differences between patients that were intubated immediately (INV-group, n = 16) or were started on non-invasive ventilation (NIV-group, n = 87). Body mass index (BMI) was lower in patients started on NIV (23.5 vs. 28.3, P < 0.02), while failure of NIV (n = 18) was not associated with greater BMI. Length of stay was shorter in the NIV-group (79 vs. 210 h, <0.001). 30-day mortality was 26/87 and 7/16 in the NIV and INV-groups, respectively (P = NS). The only significant determinant of 30-day mortality was APACHE II score with OR 3.3 per 10 points (95% CI: 1.5 to 7.5).

Conclusions: NIV was used widely in acute COPD and in agreement with current guidelines (www.goldcopd.org, www.slmf.se/kol/).

99 Acute respiratory distress syndrome treated with an interventional lung assist device for CO2 removal; a case report
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Aims: “Lung protective” ventilation (avoiding high inspiratory pressures and low expiratory pressures) has been shown to improve clinical outcome of patients with ARDS. However, such treatment may lead to small tidal volumes with hypercapnea and serious acidosis. We report a case of ARDS treated with a pumpless interventional lung assist device to reduce blood CO2.

Methods: Information gathered from hospital records.

Results: A 55 year old female with severe septic shock and ARDS, immediately needing ventilator therapy, was admitted to the ICU. Conventional pressure controlled ventilation was replaced with high frequency oscillation after 6 h because of grave hypoxia, where after oxygenation was satisfactory. However, the patient developed persistent hypercapnia (120 mmHg) and acidosis (pH 7.1) followed by cardiovascular instability. On day 18 a treatment with arterio-venous pumpless extracorporeal lung assist device (Novalung®) was started and both CO2 and pH returned to normal values within one hour with a simultaneous reduction in the need of vasoactive drugs. The patient improved significantly and the lung assist was discontinued after 12 days without any complications. While still recovering the patient died on day 46 after she unexpectedly suffered an intracerebral haemorrhage.

Discussion: Treatment with pumpless interventional lung assist device resulted in quick normalisation of arterial CO2 and pH followed by a marked improvement in the patient’s clinical condition. This type of lung assist must be considered feasible in patients with increase in CO2 due to ventilation failure, to facilitate lung protective ventilator therapy.

100 Physiological responses to positive expiratory pressure (PEP) breathing, a comparison between the PEP-bottle and the PEP-mask
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Aims: To elucidate and compare the PEP-bottle (a threshold resistor device) with the PEP mask (a flow resistance device), by comparisons of airway pressures and expiratory airflow.

Methods: During PEP-breathing, airway pressure and airflow were recorded continuously. The measurement sequence consisted of three sessions of 10 breaths with either the PEP mask or the PEP bottle, in a randomised order. A resting period of 15 minutes separated measurements of breathing through the different PEP devices.

Results: With the PEP-bottle, the expiratory phase began with a 0.39 s long zero flow period. During this period airway pressure rose 11.9 cm H2O but no airflow occurred. With the PEP-mask, the corresponding zero flow period was 0.04 s and the change in airway pressure 0.4 cm H2O. At the end of the expiration, airway pressure was 9.5 cm H2O when using the PEP-bottle and 0 cm H2O when breathing through the PEP-mask. When breathing through the PEP-bottle, the inspiration began with a zero flow period, amounting to 0.43 s. During this period, airway pressure decreased 9.6 cm H2O from the expiratory end airway pressure level. With the PEP-mask, the corresponding zero airflow period was 0.01 s, and no changes in airway pressure were observed.

Conclusions: Comparisons between the two PEP devices showed major differences in the relation between airflow and airway pressure. These findings might explain observed differences in patient compliance.

101 Using a cytology brush dipped in adrenaline, enables a cytology sample to be obtained during bronchoscopy with minimal bleeding
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Aims: To evaluate the efficacy of a cytology brush dipped in adrenaline, in obtaining a cytology sample from proximal airways tumors due to lung cancer lesions, that were considered risky to brush using the “conventional” adrenaline instillation technique that is routinely used at bronchoscopy, in order to minimize bleeding due to brushing.

Methods: We performed fiberoptic bronchoscopy in the 34 patients with the above mentioned lesions due to lung cancer available to us, in order to obtain a diagnosis. We sampled different sites of these measurable lesions: 1) By using the conventional adrenaline instillation method in some tumor sites and 2) By using a cytology brush dipped in adrenaline solution

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Comparing surgical to percutaneous tracheostomy

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Aims: Determine the mortality and morbidity of percutaneous tracheostomy with bronchoscopic guidance and compare it to the surgical open technique in the operating room.

Methods: Open, observational clinical trial in ninety four consecutive patients requiring a tracheostomy in a General Intensive Care Unit of an University Hospital. Performance of an endoscopically guided percutaneous technique unless contraindication or absence of trained personnel. We divided the percutaneous techniques in Griggs (Portex, UK) and Percutwist (Rusch, Germany). The statistical analyses were performed using Mann-Whitney and Chi-Square tests and \( P \leq 0.05 \) was considered significant.

Results: Twenty women (21%) and 74 men with a median age of 56 years and a median time of intubation of 14 days. The admission diagnoses were Trauma admissions in 53% of these patients. We performed percutaneous techniques in 65% (Griggs 44%; Percutwist 21%) and the main reason to perform a surgical tracheostomy was the lack of trained personnel. Early complications (haemorrhage \( n = 14 \); pneumothorax \( n = 1 \); hypoxia \( n = 3 \) anterior wall laceration \( n = 1 \)) happened in 22% of the patients and late ones where seen in 8.5%. Operative mortality was zero. Older patients had a significantly higher number of early complications \( (P = 0.005) \) and the Percutwist technique the one that had less complications \( (P = 0.025) \).

Conclusions: Endoscopically guided percutaneous techniques including the new Percutwist technique are safe. Percutwist offers an interesting alternative for the performance of a percutaneous tracheostomy.

Use of the PAxpress™ supraglottic device facilitates percutaneous dilatational tracheostomy

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Aims: To study the feasibility and safety of using the PAxpress™ supraglottic device for airway maintenance during percutaneous dilatational tracheostomy.

Methods: Prospective observational study of 26 consecutive patients (11M, 15F) in a general ICU. The patients’ endotracheal tube (ET) was exchanged for a PAxpress™ supraglottic device by the same ICU physician, prior to performing a percutaneous dilatation tracheostomy.

Results: Hemodynamic variables (HR, BP), arterial blood gases and ventilation parameters (Ppeak, Ppl, VTisp–VTexp) were recorded during mechanical ventilation with both the ET tube and PAxpress™ device. There was no loss of tidal volume in 22 patients, a loss of 50–100 mL/breath in 3 patients and a loss of more than 150 mL/breath in one patient. The PAxpress™ device successfully maintained the airway and allowed adequate ventilation in 25 out of 26 patients. Furthermore, there was no significant difference in HR, BP, blood gases, Ppeak and Ppl during ventilation with the ET or with the PAxpress™ device. A minute amount of blood was detected around the end of the PAxpress™ device in 3 patients.

Conclusions: The PAxpress™ is an effective ventilatory device that can successfully ventilate a patient during percutaneous dilatational tracheostomy. It may prevent the difficulties associated with the use of the ET such as cuff puncture and tube transection by the needle.
Biomechanical experimental evaluation of percutaneous tracheostomy to compare Ciaglia and Griggs techniques
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Aims: To create a method for biomechanical experimental evaluation of percutaneous tracheostomy (PCT) by Ciaglia and Griggs technique and perform their assessment in order to clarify the reasons for traumatic perioperative complications.

Methods: PCT by Ciaglia technique (n = 10) and by Griggs technique (n = 10) were performed on fresh dead pigs. During PCT special measurements were performed with the help of electronic dynamometer (MRC): piercing, penetrating, pulling and pushing forces. On the base of these measurements calculation of energy spent for stages of PCT was done. Measures of the size of tracheotomy were performed.

Results: Application of Ciaglia dilator requested more energy in 1.54 times than Griggs dilator forceps (P < 0.05). Formation of tracheotomy by Ciaglia dilator was more exact than by Griggs forceps due to special markings on the dilator. The work with Griggs dilating forceps requested more experience due to absence of any markings on the dilator. The most dangerous moments of PCT for laceration were: dilation of hole in Griggs technique and insertion of tracheotomy tube loaded on dilator in Ciaglia technique. Appearance and diameter of tracheotomies were the same in spite of different instruments used for dilation (P < 0.05).

Conclusions: PCT by Ciaglia and Griggs techniques has almost similar biomechanical characteristics and the same parameters of tracheotomy. Both of them have dangerous moments. In order to prevent laceration of the cervical trachea during PCT some improvements must be done in instrumentation.

Experimental sepsis

Vasopressin has profound effects on the distribution of splanchnic blood flow in septic shock
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Introduction: Vasopressin has been proposed for treatment of catecholamine-resistant septic shock. The aim of this study was to measure hepato-splanchnic, as well as microcirculatory blood flow in the liver, the pancreas and the kidney during administration of low-dose vasopressin in septic shock.

Methods: Four groups of pigs (27–34 kg, n = 8 in each group) were anaesthetised and ventilated. Blood flow was measured in the hepatic and renal arteries, portal vein and in celiac trunk using ultrasonic transit time flowmetry. Microcirculatory blood flow was measured in liver, kidney and pancreas using laser Doppler flowmetry. Group S (sepsis) and group SV (sepsis/vasopressin) were made septic by fecal peritonitis. Group C and group V were non-septic control groups. After 300 min of sepsis group V and group SV received intravenous infusion of vasopressin 0.06 IU.·kg⁻¹·h⁻¹ for 3 hours.

Results: In both septic and nonseptic groups, vasopressin increased MAP and decreased CO. Regional blood flow decreased in the portal vein and the renal artery while it increased in the celiac trunk and the hepatic artery. Total hepatic blood flow remained unchanged. Microcirculatory flow decreased in pancreas and kidney but was unchanged in the liver.

Conclusion: In this porcine model of fluid resuscitated septic shock, administration of vasopressin resulted in profound changes in the distribution of blood flow in the splanchnic region. While total hepatic blood flow appeared to remain preserved, regional and microcirculatory blood flow significantly decreased in the kidney and pancreas.
Vasopressin decreases microcirculatory blood flow in the stomach and small intestine in septic shock

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Background: Vasopressin can raise arterial pressure in septic shock even when alpha adrenergic agonists appear ineffective. The aim of this study was to investigate the effects of vasopressin on superior mesenteric artery- and microcirculatory blood flow during septic shock in pigs.

Methods: Thirty-two pigs were anesthetized, mechanically ventilated and randomly assigned to one of four groups (n = 8 in each). Group S (sepsis) and group SV (sepsis/vasopressin) were made septic by fecal peritonitis. Group C and group V (sepsis/vasopressin) were non-septic control groups. After 300 min of sepsis group V and group SV received intravenous infusion of vasopressin 0.06 IU · kg⁻¹ · h⁻¹. In all groups cardiac index and superior mesenteric artery flow were measured. Microcirculatory blood flow was recorded with laser Doppler flowmetry in both mucosa and muscularis of the stomach, jejunum and colon. Intramucosal CO₂ tension in the jejunum was measured with tonometry.

Results: While vasopressin significantly increased MAP in group SV (P < 0.01) superior mesenteric artery flow decreased by 50% (P < 0.01). Microcirculatory blood flow decreased in stomach mucosa (23%, P < 0.05) and muscularis (48%, P < 0.01) and in jejunal mucosa (27%, P < 0.01). There was increase in mucosal to arterial CO₂ gap (P < 0.01). Conclusion: Vasopressin decreased mesenteric blood flow as well as microcirculatory flow in the stomach and small intestine. This flow reduction together with increase in arterial to jejunal CO₂ gap suggests compromised mucosal blood flow during vasopressin administration.

Treatment with rescueflow™ (hypertonic saline/dextran) and/or endothelin receptor antagonist tezosentan of LPS-induced endotoxin shock in anaesthetized pigs

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Aims: We evaluated the effect of endothelin receptor antagonist Tezosentan and/or iv infusion of HSD in anaesthetized pigs.

Methods: In 32 anaesthetized pigs, a continuous infusion of endotoxin (0111:B4) was increased during 30 min to 5 μg/kg/h. The infusion was discontinued after 3 hours and the animals were observed for another 2 hours. After one hour of infusion, 8 animals were randomised to receive Tezosentan, 8 animals to HSD and 8 animals to a control group. Central hemodynamics and SvO₂ were measured using a pulmonary artery catheter. Regional blood flow rates were measured continuously using perivascular ultrasonic flow probes. Blood oxygenation and acid-base balance were also analyzed.

Results: The LPS-infusion resulted in a septic shock within one hour in all animals. There was an increased mortality in the treatment groups compared to the control group. Survival rate: Tezosentan group, 6 of 8, HSD group, 7 of 8, Tezosentan and HSD in combination, 6 of 8, and in the control group, 2 of 8. Tezosentan had beneficial effects on splanchnic blood flow associated with a decreased blood pressure, while HSD had beneficial effects on systemic blood pressure and renal blood flow.

Conclusion: Resuscitation with Tezosentan or HSD demonstrates beneficial effects in terms of survival. The results of an combination of Tezosentan and HSD did not show any improvement of the survival rate, even though this combination increased blood pressure and regional perfusion compared to single treatment or control group.

The inflammatory response during hyperglycemia and hyperinsulinemia in a porcine endotoxemic model


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Aims: To elucidate whether acute hyperglycemia and hyperinsulinemia modify the cytokine content in organs during LPS challenge in a porcine model.

Methods: Pigs (35-40 kg) were randomised to normoglycemia (group 1, plasma glucose = 5 mM, n = 8) or hyperglycemia (group 2, plasma glucose = 15 mM, n = 8). Anesthetized and mechanically ventilated. Both groups received LPS infusion (180 min, total 10 μg/kg). Group 1 maintained a baseline insulin level while the hyperglycemic group exhibited increased insulin levels.

Results: Circulating cytokines, cytokine mRNA and cytokine protein content were examined in essential organs. After LPS exposure, in both groups vast and equal plasma cytokines were elicited by approximately 70–5000 fold. A 10-fold higher level of IL-10, IL-6 and TNF-α protein was found in kidney tissue compared to the other organs together with a 3–10 fold increase of TNF-α in adipose tissue. However, cytokine mRNAs as well as organ function were without statistical difference between the groups, except for muscle tissue.

Conclusion: Endotoxemia elicited a pronounced cytokine response in both plasma and at organ level. The kidneys and adipose tissue showed the highest cytokine protein content. Acute hyperglycemia apparently counteracts the well-established anti-inflammatory effects of insulin in the inflammatory response in an LPS challenged porcine model. Whether the observation can be extrapolated to more long-term stress-exposure remains to be clarified.

Effect of 1.25-dihydroxy-vitamin D₃ in experimental sepsis

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Aim: In addition to the regulation of calcium homeostasis, vitamin D affects the immune system cell differentiation, the interaction of macrophages and monocytes, and the lymphocyte activity. We therefore examined the effect of 1.25-dihydroxy-vitamin D₃ on coagulation and organ failure in three models of sepsis in the rat.

Methods: Three series of placebo-controlled studies were conducted. All rats were pretreated with daily SC injections of 1.25-dihydroxy-vitamin D₃, 100 ng/kg or placebo for 3 days. In study A, sepsis was accomplished by abdominal surgery comprising...
36 Experimental sepsis

a coecal ligation and puncture with a 1.2 mm needle, or sham surgery. In study B, the rats had a single IP injection of lipopolysaccharide from E. Coli 0111:B4 (LPS) 8 mg/kg, or placebo. In study C, an hour-long IV infusion of LPS 7 mg/kg, or placebo was given.

Results: In all three models of sepsis a significant effect on coagulation was obtained with reduced platelet count and AT, and increased APTT and prothrombin time (P < 0.05). Also, a significant effect on liver function was induced in all sepsis groups comprising elevated ALT, AST, ALP, and bilirubin (P < 0.05). However, we found no differences between vitamin D and placebo-treated rats with regards to either coagulation or liver function.

Conclusion: The present data does not suggest a modulating effect of 1,25-dihydroxy-vitamin D₃ supplementation on sepsis-induced failure of coagulation or liver in rats.

112 Rosiglitazone, a ligand of peroxisome proliferator-activated receptor-γ, attenuates pulmonary inflammation and NF-κB activation in endotoxic rats

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Aims: The purpose of this study is to investigate the protective effect of rosiglitazone (ROS), a ligand of peroxisome proliferator-activated receptor-γ (PPARγ), on endotoxin-induced acute lung injury in rats.

Methods: 24 anesthetized male Wistar rats were randomly assigned into four groups (n = 6 per group): (1) Sham-DMSO group, rats received the vehicle for ROSI (10% dimethyl sulfoxide (DMSO), i.v.) 30 min prior to saline; (2) Sham-ROSI group, same as the Sham-DMSO group but that ROSI (0.3 mg/kg, i.v.) was administered instead of DMSO; (3) LPS group, identical to the Sham-DMSO group except that lipopolysaccharide (LPS, 6 mg/kg, i.v.) was given instead of saline; (4) LPS-ROSI group, rats received for ROSI (10% dimethyl sulfoxide, i.v.) 30 min prior to saline. 4 h after LPS injection, lung injury was evaluated in terms of tissue neutrophil infiltration (Myeloperoxidase activity) and histopathological changes. Concentrations of tumor necrosis factor-α (TNF-α) and cytokine-induced neutrophil chemottractant-1 (CINC-1) and nuclear factor-κB (NF-κB) activation were also measured in lung tissues using commercial ELISA kit.

Results: Pretreatment with rosiglitazone attenuated LPS-induced lung histological injury and neutrophil infiltration. Furthermore, rosiglitazone significantly reduced the increases of TNF-α and CINC-1 concentrations in the lung tissues caused by LPS (P < 0.01). These beneficial effects of rosiglitazone were associated with the inhibition of NF-κB activation.

Conclusions: Rosiglitazone could reduce endotoxin-induced pulmonary inflammation and lung injury in rats.

113 Antimicrobial peptides based on human cathelicidin LL-37 as candidates for treating sepsis

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Antimicrobial peptides have been evaluated as alternatives to conventional antibiotics. Human antimicrobial peptide LL-37 not only possess antimicrobial activity against Gram-negative and -positive bacteria and fungi, but also binds and neutralizes endotoxin, a trigger of SIRS. It could thus be beneficial in sepsis treatment but clinical trials have been hampered by indications that native LL-37 is cytotoxic. Although the toxicity is inhibited by binding to plasma proteins, the binding of LL-37 unfortunately also abolishes its antimicrobial effects.

Aim: Investigate if removal of hydrophobic amino acids from LL-37 decreases cytotoxicity and plasma protein binding without affecting antibacterial activity, endotoxin neutralization and chemotactic activity.

Methods: LL-37 was compared to two less hydrophobic fragments obtained by N-terminal truncation, named 106 and 110 and one previously described hydrophobic variant, 18 mer LLKKK.

Results: All peptides inhibited the growth of Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus and Candida albicans, inhibited endotoxin-induced vascular nitric oxide production and attracted granulocytes similarly. While fragment 106 and 110 caused less hemolysis and apoptosis in human cultured smooth muscle cells than LL-37, 18 mer LLKKK induced severe hemolysis. As opposed to LL-37 the antibacterial effect of fragments 106 and 110 was not affected by serum.

Conclusions: Removal of N-terminal hydrophobic amino acids from LL-37 decreases its cytotoxicity as well as its inhibition by serum while antimicrobial and endotoxin neutralization are maintained. These results suggest that analogs of LL-37 may be used as a novel peptide-based systemic treatment of sepsis.

114 Flowmotion of colon mucosal microcirculation during short-term administration of norepinephrine

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Aims: Rhythmic variations of microcirculatory blood flow have been observed in skeletal muscle and other tissues in low flow states. A similar looking flowmotion occurs in the intestinal mucosa under conditions of normal blood flow, however it disappears when blood flow is severely reduced. The physiological importance is not known but an involvement in transcapillary fluid exchange has been suggested. The aim of the study was to test the effects of norepinephrine on flowmotion of the colon mucosa.

Methods: Eight pigs were anaesthetized and mechanically ventilated. Systemic blood flow was measured using thermodilution. Microcirculatory blood flow (MBF) in the colon mucosa was measured using laser Doppler flowmetry (LDF). After surgery and stabilization, an intravenous infusion of norepinephrine was administered at a rate of 0.2 mcg kg⁻¹ min⁻¹. The LDF signal was recorded continuously and analyzed offline.

Results: At baseline, regular flowmotion with a median frequency of 72 (68–73) mHz was observed in the colon mucosa in three of eight animals. In two animals, oscillations of the LDF signal were irregular and in three animals flowmotion was absent. After 15 minutes of norepinephrine, arterial blood pressure and cardiac output increased. MBF of colon mucosa decreased to 83% (59–103; P = 0.02) of baseline and regular flowmotion with a median frequency of 78 (68–100) mHz was observed in seven out of eight animals.

Conclusions: Despite decreased MBF in the colon mucosa during administration norepinephrine, regular flowmotion appeared to be induced rather than depressed.
Evaluation of microdialysis as a method to investigate inflammation

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Aim: To study whether microdialysis can be used to investigate an inflammatory reaction as reflected by cytokines, chemokines and complement activation products.

Methods: Lepurin-anticoagulated human whole blood was incubated with lipopolysaccharide (0.1 μg/mL) at 37°C for 1, 4 and 24 hours and plasma obtained as resource for cytokines (TNF-α, IL-1β, IL-6 and IL-10) and chemokines (IL-8, IP-10, MCP-1, MIG and RANTES). Complement activation products (C3a, C4a and C5a) were obtained by incubating normal human serum with heat-aggregated IgG (1 mg/mL) at 37°C for 30 minutes. The activated plasma and serum samples were tested with CMA microdialysis catheters with 20 and 100 kD pore sizes, respectively.

Results: None of the mediators tested passed through the 20 kD filter with significant recovery (<10% for all). With the 100 kD filter the following results were obtained: 1) The cytokines IL-1β and IL-6 showed high (>50%) and low (10%) recovery, respectively, whereas TNFα and IL-10 did not pass. 2) The chemokines in general showed high recovery, consistent with their low molecular weight; MCP-1 and MIG: 50%, IL-8: 30–50% and IP-10: 20–25%. 3) All three anaphylotoxins were detected with a recovery of 20–30%.

Conclusions: These data indicate that the 100 kD CMA microdialysis system can be used as a reliable method to detect an inflammatory reaction, defined by certain specific markers. Importantly, the actual markers cannot be predicted by their molecular weight alone; other physical and chemical properties may influence their passage through the filter. The findings may have important implications in future clinical studies.

Sustained effects of repeated trauma team training with simulation arranged locally in hospitals

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Aims: To study whether trauma management and the correct order of interventions was improved from first training course to last training course was assessed by questions evaluating overall performance of the hospital's trauma team. The development in each hospital from the time of the first training to the last training was assessed by questions assessing changes in team cooperation, communication and leadership.

Methods: 16 of the hospitals had more than one training course. The development in each hospital from the time of the first training course to the last training was assessed by questions comparing participants at first course with new participants in later courses in the same hospital (95% CI of difference <0.27 to 0.11 and <0.37 to 0.02 respectively, P = 0.391 and 0.063). Six months after the training 79% reported that the training gave them experience in trauma handling they would not have gained otherwise.

Conclusions: Trauma management and the correct order of interventions was improved from first training course to later courses evaluated by new participants. Knowledge seems to have been transferred to the organisation, while individual knowledge and confidence in new participants remains unchanged.

References

Marked improvement in Norwegian hospitals’ trauma care during four years

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Aims: To study whether trauma management and the correct order of interventions was improved from first training course to last training course was assessed by questions evaluating overall performance of the hospital's trauma team. The development in each hospital from the time of the first training to the last training was assessed by questions assessing changes in team cooperation, communication and leadership.

Methods: 16 of the hospitals had more than one training course. The development in each hospital from the time of the first training course to the last training was assessed by questions comparing participants at first course with new participants in later courses in the same hospital (95% CI of difference <0.27 to 0.11 and <0.37 to 0.02 respectively, P = 0.391 and 0.063). Six months after the training 79% reported that the training gave them experience in trauma handling they would not have gained otherwise.

Conclusions: Trauma management and the correct order of interventions was improved from first training course to later courses evaluated by new participants. Knowledge seems to have been transferred to the organisation, while individual knowledge and confidence in new participants remains unchanged.

References
118 Effect of prehospital advanced life support with rapid sequence intubation (RSI) on outcome of severe head injury
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Aim: The role of prehospital trauma care and the effect of prehospital RSI is still not clear. This study evaluated the impact of the prehospital trauma care with emergency medical doctors on the mortality from severe head injury and 180-day Glasgow Outcome Scale (GOS).

Methods and patients: A 48-months retrospective study of 63 patients with severe head injury (GCS < 9 and ISS > 15) who received ATLS and RSI and were transported by EMD to the hospital (EMD group). This group was compared with 60 patients who were injured before the beginning of prehospital care system with EMD in our region and did not receive RSI or appropriate ATLS (EMT group).

Results: There were no significantly statistical differences between both groups in age (P = 0.79), mechanism of injury (P = 0.68), gender (P = 0.82), initial GCS (P = 0.63) and hospital mortality (EMD group: 40% 95% CI: 34–45 vs. EMT group: 42% (95% CI 36–47), P = 0.76). In EMD group there was significantly better first hour survival (97% vs. 79%, P = 0.02), first day survival (90% vs. 75%, P = 0.02), better outcome (GOS 4–5 (53.1% vs. 33.3%, P = 0.01), GOS 2–3 (7.8% vs. 20%, P = 0.01)), shortened time of hospitalization in ICU (P = 0.03) or other departments (P = 0.04).

Conclusion: After starting trauma care system (and RSI) with emergency medical doctors in our region, there was a decrease in number of deaths at hospital admission, a change in temporal distribution of deaths, an improvement in functional outcome and a shortened time of hospitalization.

119 Clonidine and motion sickness in prehospital trauma care
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Aims: The study of an a2 agonist clonidine in prevention of motion sickness in prehospital trauma care. Clonidine has been used with success in the postoperative nausea and vomiting. Risk factors for motion sickness are the transport by ambulance, the trauma and the type of drugs that the patient has received. Oxygen and antiemetic drugs are the major care for this problem.

Methods: Sixty (60) patients, ages 18–60 years old, all traffic accident victims were included in this prospective, randomized trial. The patients had one or two long bone fractures. They were haemodynamically stable and conscious. The fractures were stabilized. The patients received loroxinbac 8 mg intravenous (iv) as analgesic agent and ranitidine 50 mg iv for gastric mucous protection. They were divided in two groups of thirty (30) persons each. Group A was the placebo group. Group B received clonidine 150 g iv after the stabilization of fractures and before the use of analgesic agent. The transport average time was 20 minutes. They all received oxygen as supplemental therapy.

There were excluded patients with medical history of predisposing factors to motion sickness.

Results: The type of medicine and the appearance of motion sickness, are not independent (P = 0.001).

Conclusions: The emesis center is connected with area postrema. Clonidine as an a2 agonist probably interacts with these receptors.

120 Anaesthesiologist in 2 different field hospitals
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Aims: In disaster and military conflict areas anaesthesiologists have to work under exceptional circumstances encountering special problems and unusual pattern of traumatized patients. I present my own mission experiences in International Red Cross Committee field hospital of Quetta for victims of civil war in Afghanistan 1993–1994 and in Finnish Red Cross Society’s field hospital in Bhuj, after earthquake 2001.

Methods: 1st mission in Quetta field hospital lasted 6 months, over 800 anesthesias for war surgery. Gun shot wounds 30%, land mine injuries 30% and shrapnel injuries 30%. Ketamine intravenous anaesthesia dominated >90%. 2nd mission after earthquake which destroyed the city of Bhuj was field hospital (totally functioning in tents) supported by Red Cross Societies of Norway, Germany and Finland lasting 2 months. During 6 first weeks, 480 patients were operated. Soft tissue injuries, infected wounds dominated, but cesarean sections for 33 mothers, and normal surgical diseases were done.

Results
1. working conditions, climate, local culture different
2. war and disaster traumas and anaesthesia need special training in anaesthetic and surgical care

Conclusions
1. training program in disaster medicine and field hospital anaesthesiology mandatory for successful outcome of missions, both for professional reasons and economical reasons: field hospitals are costly.
2. ERU-concept (emergency response unit) worked well in BHUJ
3. preplanned ready to use hospital documentation needed.

121 Regional anaesthesia for high risk patients in difficult circumstances
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The perception that regional anaesthesia is safer than general anaesthesia has been growing among physicians; in particular anaesthesiologists. The aim of this study is to evaluate the use of different regional anaesthesia procedures for surgery in high risk patients; in difficult circumstances (during embargo, war and post – war conditions). The study includes 49 patients (40 male and 9 female). All patients were judged as high-risk associated with multiple medical problems and rank in ASA class III (32 patients) and ASA class IV (17 patients). Various surgical procedures were done for them; 23 general surgery, 18 orthopedic and 8 urological operations. Different regional anaesthesia techniques were used depending on the surgical procedures, availability of regional anesthetic agents and instruments as well as author preference. Those regional anaesthesia techniques include 13 spinal, 20 epidural (8 lumbar and 13 caudal) and 15 peripheral nerve blockade. Lignocaine was used for 32, bupivacaine for 12, levo-bupivacaine (chirocaine) for 3 and mivipacaine for 2 patients. Freshly prepared mixtures of the local anesthetics and additives (adrenaline, sodium bicarbonate or fentanyl) were used in most of the cases. 39 patients did not required sedation or analgesia or supplemented light general anaesthesia. The
remaining ten patients were judged to be apprehensive and were sedated with medazolam 1 mg (2 patients) or Fentanyl 50 micrograms (3 patients) and light general anaesthesia; 60% N₂O in oxygen and halothane with Magill’s circuit (5 patients) peroperatively. Post operatively, the patients were pain free for three to twenty hours (depending on local anesthetic agents and additives used). Three patients had mild hypotension peroperatively (2 epidural and one intrathecal) that had been managed successfully with intravenous fluid with or without vasopressors. In conclusion; with careful selection and preparation of high-risk patients and with proper understanding and selection of the regional anaesthesia techniques, peroperative observations and early post operative follow up reveal high degree of patients satisfaction with minimal metabolic and cardiovascular disturbances.

122
Smoking prevalence and patients motivation to change behaviour in young trauma patients with minor trauma in an inner city emergency department
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Aims: To evaluate the prevalence of smoking and patients motivation to change behaviour in trauma patients in an emergency department.

123
The effect of different doses of alfentanil on the intubation conditions during rapid sequence induction with thiopental and rocuronium
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Aims: Determine the dose of alfentanil needed to achieve perfect intubation conditions within 40 s after rapid sequence induction with thiopental and rocuronium.

Methods: 60 ASA 1 patients were randomly allocated to five different alfentanil dose groups (NaCl15, 30, 45, or 60μg/kg). A blinded dose of alfentanil, thiopental 4 mg/kg, and rocuronium 1 mg/kg were administered in rapid succession. Laryngoscopy followed by tracheal intubation was performed 40 s after rocuronium. Intubation conditions were graded according to five different criteria. Logistic regression was used to analyze the relationship between the alfentanil dose and the probability of having perfect intubation conditions within 40 s. Doses of alfentanil which gave 50, 90 and 95% probability (D50, D90, D95) of success were calculated.

Results: D50, D90, and D95 of alfentanil, and their confidence intervals were 21.5 (19.0–23.8), 33.1 (30.1–35.8), and 36.4 (33.4–39.4) μg/kg, respectively.

Conclusions: Approximately 36 μg/kg of alfentanil was needed to obtain perfect intubation conditions in 95% of the patients during rapid sequence induction with thiopental and rocuronium. When ideal intubation conditions are needed, our technique represents a satisfactory alternative to regimen involving succinylcholine.

124
Pharmacology of intranasal midazolam: Discrepancy between pharmacokinetics and subjective sedation
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Aims/Background: Bidirectional nasal drug delivery is a new administration principle with improved deposition pattern. Its potential for a more rapid and complete nasal uptake of midazolam was studied in healthy volunteers.

Methods: Twelve subjects were included after ethics committee approval to this 3-way crossover (3.4 mg midazolam iv; bidirectional and traditional spray) study. Primary outcomes were bioavailability and time to maximum serum concentrations, secondary outcomes were sedation, adverse effects, and relations between nasal dimensions and pharmacokinetics. Serum concentrations were measured by a validated GC-MS method, pharmacokinetic calculations were based on non-compartmental modelling, sedation assessed by a subjective 0–10 numerical
Remifentanil as a single agent for extracorporeal shock wave lithotripsy: comparison of infusion doses in terms of analgesic potency and side effects


Aims: The goal of this randomised, double-blind study was to compare the analgesic effectiveness and side effects of two remifentanil infusion rates in patients undergoing extracorporeal shock wave lithotripsy (ESWL) for renal stones.

Methods: 200 patients undergoing ESWL were administered either remifentanil 0.05 micrograms kg\(^{-1}\) min\(^{-1}\) (n = 100) or 0.1 micrograms kg\(^{-1}\) min\(^{-1}\) (n = 100) plus demand bolus of 10 micrograms of remifentanil via a patient controlled analgesia (PCA) device. No other sedating agents were given. The frequency of PCA demands and deliveries were recorded. Blood pressure, oxygen saturation and respiratory rate were recorded throughout the procedure. Nausea and vomiting (PONV), dizziness, itching, agitation and respiratory depression were measured post treatment. Visual analogue scale (VAS) scores were taken preoperatively, directly postoperative and 30 minutes after finishing the procedure.

Results: There were no statistically significant differences in the frequency of PCA demands and delivered boluses, nor between perioperative VAS scores. The extent of PONV and frequency of dizziness and itching immediately after and dizziness 30 minutes after the end of treatment were significantly reduced in the lower dose group.

Conclusions: A remifentanil infusion of 0.05 micrograms kg\(^{-1}\) min\(^{-1}\) plus 10 microgram demands is superior to 0.1 micrograms kg\(^{-1}\) min\(^{-1}\) plus demands, as there was no difference in the pain scores recorded between groups and it has a lower incidence of side effects in patients receiving ESWL.

Propofol uses the phosphatidylinositol-3-kinase to regulate actin reorganisation

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Aims: The cellular pharmacology of anaesthetics are not fully understood. Propofol interacts with the cytoskeleton by recruiting actin to the cell membrane and by reorganising the cytoskeletal actin into ring structures. Actin reorganisation often involves modulation via the phosphatidylinositol-3-kinase (PI3-kinase). To explore the anaesthetic cellular mechanisms, the signal system used by propofol to cause actin rings was studied.

Methods: Cultured newborn rat neurons were exposed to propofol (3\(\mu\)g ml\(^{-1}\)) with or without wortmannin, a inhibitor of PI3-kinase, in calcium medium at 37°C. Wortmannin was used in both a dose-response (0.1 nM–10 \(\mu\)M for 20 minutes) and a time-response study (1 \(\mu\)M, 0.5–35 minutes). ALEXA-phalloidin was used to visualize cytoskeletal actin and percentage cells with ring structures were counted using fluorescence microscopy.

Results: The amount of ring structures caused by propofol was decreased in a dose-dependent manner with EC50 at 1 \(\mu\)M (n = 4). No difference in the amount of rings was detectable in the time study (n = 4).

Conclusions: Propofol reorganise neuronal actin by signalling via PI3-kinase, and provides another piece towards understanding anaesthetic cellular pharmacology.

Different effects of sevoflurane and isoflurane on neuronal actin cytoskeleton

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Aims: To explore the anaesthetic cellular mechanisms, effects on the neuronal cytoskeleton caused by sevoflurane and isoflurane was studied to compare the effects of volatiles with the effects of propofol. Propofol interacts with the cytoskeleton by recruiting actin to the cell membrane and by reorganising the cytoskeletal actin into ring structures.

Methods: Cultured newborn rat neurons were exposed in a time-response study (1–35 minutes) to either sevoflurane (4%) or isoflurane (2.5%) in air, air alone or propofol (3 \(\mu\)g ml\(^{-1}\)) in a calcium medium at 37°C. ALEXA-phalloidin was used to visualize cytoskeletal actin and percentage cells with ring structures were counted using fluorescence microscopy.

Results: Propofol is known to cause maximal ring structures at 20 minutes (25% rings), and was used as positive control. Sevoflurane (n = 3) had a time maximum at 20 to 25 minutes (30% rings), but for isoflurane (n = 3) the amount of rings were 15% for all times studied. Air alone gave 5% rings with no difference between stimulation times.

Conclusions: Sevoflurane and propofol are equal in their effects on actin rings, but the structurally related volatiles sevoflurane and isoflurane have different cytoskeletal effects. This difference in cellular dynamics might play a part in their clinical appearance as fast and slow agents.

Orexin A: A propofol antagonist?

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Aims: To elucidate the anesthetic mechanisms, we studied orexin A, a hypothalamic peptide known to regulate arousal. We investigated its effect on propofol induced reorganization of the actin cytoskeleton evaluated as ring structures in neurons.

Methods: Primary cultures of rat neurons were stimulated in a dose-response experiment by propofol 3 \(\mu\)g ml\(^{-1}\) for 1 min before adding a premixed solution of orexin A and propofol in calcium medium for 20 min. In a time-response titration, rat neurons were treated initially by propofol 3 \(\mu\)g ml\(^{-1}\) and after 1 min with a premixed solution of orexin A 10 \(^{-8}\) M and propofol in calcium medium. Fluorescence microscopy of ALEXA-phalloidin labelled actin was used to visualize the number of actin ring structures.

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**Novel mutations in the butyrylcholinesterase gene**

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Hereditary low butyrylcholinesterase (BChE) activity may result in prolonged duration of action of succinylcholine and mivacurium. In 25% of the patients referred to Danish Cholinesterase Research Unit, the phenotypes cannot be established using conventional biochemical method, and DNA-based diagnosis is therefore used.  

**Aims:** To identify novel mutations in the butyrylcholinesterase gene in patients who have experienced a prolonged duration of action of mivacurium or succinylcholine.  

**Materials and methods:** A total of 268 subjects (proband and family members) were studied. Genotyping was performed with complete nucleotide sequencing of the 4 exons and the intron-exon boundaries.  

**Results:** Fourteen new mutations were identified in 6 families and 8 individuals. Eleven nucleotide substitutions caused single amino acid changes and one was a deletion of two nucleotide bases. Two mutations were located on the untranslated parts of the gene. The mutations were associated with prolonged duration of action of the drugs.  

**Discussion:** Surprisingly many new mutations were found. One fourth of the patients had equivocal phenotypes, and in some families there were subjects who were homozygous for silent genes. The significance of the new mutations for the reactions to mivacurium and succinylcholine is discussed. Genetic investigations may help identifying subjects at risk and thus increase perioperative safety.

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**Post op pain and PONV**

**Patient-controlled analgesia: an experimental assessment of the PCA delivery systems of six hospitals**

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**Aims:** To assess the design safety of Patient-Controlled Analgesia (PCA) systems used clinically, with attention to (i) risk of siphoning of opiate from the syringe into the patient and (ii) risk of reflux of opiate retrogradely into the intravenous fluid line and fluid bag.  

**Methods:** The PCA delivery systems in six major Australian paediatric hospitals were studied. Safety features during normal operation and during simulated distal cannula occlusion were examined. Methylene blue was used in the opiate syringe as visual identification for siphoning and reflux. Bench tests were performed in triplicate.  

**Results:** Important findings were: (i) Siphoning of opiate syringe contents was demonstrated in two of the six PCA systems studied (siphoning flow rates up to 10.2 ml per minute when the opiate syringe was 60 cm higher than the cannula). Using the corresponding hospital opiate protocols, this represented infusions of 1.0 mg/kg morphine intravenously in five minutes. The two systems displaying siphoning did not incorporate anti-siphon devices. (ii) One PCA system revealed the potential for opiate reflux into the intravenous fluid bag. This system did not have a non-reflux device. (iii) In four of the PCA systems the bolus took greater than 5 minutes to be delivered to the cannula. (iv) There was wide inter-hospital variation in the PCA systems used.  

**Conclusions:** This study raises concerns about design safety features of Patient-Controlled Analgesia systems in clinical use and their potential for adverse incidents. The authors encourage other anaesthetists to assess the safety of their own Patient-Controlled Analgesia systems.

**Quality of segmental epidural pain management by two different age groups after abdominal surgery. Survey by 966 patients in the University Hospital Landspítalinn Reykjavík Iceland**

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**Introduction:** Optimal postoperative epidural analgesia reduces complications and shortens the postoperative course after major surgery. In the year 1996 triple component segmental epidural analgesia treatment was implemented on the surgical ward in our hospital. A specific pain monitoring flow-sheet served as a tool in the observation of post-operative pain, pain treatment and side effects as well as an accurate documentation of the treatment. This study describes the result of the pain treatment in two different age groups after abdominal surgery in the years 1996 to 2004.  

**Methods:** Patients undergoing laparatomy were studied retrospectively. Postoperatively a BFA-mixture (bupivacaine 0.1 mg/ml, fentanyl 2 ug/ml and adrenaline 2 ug/ml) was infused in an thoracic epidural catheter for pain treatment. The patients were divided into two age groups, Group I, with patients ≤50 years of age and group II, with patients ≥70 years of age. The information in the pain monitoring flow-sheets was evaluated on the first and second postoperative day. Post-operative pain intensity (VAS 1–10), infusion rate of...
BFA-mixture, and the use of rescue drugs were compared between the two age groups.

**Results:** 966 patients were included in the study, 333 in group I (mean age 38.8) and 633 in group II (mean age 77.5). Analgesia at rest and by movement was better on day one and day two in group II than group I.

<table>
<thead>
<tr>
<th>Analgesia by rest/movement</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day one VAS ≤ 3, at rest.</td>
<td>84%</td>
<td>94%</td>
</tr>
<tr>
<td>Day one VAS ≤ 3, by movement.</td>
<td>63%</td>
<td>79%</td>
</tr>
<tr>
<td>Day two VAS ≤ 3, at rest.</td>
<td>86%</td>
<td>92%</td>
</tr>
<tr>
<td>Day two VAS ≤ 3, by movement.</td>
<td>75%</td>
<td>84%</td>
</tr>
</tbody>
</table>

The average use of BFA-mixture was higher in group I (6.3 ml/h.) than group II (6.7 ml/h.). Also the need to apply rescue drugs was higher in group I.

Conclusions: Insufficient postoperative epidural analgesia depends on many factors as unskilled anaesthesiologists, not motivated patients, technical problems by epidural puncture and catheterization. The age of the patients also seems to be factor which may influence the quality of the postoperative pain management and patients satisfaction.

133

Effects of epinephrine in patient controlled epidural analgesia after subtotal gastrectomy

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**Aims:** Local anesthetics and opioids have been widely used for epidural patient controlled epidural analgesia (PCEA). Epinephrine has also been shown to potentiate the analgesic effect of epidural infusion of local anesthetics or opioids. The aim of this study was to compare analgesic effects and side effects of PCEA with ropivacaine mixed with either morphine, fentanyl, or epinephrine.

**Method:** Sixty-seven subtotal gastrectomy patients treated postoperatively with PCEA were randomly allocated into group M; 0.2% ropivacaine and 40 μg/ml morphine, group F; 0.2% ropivacaine and 4 μg/ml fentanyl, or group E; 0.2% ropivacaine and 2 μg/ml epinephrine. Visual analogue scale (VAS) was used to estimate pain and side effects at 6 and 24 hours postoperatively.

**Result:** The VAS score was significantly higher in group E compared to group M and F at 6 hours postoperatively and higher than group F at 24 hours. The total doses of PCEA was lower in group M than in groups F and E. The incidence and severity of postoperative nausea was higher in group M than in groups F and E at 6 and 24 hours postoperatively.

**Conclusion:** Epinephrine-ropivacaine provided less side effects and higher pain score than fentanyl-ropivacaine or morphine-ropivacaine for patient controlled epidural analgesia after major abdominal surgery. It is suggested that epinephrine should be considered as an alternative to opioids in analgesic solutions used for patient controlled epidural analgesia.

133

Experience of pain control by regional block in advanced malignancy

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**Background:** Neurolytic block is one of the methods for control of intractable pain in advanced malignancies and some times it is the only method where 20% will not respond to NSAID’s or opiates.

**Objectives:** The purpose of our research is to prove the effectiveness and promote our experience of pain control in advanced malignancy of abdominal, pelvic and secondary rib metastasis.

**Methods:** 100 patients were included in this study, their ages ranging (20–75) years. Mean age is 50 years with advanced abdominal and pelvic malignancies, and secondary rib metastasis. The patients were referred from surgical department and medical department of oncology in Baghdad teaching hospital between Feb. 1999–Apr. 2001, we used celiac block pain in advanced abdominal malignancies, intrathecal absolute alcohol for pelvic malignancies and paravertebral intercostals block to control pain due to secondary metastasis of ribs. Using visual analogous scale to know the effect versus of these techniques.

**Results:** Out of 75 patients who received celiac block for pain due to abdominal malignancies, 69 patients had pain control dramatically (92%) out of 20 patients who received intrathecal alcohol for pain due to pelvic malignancies, 18 patients had satisfactory pain control (90%). All patients who received intercostals block responded very well to this modality of pain control (100%).

**Conclusion:** In expert hands these methods of pain control can be used safely to decrease the suffering of these patients, thus improving their life quality, this objective calls for the establishment of a specialized teaching centre to train coming generations of doctors.
POSTERS

134
Introduction of HFOV is more beneficial in adult patients with extrapulmonary form of acute respiratory distress syndrome
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Aims: Recently known differences between pulmonary and extrapulmonary acute respiratory distress syndromes (ARDSp, ARDSexp) are the main reasons of scientific discussion on potential differences in effects of current ventilatory strategies. The aim of this study is to assess whether the presence of ARDSp or ARDSexp can differently affect the beneficial effects of HFOV upon physiological and clinical parameters.

Methods: 30 adults (55 ± 19 years old, M/F = 16/14) fulfilling the ARDS criteria were indicated for HFOV in case of failure of conventional ventilation strategy. According to ARDS type, each patient was included either to the group of patients with ARDSp or ARDSexp (15/15 patients). HFOV: Sensormedics 3100B, f = 5 Hz, ΔP set to reach normocapnia, CDP (i.e. MAP during HFOV) changed iteratively to reach the best PaO₂/FIO₂.

Results: Six hours after introduction of normocapnic HFOV there was no significant increase in PaO₂/FIO₂ in ARDSp group (from 129 ± 47 to 133 ± 50 Torr), but a very significant improvement in ARDSexp (from 114 ± 54 to 200 ± 65 Torr, P < 0.01). Despite the insignificant difference in the latest MAP on CMV between both groups, initial optimal CDP for the best PaO₂/FIO₂ during HFOV was 2.0 ± 0.6 kPa in ARDSp and 2.8 ± 0.6 kPa in ARDSexp (P < 0.01).

Conclusion: HFOV recruits and thus it is more effective in ARDSsp patients with increased amount of recruitable atelectatic lung tissue. ARDSexp patients require higher CDP levels than ARDSp patients during HFOV. The testing period for positive effect of HFOV is recommended not to be longer than 24 hours.

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135
Studying the interaction between the mechanical properties of the respiratory system and artificial lung ventilation
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Aims: Different effects of artificial lung ventilation can be observed when conventional ventilation (CV) or high frequency ventilation (HFV) are used. The aim of this work was to develop a model of the human respiratory system that can be used during both CV and HFV and that can explain differences in the intrapulmonary conditions and consequential different effects of CV and HFV.

Methods: The anatomical structure of the respiratory system is considered as an acoustical system. The whole model, comprising 67 108 859 individual components, can be represented as an electric circuit and a special algorithm for solution of that complicated structure was developed. The pressure distribution along the bronchial tree, distribution of tidal volume among the generations of the bronchial tree, etc can be simulated. The intrapulmonary conditions were studied under various parameters of CV and HFV.

Results: The results obtained by the model suggest that HFV should be more suitable when the alveolar compliance has been decreased, while changes in airways resistance do not affect parameters of CV as much as parameters of HFV. The modelling confirms that almost 95% of proximal pressure amplitude is present inside the lung structure during CV, while only 5-10% of the input pressure amplitude is transferred deep inside the lung structure during HFV.

Conclusions: The unique model of the human respiratory system was developed according to the real anatomical lung structure. Results from the presented study may be used for explanation of the effects observed in the clinical practice.

136
Improvement in alveolar oxygen fraction by introduction of tracheal gas insufflation
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Aims: Tracheal gas insufflation (TGI) has been examined on animal experiments for a long time but still it is far from a routine clinical application. Combination of TGI and high-frequency oscillatory ventilation (HFOV) offers another protective ventilatory technique improving oxygenation. The aim of the study is to create a gas-flow model of the respiratory system suitable for studying effects of TGI during HFOV and during conventional ventilation (CV).

Methods: A mathematical model was created based on convection-diffusion equation of gas in the respiratory system. The complicated lung structure is modelled as an axial symmetrical straight pipe with a growing radius. The TGI catheter is modelled as an axial symmetrical straight pipe with a growing radius. The TGI catheter is modelled as an axial symmetrical straight pipe with a growing radius. The TGI catheter is modelled as an axial symmetrical straight pipe with a growing radius. The TGI catheter is modelled as an axial symmetrical straight pipe with a growing radius.

Results: The results obtained by the model suggest that HFV effect is much stronger during HFOV contrary to CV. Furthermore, many other results, which are observed during HFOV or TGI applications, can be explained using the model, e.g. influence of VT on oxygenation in HFOV contrary to CV, etc. The precision of the calculation can be demonstrated by agreement of the results of the animal experiment (the difference in increased oxygenation was ΔP₂O₂HV - CV = 11.2 ± 3.6% and calculations (ΔP₂O₂HV - CV = 14.4%) under equivalent conditions.

Conclusions: The developed model is useful for describing and studying TGI effects during both CV and HFOV that can be observed in the clinical practice.
A comparison of propofol-remifentanil and propofol-alfentanil infusion for posterior spinal fusion with wake-up test

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Aims: Wake-up test can be used during posterior spinal fusion (PSF) to ensure that spinal function remains intact. The goals of this study were assessment of wake-up test time and their quality, hemodynamic changes, and costs between propofol-remifentanil (PR) versus propofol-alfentanil (PA) infusions during PSF surgery.

Methods: Intraoperative wake-up tests were performed in 40 patients randomized to either alfentanil or remifentanil infusions for PSF surgery. In both groups, after premedication with midazolam 30 mcg kg⁻¹ and alfentanil 30 mcg kg⁻¹, anesthesia was induced with thiopental 5 mg kg⁻¹ and atracurium 0.6 mg kg⁻¹. After endotracheal intubation, anesthesia protocol was continued with propofol or remifentanil 0.2 mcg kg⁻¹ min⁻¹ and alfentanil 0.5 mcg kg⁻¹ min⁻¹. All patients received isoflurane and nitrous oxide, and the ventilation was adjusted to maintain arterial carbon dioxide tension at 35–45 mmHg and arterial oxygen saturation at 98–100%.

Results: Blood pressure was lower in PR than PA (4.5 min) (P < 0.0001). IOP in supine 1 group (132 ± 18.9 mmHg) was higher than in group 2 (132 ± 8.9 mmHg), and the duration in group 1 (132 ± 8.9 mmHg) was longer than in group 2 (P < 0.005). There was no significant difference between systolic and diastolic blood pressure and heart rate before and after block in these three groups.

Conclusion: Addition of verapamil with or without sufentanil to lidocaine solution for axillary plexus block significantly prolonged the duration of axillary plexus block.

The intraocular pressure alterations in anesthetized patients under percutaneous nephrolithotomy

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Aims: Regarding the effect of prone position on intraocular pressure (IOP) and consequent effect on ocular perfusion pressure (OPP) and probable threat of post-operative visual loss (PVL), this study was carried out to measure the time dependent correlation between IOP and prone position during Percutaneous nephrolithotomy (PCN) procedures.

Methods: The IOP of 20 patients (18–60 y/o, ASA status I–III) without history of eye disease, ophthalmic surgery or allergy, scheduled for PCN surgery were measured in the status below: (1) Awake patient in supine position (baseline). (2) 10 minutes after anesthesia in supine position (supine I). (3) 10 minutes after prone position (prone I). (4) End of procedure in prone position (Prone II). (5) 10 minutes after returning to supine position (supine II). The patient head was positioned with a gelatine head holder. The data were analyzed with repeated measures analysis of variances and paired t test.

Results: The mean values for IOP in successive measurements had statistically significant difference (P < 0.000). IOP in supine I was less than baseline IOP (15.4 ± 2.9 to 12.5 ± 2.5 mmHg, P < 0.000). IOP in prone I (25.5 ± 1.5 mmHg) was higher than both IOP in supine I (P = 0.000) and baseline (P = 0.000). IOP in prone II (38.9 ± 0.9 mmHg) was higher than all the other measurements (P = 0.000). IOP in supine II (37.3 ± 0.4 mmHg) decreased in comparison with IOP in prone II (P = 0.000). There was a positive
linear correlation between IOP and time in prone position ($r = 0.67, P = 0.001$).

Conclusions: IOP decreased after anesthesia and increased significantly after prone position. There was a linear correlation between increasing IOP and duration of prone positioning. IOP was doubled after 2 hours. Therefore precautional efforts and continuous consideration are strongly recommended during long term procedures (more than 2 hours) in prone position anesthetized patients to prevent probable post-operative visual loss.

141 Blood pressor response and airway effects of cricoid pressure during induction of general anaesthesia

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Aims: Cricoid pressure (CP) has been used to protect the patient from regurgitation and gastric insufflation. The aim of this study is to evaluate the pressor response and airway effects of this maneuver.

Methods: Eighty ASA I adult patients were prospectively included in the study. Patients were randomly divided into Cricoid and Placebo groups. In the Cricoid group, after the induction of anesthesia, bimanual CP was performed, and in the Control group, simple placement of hands without exerting pressure was performed. Peak inspiratory pressure and exhaled tidal volume were recorded before and during the application of CP. Arterial blood pressure and heart rate were recorded before and after application of CP. The data were compared between and within groups by using the mixed-design analysis of variance.

Results: Peak inspiratory pressure increased and tidal volume decreased significantly after the application of CP compared with the Control group and baseline values. Arterial blood pressure and heart rate increased significantly after the application of CP compared with the baseline values and with those of the Control group.

Conclusions: The result of this study shows that cricoid pressure can cause a relatively strong blood pressor response, which could be risky in old patients with borderline heart disease.

142 Perioperative course of patients with active infective endocarditis in Estonia in 1995–2004

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Aims: To evaluate indications for surgery, perioperative course and microbiological data of active infective endocarditis (AIE) in Estonia.

Methods: Retrospective analysis of 96 patients (pts) in 1995–2004 via hospital chart review.

Results: In 1995–2004 103 valve replacements were performed on 96 pts with AIE (re-replacements on 7 pts), 75 of them due to native and 21 due to prosthetic valve endocarditis (PVE) with 7 early and 14 late PVE cases. Mean age was 50 (19–79) yrs, 75% of pts were males. Targets of septic destruction were aortic valves (70.8%) with 41.2% of them spreading to mitral valve or adjacent structures. Blood cultures were negative in 40.6% of pts. No pathogen was identified in 25% of cases. Staphylococci were most important pathogen. Indications for surgery were severe heart failure in 47.9%, uncontrolled infection in 23.9%, or both in 13.5% of pts. 19.8% of pts were operated on as emergency due to septic or cardiogenic shock. Due to coagulopathies 60.4% of pts received platelet transfusion. 8 units of red blood cells and 4 units of plasma were transfused perioperatively as mean, 8 rethoracotomies. Despite of severe preoperative condition 72.9% of pts needed no or moderate inotropic support and mechanical ventilation of the lungs (MVL) less than 24 h. 27.1% of pts developed septic or cardiogenic shock needing aggressive inotropic support and prolonged (13 days as mean in survivals) MVL. Hospital mortality was 16.7%, MOF and uncontrolled infection as main course.

Conclusions: Early surgical treatment of AIE seems to be effective despite severe preoperative conditions.

143 The hemodynamic time course of landiolol hydrochloride, a ultra-short-acting β-blocker: Comparison with those of esmolol hydrochloride

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Aims: Landiolol hydrochloride is a half-life 3.96 minutes, selective β-blocker ($\beta_1/\beta_2 = 277:1$). We compared landiolol hydrochloride with esmolol hydrochloride by hemodynamic change to evaluate the effect on sinus tachycardia cases.

Methods: The study was focused retrospectively on 20 perioperative sinus tachycardia (heart rate > 100/min) patients: 10 cases landiolol hydrochloride (group L), 10 cases esmolol hydrochloride (group E). Heart rate (HR) and systolic & diastolic blood pressure (SBP&DBP) monitored by arterial tonometry method as a non-invasive continuous measurement were recorded by every 2 seconds with a computer.

Results: HR decreased significantly ($P < 0.05$) after 52 seconds in group L, 22 seconds in group E from baseline (drug administration). The 10% decrease of HR was shown after 115 seconds in group L, 22 seconds in group E. The 10% decrease of HR was shown after 115 seconds in group L, 22 seconds in group E. Additional injection was needed in 2 patients of group L and 4 patients of group E. BP was temporary increased, especially SBP; and decreased in both group afterwards. Peak SBP was monitored after 58 seconds in group L, 32 seconds in group E. Administration of vasopressor drug for excessive hypotension was required in 1 patient of group L, 4 patients of group E.

Conclusions: The rapid bradycardiac change and hypotension after temporary hypertension occurred in both groups. In group L, bradycardia and hypotension were mild and adequate. We’ll refer to tonometry method as more precious monitoring system in our presentation.

144 Late alveolar haemorrhage in a patient recovering from leptospirosis

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Aims: Although not uncommon, alveolar haemorrhage due to pulmonary vasculitis in the course of leptospirosis, is rarely included in the differential diagnosis of pulmonary haemorrhagic syndromes. We present a case of a patient, being treated in the ICU for leptospirosis infection, with a late onset of diffuse alveolar damage presenting as severe haemoptysis.

Case presentation: A 68-year-old man was admitted in the hospital and three days later he was transferred in the ICU after a progressive CNS impairment and finally a cardiac arrest. He
145 The effects of anesthetic preconditioning on neurologic injury and Bcl-2 family protein mRNA expression after transient spinal ischemia in the rat

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Aims: The aim of this study was to evaluate the effects of anesthetic preconditioning on neurologic outcome and Bcl-2 family protein gene expression in transient spinal ischemia.

Methods: Rats were anesthetized with intraperitoneal propofol, and enflurane (EP group), sevoflurane (SP group), isoflurane (IP group) were given during 30 minutes and 14 minutes of spinal ischemia was induced 30 minutes later. Spinal ischemia was produced by both induced hypotension and thoracic aortic cross clamping. Neurologic scores were assessed 1, 3, 24, 48 hours after transient spinal ischemia. After 48 hours, rats were killed under anesthesia and spinal cords were removed for the assay of Bcl-2 family protein mRNA expression.

Results: 30 minutes of anesthetic preconditioning with enflurane, sevoflurane, and isoflurane showed significantly better neurologic outcome compared to propofol anesthetized rats. Bcl-2 family protein mRNA expression of IP group was lesser than that of the other groups.

Conclusions: Anesthetic preconditioning with volatile anesthetics for 30 minutes could reduce ischemic injury during transient spinal ischemia. The degree of neurologic injury may not be related to the expression of pro-apoptotic protein Bax. Isoflurane may have different influence on apoptosis after spinal ischemia compared to enflurane or sevoflurane.

146 Advantages of nalbuphine, compared with fentanyl and midazolam extracorporeal shock-wave lithotripsy: an evaluation of postoperative analgesia and adverse effects

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Aims: The purpose of this study is to examine the advantages of nalbuphine, for postoperative analgesia and adverse effects compared with fentanyl and midazolam, in extracorporeal shock-wave lithotripsy.

Methods: Sixty healthy patients who were scheduled for extracorporeal shock-wave lithotripsy with anesthesia were enrolled. They received 2 mg midazolam with either fentanyl 100 ug (Group 1), nalbuphine 5 mg (Group 2), nalbuphine 10 mg (Group 3), or nalbuphine 15 mg (Group 4). Only patients in Groups 1 and 2 reported pain during surgery. Postoperative analgesia lasted significantly longer in the fentanyl group, compared with the nalbuphine groups (P < 0.0001). In the nalbuphine groups, postoperative analgesia lasted longest with the 15-mg dose. The additional increase to 20 mg did not increase efficacy. The incidence of pruritus was significantly higher in Group 1 (11 of 14), compared with other Group 2 (0 of 13, P < 0.0002), Group 3 (0 of 15, P < 0.0001), and Group 4 (3 of 14, P < 0.02). Postoperative nausea and vomiting were more frequent in Group 1 (5 of 14), compared with Group 2 (0 of 13, P < 0.05), Group 3 (0 of 15, P < 0.05), and Group 4 (0 of 14, P < 0.05). There was no respiratory depression.

Results: Small doses of intravenous nalbuphine produce fewer adverse effects, such as pruritus and postoperative nausea and vomiting, compared with intravenous fentanyl. This may allow earlier discharge of patients from the recovery room.

Conclusions: We conclude that 10 mg of intravenous nalbuphine improves intraoperative analgesia and prolongs early postoperative analgesia, without increasing the risk of side effects.
Conclusions: 

In partial curarization.

Methods: 

Ondansetron or granisetron was added. Twitch heights at 10 min after rocuronium and each drug administration were compared.

Results: There were no differences between the different groups in partial curarization.

Conclusions: Ondansetron and granisetron did not enhance the rocuronium-induced partial curarization.

Comparison of skin blood flow between closed-circuit and semi-closed isoflurane anaesthesia


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Aims: Closed-circuit anaesthesia (CCA) has been suggested to provide better hemodynamic stability and peripheral tissue perfusion than semi-closed circuits (SCA). The less severe circulatory response and autonomic reactivity to surgical stimulation during anaesthesia with CCA might indicate more adequate anesthetic depth than with SCA. We hypothesize that patients under CCA might have favourable peripheral skin blood flow than patients anesthetised with semi-closed anaesthesia (SCA). This study compared the changes in skin blood flow (SBF) during maintenance anesthesia using either CCA or SCA.

Methods: Twenty-seven patients, ASA class I or II, aged 28–56 y, weighing 41–79 kg, underwent explorative laparotomy. Patients were randomly divided into two groups CCA (n = 13) and SCA (n = 14). General anaesthesia was induced with fentanyl and thiopental and maintained with isoflurane in both groups. A laser Doppler velocimeter (Moore instrument, Axminster, England) was used to measure noninvasively and real time skin blood flow at the thenar eminence of left hand. Skin blood flow was measured at baseline (100%), 10 min after tracheal intubation, and every 30 min for two hours after that.

Results: In the group anesthetized with closed circuit skin blood flow remained virtually unchanged during surgery, as compared to baseline. In the group receiving semi closed circuit, on the other hand, there was 18–25% decrease in skin blood flow (P < 0.05).

Conclusions: Closed circuit isoflurane anaesthesia provides more favorable skin blood flow than semi closed circuits.

A potential of intrathecal implantation of bio-engineered chromaffin cells as analgesic source to treat chronic pain

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Aims: We investigated intrathecal chromaffin cells with transfected enkephalin gene effectively produce the analgesic effects in a rat model of chronic neuropathic pain induced by unilateral chronic constriction injury (CCI) of the sciatic nerve.

Methods: To form DNA/polymer complex, Cationic polymer was made with 1,4-butanediol diacrylate and 4,4-trimethylene-dipiperidine and cell toxicity and characters of DNA/polymer were evaluated. After transfecting enkephalin gene into bovine chromaffin cells, enkephalin from cells was measured by radioimmunoassay. Prior to implantation, the cells were encapsulated with alginate and poly-L-lysine to circumvent the host immune system. A week after CCI, the encapsulated cells were transplanted into rat spinal space. Mechanical allodynia was measured using von frey hair. At 30 days after implantation, viability of implants was evaluated upon retrieval of the capsule. In enkephalin measurements, a Students t test was done and data from the von Frey hair test were analysed using non-parametric statistical tests including the Wilcoxon signed-rank tests, the log-rank test and analysis of variance. P < 0.05 was considered as statistically significant.

Results: The cells with transfected gene significantly produced enkephalin and significantly reduced mechanical allodynia when implanted intrathecally, compared to those without transfected gene. In addition, viability of retrieved implants was observed.

Conclusions: Application of intrathecal implantation of bio-engineered chromaffin cells can be an alternative method for treating chronic pain.

Effect of ondansetron and granisetron on the dose-response curve of rocuronium in the rat hemidiaphragm preparation

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Aims: Ondansetron and granisetron exert their antiemetic effects via blockade of 5-hydroxytryptamine3 receptor (5HT3R). Because the 5HT3R exhibits structural similarities with the nicotinic acetylcholine receptor (nAChR), 5HT3R antagonist may also act as a competitive inhibitor of the AChR. We investigated the effects of 5HT3 antagonists, ondansetron and granisetron, on rocuronium-induced partial curarization in vitro.

Methods: The hemidiaphragm with phrenic nerve of a SD rat was dissected and mounted in a bath containing 100 ml of Kreb’s solution at 32 degrees C. The phrenic nerve was stimulated with supramaximal intensity using a stimulator. Twitch responses were measured using precalibrated force displacement transducer and recorded. After 1 hour’s stabilization, the studies were done. For the partial curarization study, seventy rats were allocated into seven groups (control, ondansetron 1, 10, 100 μg/ml, granisetron 0.1, 1, 10 μg/ml). Rocuronium 300 μg was administered to the bath. 10 minutes later, each dose of ondansetron or granisetron was added. Twitch heights at 10 minutes after rocuronium and each drug administration were compared.

Results: There were no differences between the different groups in partial curarization.

Conclusions: Ondansetron and granisetron did not enhance the rocuronium-induced partial curarization.
each dose of ondansetron and granisetron were administered to the bath simultaneously. When a stable 3–5 twitch was obtained, incremental 50μg of rocuronium were added to obtain more than 95% twitch inhibition. The dose-response curve of rocuronium in each group was calculated by logit model.

Results: The rocuronium dose-response curve of ondansetron 100μg/ml and granisetron 10μg/ml groups were significantly shifted to the left.

Conclusions: Ondansetron and granisetron in high concentrations can enhance neuromuscular blockade of rocuronium.
Muscle protein turnover in muscle following an endotoxin challenge

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Background

ICU patients with multiple organ failure and long stay in the ICU suffer from pronounced muscle protein depletion. The degree of depletion is often referred to as one of the important contributing factors to the additional mortality seen in this patient group during the initial 6 months following ICU discharge. For patients older than 50 years this additional mortality is of the same magnitude as the ICU mortality (25 ± 20%). Measurements of muscle protein content by imaging techniques have been used (1). The variable water content in muscle tissue, however, gives a rather large scatter in such estimates. Clinical analysis of muscle biopsy material for total protein content also suffers from problems of variability and reproducibility (2). Muscle protein content is the difference between the rates of degradation and de novo synthesis of muscle protein. Such dynamic measures of muscle protein turnover may have the potential to give a higher precision in the measure of muscle protein balance.

Standard technique to determine muscle protein synthesis and degradation involves the use of amino acids labelled with a stable isotope as a tracer. The use of such tracer techniques involves a number of underlying assumptions, which must be thoroughly considered in order to obtain a high precision in the measurements. To develop and validate a technique which will enable measures of muscle protein turnover in ICU patients, healthy volunteers were studied following an endotoxin challenge representing the initial phase of sepsis as a standardised human model. Muscle protein synthesis and degradation are necessary. These results indicate that such measurements are possible, provided that proper protocols are designed, meticulous attention is given to the details of the experimental procedure as well as the analysis. In addition the underlying assumptions made must be discussed properly.

Materials and methods

The protocol in healthy volunteers (n = 6) contained a run in period of 4 h to establish a base line and a steady state of isotope tracer. D3-3methylhistidine and D5-phenylalanine were used as tracers. Leg blood flow was measured using venous occlusion plethysmography and isotope enrichment were analysed by gaschromatography/massspectrometry. After the endotoxin injection (4µg/kg body weight) the volunteers were studied for another 4 h. Muscle biopsies were taken before and after endotoxin administration.

Results

Phenylalanine net balance across the leg, reflecting the net sum of protein synthesis and degradation was negative in the basal state and further decreased following endotoxin administration. Using a 2-pool model, the rate of appearance and the rate of disappearance of phenylalanine from the leg, reflecting protein degradation and synthesis respectively, indicated a decrease in muscle protein synthesis 9.4 ± 1.8 v. 3.5 ± 4.7 nmol/min/100ml leg volume (P < 0.05), while protein degradation was not altered significantly 15.4 ± 2.4 v.15.8 ± 2.9 nmol/min/100ml (NS). The rate of appearance of 3-methylhistidine from the leg was also unaltered 1.1 ± 0.9 v. 1.7 ± 0.8 nmol/min/100ml (NS), indicating degradation of contractile proteins to be unaffected. When applying a 3-pool model taking the enrichment of tissue free amino acids into account, similar results as in the 2-pool model was obtained. For the calculations of muscle protein synthesis and degradation by the 3-pool model a steady state of the concentration of phenylalanine in tissue is an underlying assumption. As the concentration of phenylalanine in muscle tissue changed the underlying assumption for that calculation was not fulfilled. Caution must therefore be recommended when interpreting that specific result.

Conclusion

An endotoxin injection in healthy volunteers used as a human model of the initial phase of sepsis demonstrated a decrease in muscle protein synthesis while muscle protein degradation was unaffected. Taken together this resulted in a more negative muscle protein balance. These results differ from what is reported in critically ill patients studied after admission to the ICU (4–6). Measurements on muscle protein synthesis rate show values that are not different from those seen in healthy individuals. The scatter, however, is larger. For degradation there are few reports using quantitative techniques, but qualitative techniques indicate an increase in muscle protein degradation (7–9). Although the muscle protein loss in ICU patients is obvious, to evaluate strategies to counteract this process, a meticulous use of available techniques combining measurements of protein synthesis and degradation are necessary. These results indicate that such measurements are possible, provided that proper protocols are designed, meticulous attention is given to the details of the experimental procedure as well as the analysis. In addition the underlying assumptions made must be discussed properly.

References


153

New methods to measure the size of the extracellular fluid space
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Introduction
There is a need to find methods for assessment of the size of the extracellular fluid (ECF) volume without involving radioactive tracers. While in healthy man ECF is remarkably constant, marked changes occur in severe trauma and critical illness.

Methods
Three methods for measuring the ECF volume were applied in 10 male volunteers (mean age, 34 years). Steady-state plasma bromide concentration (control) was compared to the results of a two compartment kinetic analysis of plasma iohexol (an X-ray contrast medium) and to a volume-of-fluid-space kinetic analysis of the dilution of serum sodium after intravenous infusion of 1 L of isotonic mannitol. The volume of distribution of these tracers was used to indicate the ECF volume.

Results
The results disclosed statistically significant correlations between the results of all three methods, although the average sodium dilution showed 0.7 L lower values than iohexol and 1.4 L lower than bromide. All three methods correlated significantly with body weight. The percentage of the body weight indicated lower than bromide. All three methods correlated significantly between the results of all three methods, although the average sodium dilution showed 0.7 L lower values than iohexol and 1.4 L lower than bromide.

Conclusions
We conclude that sodium dilution may be carried out at bedside but iohexol and bromide showed lower inter-individual variability. Iohexol simultaneously measures the glomerular filtration rate and should be a viable clinical option for the measurement of ECF, if the hospital performs routine assessments of kidney function using this tracer.

References

154

Myocardial dysfunction and metabolism in porcine endotoxic shock
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Introduction
Sepsis is the most common cause of death in the ICU. Organ dysfunction, particularly myocardial and circulatory failure, dominate the clinical picture. It has been suggested that sepsis creates a mismatch between local oxygen delivery and demand, contributing to local oxygen debt and organ dysfunction (1). Indeed,
improved oxygen delivery to tissues may lower mortality, especially if treatment is initiated early (2).

It has become clear that microcirculatory changes are pronounced in sepsis (3), and that defects in metabolic pathways may be important in the development of organ failure (3-6). Although myocardial dysfunction has been documented in sepsis, it is not known if this is caused by inflammatory, microcirculatory or metabolic derangements. Regional microcirculation and metabolism are poorly studied, partly due to difficulties in the measurement of tissue metabolite concentrations. The recent introduction of microdialysis has made it possible to measure interstitial lactate and pyruvate concentrations with time, and no intergroup differences were detected. Interstitial pyruvate increased over time with peak concentrations at t=4 (Table 2).

Aims
The aim of this study was to investigate whether sepsis-induced myocardial depression and circulatory failure is due to myocardial dysoxia and impaired metabolism.

Methods
18 pigs were assigned to control (n=6) and endotoxin (n=12) groups. The animals in the endotoxin group were infused with E.coli lipopolysaccharide (LPS, 2 mg/kg/min, 3000/000 EU/mg) for six hours. The endotoxin group was further sub-grouped into survivors (S) and non-survivors (NS) post-hoc, with S being those animals surviving the 6 hour duration of the endotoxin infusion, and NS being those surviving ≥4 but <6 hours.

The animals were anaesthetised, intubated and ventilated. Monitoring consisted of 3-lead ECGs, invasive arterial blood pressure and central venous pressure. A pulmonary artery catheter was inserted for the measurement of mean pulmonary pressure and central venous pressure. A pulmonary artery monitoring consisted of 3-lead ECGs, invasive arterial blood pressure, and NS being those surviving the 6 hour duration of the endotoxin infusion, and S being those surviving ≥4 but <6 hours.

In the endotoxin group, 6 pigs survived the duration of the experiment, and 6 pigs survived less than 6 hours.

LPS infusion induced profound haemodynamic changes, seen as significant rises in heart rate (HR) and MPAP, and decreases in SVI, LVSWI and Svo2 in S and NS groups compared to controls. These changes were seen as early as one hour after the start of LPS infusion, with maximal changes seen generally at t=4 in the NS group (Table 1).

A microdialysis catheter (20 kDa cut-off, 10 mm membrane) was inserted into the anterior surface of the myocardium, and perfused with Ringers-Dextran (1:1 solution) at a rate of 0.3 μL/min. The samples were collected 2 hourly and immediately frozen at −70°C until analysis for interstitial glucose (MD-gluc), lactate (MD-lac) and pyruvate (MD-pyr) concentrations.

Blood samples were also drawn 2-hourly for the measurement of arterial blood gases as well as plasma glucose (P-gluc) and lactate (P-lac) concentrations.

After testing for normality, the data were compared for within-group temporal changes using Repeated Measures ANOVA (on Ranks, if non-parametric data). Between-group comparisons were made using One-way ANOVA (on Ranks, if non-parametric data), with a Bonferroni correction applied for multiple analyses.

Results
In the endotoxin group, 6 pigs survived the duration of the experiment, and 6 pigs survived less than 6 hours.

LPS infusion induced profound haemodynamic changes, seen as significant rises in heart rate (HR) and MPAP, and decreases in SVI, LVSWI and Svo2 in S and NS groups compared to controls. These changes were seen as early as one hour after the start of LPS infusion, with maximal changes seen generally at t=4 in the NS group (Table 1).

Plasma glucose concentrations decreased with time in the C and S group, but remained stable in the NS group. Intergroup analysis showed a significant difference between C and NS, also S and NS at t=4. Plasma lactate concentrations rose significantly over time with peak concentrations at t=6 and t=4 for S and NS respectively. Intergroup analysis showed significant differences when comparing C vs NS at t=2 and t=4, as well as between S and NS at t=4 (Table 2).

There were no significant changes in interstitial (microdialysis) glucose and lactate concentrations with time, and no intergroup differences were detected. Interstitial pyruvate increased with time in the C and S groups. There was concomitant temp.
Discussion and conclusions

Distinct haemodynamic changes were induced in this porcine model of sepsis, with an early mortality (6 hours) of 50%. Left ventricular function was depressed, reflected by decreased SVI and LVSWI. SvO2 decreased to very low values at the same time as plasma lactate increased, suggesting inadequate O2 delivery to meet aerobic metabolic demands. Plasma glucose decreased in the C and S groups, but remained stable in the NS group. These haemodynamic and plasma metabolic changes were seen in endotoxic shock is a result of local tissue hypoxia. These data, taken together, our data does not support that myocardial dysfunction results from dysoxia. This is contrast to the work by Klaus et al (7, 8) in which increases in interstitial lactate and glyceroI were seen in subcutaneous fat, skeletal muscle and the liver implying hypoxia in these tissue beds. It must however be emphasized that their studies do not report results for interstitial pyruvate hence hypermetabolism in fully aerobic conditions cannot be excluded. Moreover, the heart was not studied, and we cannot exclude differences in metabolism from organ to organ. Our results are consistent with those of Mutschler et al (10), where endotoxic shock induced myocardial depression without any changes in interstitial pyruvate or lactate. Taken together, our data does not support that myocardial dysfunction in endotoxic shock is a result of local tissue hypoxia. These data require confirmation, and other mechanisms for myocardial depression, such as inflammation and intrinsic defects in cellular respiration are potential areas for exploration.

References


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Table 2. Interstitial and plasma metabolites. C = controls, S = survivors, endotoxin group, NS = non-survivors, endotoxin group, L: P = lactate-to-pyruvate ratio

<table>
<thead>
<tr>
<th>MICRODIALYSIS</th>
<th>t = 0</th>
<th>t = 2</th>
<th>t = 4</th>
<th>t = 6</th>
<th>P (temporal changes)</th>
</tr>
</thead>
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<tr>
<td>MD-Glucose</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>C</td>
<td>3.63 (2.85–4.44)</td>
<td>5.56 (4.83–6.08)</td>
<td>4.81 (3.14–6.09)</td>
<td>4.84 (1.42–5.22)</td>
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</tr>
<tr>
<td>S</td>
<td>3.59 (3.35–4.12)</td>
<td>4.89 (3.49–4.84)</td>
<td>3.66 (2.46–4.85)</td>
<td>2.52 (1.79–3.31)</td>
<td>NS</td>
</tr>
<tr>
<td>NS</td>
<td>2.67 (1.66–3.50)</td>
<td>4.98 (2.67–9.67)</td>
<td>2.38 (0.88–5.35)</td>
<td>–</td>
<td>NS</td>
</tr>
<tr>
<td>P (C vs S vs NS)</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
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<tr>
<td>MD-Lactate</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>C</td>
<td>1.11 (0.48–2.69)</td>
<td>1.36 (0.87–2.54)</td>
<td>1.79 (0.95–3.09)</td>
<td>2.41 (1.56–4.05)</td>
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<tr>
<td>S</td>
<td>1.53 (1.16–1.83)</td>
<td>2.06 (1.94–4.44)</td>
<td>2.30 (1.49–5.26)</td>
<td>2.55 (1.98–3.16)</td>
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<td>NS</td>
<td>1.80 (0.51–4.88)</td>
<td>2.82 (2.07–4.71)</td>
<td>2.46 (2.39–4.95)</td>
<td>–</td>
<td>NS</td>
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<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>MD-Pyruvate</td>
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<td>C</td>
<td>40.2 ± 28.7</td>
<td>102.8 ± 45.7</td>
<td>158.5 ± 52.6</td>
<td>175.6 ± 48.6</td>
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</tr>
<tr>
<td>S</td>
<td>59.0 ± 20.7</td>
<td>135.8 ± 52.6</td>
<td>175.3 ± 79.9</td>
<td>194.6 ± 63.1</td>
<td>&lt;0.001</td>
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<tr>
<td>NS</td>
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<td>80.9 ± 42.6</td>
<td>157.3 ± 138.6</td>
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<td>NS</td>
<td>NS</td>
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<tr>
<td>MD-L:P</td>
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<td>C</td>
<td>34.2 ± 12.1</td>
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<td>12.6 ± 6.1</td>
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<td>6.95 (6.58–7.10)</td>
<td>5.72 (4.65–6.70)</td>
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</table>

*p = P < 0.05 for C and NS, ** = P < 0.05 for C vs NS and S vs NS, *** = P < 0.05 for C vs S, C vs NS and S vs NS.
REFRESHER COURSES

155
Prevention and treatment of postoperative renal failure
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Acute renal dysfunction, defined as a rise in serum creatinine above baseline, is a common postoperative complication following cardiac or major vascular surgery (1–4). Ten to twenty percent of patients with acute renal dysfunction after cardiovascular surgery may develop dialysis-dependent acute renal failure (1–4), with a reported mortality of 30–60% (1–4). Dialysis-dependent acute renal failure has been considered an independent risk factor for early mortality in such patients (5).

Pathophysiology of acute renal failure
Repeated or prolonged episodes of hypotension, in turn caused by low cardiac output or low systemic vascular resistance, decrease renal blood flow (RBF) and glomerular filtration rate (GFR). Episodes of decreased RBF will cause tubular injury with cellular oedema and necrosis with a consequent tubular obstruction to flow, which in turn will further decrease GFR. The medullary thick ascending limbs of Henle’s loops and the proximal tubules are particularly sensitive to renal ischaemia due to their high oxygen demand caused by the reabsorptive work (6). Glomerular filtration of pro-inflammatory cytokines might also contribute to proximal tubular damage in cardiac surgery (7).

Prevention of acute renal failure in cardiac surgery
Various therapeutic strategies have been evaluated for the prevention of ARF in cardiac surgery. These include: loop-diuretics (furosemide), inotropic agents with renal vasodilatory properties (dopamine and doxapram) and renal vasodilators (fenoldopam). The preventive effects of these agents have only been studied in patients with preoperative normal renal function undergoing uncomplicated cardiac surgery followed by a transient decrease in GFR.

Furosemide inhibits sodium reabsorption in the medullary thick ascending Henle’s loop (mTAL) and reduces tubular oxygen consumption. The mTAL is responsible for the generation of the osmotic gradient by active reabsorption of sodium, a process that requires a large amount of oxygen. Medullary hypoxia is therefore seen under normal conditions with a medullary tissue pO2 requires a large amount of oxygen. Medullary hypoxia is therefore seen under normal conditions with a medullary tissue pO2

Dopamine is a less potent dopamine-receptor stimulator and therefore a less potent renal vasodilator when compared to dopamine. In addition, doxapram is a potent β2-agonist with no α-adrenergic effects. Berendes et al evaluated the preventive effect of doxapram on acute renal dysfunction after cardiac surgery (10). Dopexamine improved creatinine clearance compared to placebo.

Fenoldopam is selective dopamine-1-receptor stimulator with no dopamine-2, beta- or α-receptor stimulatory effects. It has recently been shown in male volunteers that fenoldopam increases RBF with no major change in GFR, indicating a balanced action on both pre- and postglomerular resistance vessels (11). Halpenny recently showed that fenoldopam improved creatinine clearance when compared to placebo after CABG (12).

Treatment of ARF
There are no studies on the effects of loop-diuretics or dopaminergic agents for treatment of ARF after cardiovascular surgery. In a recent study in patients with ARF treated in a general ICU mainly because of infections, intermittent bolus doses of loop-diuretics did not affect renal recovery, incidence of dialysis or mortality when compared to placebo (13). The effects of low-dose dopamine on patients with early ARF treated in a general ICU because of systemic inflammatory response syndrome, were recently evaluated (14). 60% of the patients were treated with inotropic agents and 85% of the patients were on mechanical ventilation. Low-dose dopamine had no effects on peak s-creatinine, increase in creatinine, incidence of dialysis, hospital stay or mortality. One explanation why low-dopamine does not have significant effects on renal outcome in patients with ARF, could be the fact that the beneficial renal effects of dopamine are transient because of development of tachyphylaxis (15).

Recombinant human atrial natriuretic peptide (ANP) in the treatment of postoperative ARF
ANP is a cardiac hormone with potent diuretic, natriuretic and renal vasodilatory effects. Infusion of ANP increases both RBF and GFR in experimental models of ischaemic and cyclosporine-induced ARF (16). Our group has previously demonstrated that ANP infusion at a dose of 50–100 ng/kg/min increases RBF and GFR by 30–40% in patients with ischaemic ARF after cardiac surgery and in patients with cyclosporine-induced ARF after heart transplantation (17,18). These beneficial effects of ANP on renal function are maintained during a long-term infusion (<48 hours) (19), in striking contrast to what was shown for low-dose dopamine infusion (see above).

We recently evaluated the effects of ANP infusion (50 ng/kg/min) on the incidence of dialysis and dialysis-free survival in patients with ischaemic ARF after complicated cardiac surgery (20). These patients were all treated with two or more inotropic agents and had diuretic support with furosemide infusion. The incidence of dialysis at day 21 after surgery was lower with ANP compared to placebo (21% vs. 47%, P = 0.009). Dialysis-free survival was 72% with ANP and 43% with placebo (P = 0.017).

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Transpulmonal thermodilution
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Circulatory dysfunction is common in the ICU, and one of the most common problems encountered in the operating room (OR) during anaesthesia. In these settings the patients haemodynamic conditions may change rapidly and continuous monitoring of circulatory data in order to change therapy is considered important by most intensivists and anaesthetists. The tools to provide such data are however a matter of debate, especially since the publication by Connors et al in 1996 where the use of pulmonary artery catheter (PAC) was criticized (1).

There are several desirable characteristics for a system to provide monitoring of cardiac and circulatory data. The system should be accurate, data must be reproducible, having fast response time, being operator independent, easy to use, provide continuous data, to be cost-effective and should not be harmful to the patient (Jansen J; Eurosova 2004).

An alternative to the PAC is transpulmonary dilution techniques. Traditionally the double indicator technique was used, but in the later years only thermal (thermodilution, PiCCO) or an indicator (dye or substance) have been used. The lithium dilution method (LiDCO) is an example of the latter.

TTT have been in use for more than 20 years (2) but only in recent years this technique has gained popularity, especially after the introduction of PiCCO (Pulsion) (3).

How it works
Transpulmonary thermodilution consider five different intravascular compartments (right atrial, right ventricular, pulmonary, left atrial and left ventricular volumes) where the indicator is diluted. Using the Steward-Hamilton method the cardiac output (CO) may be estimated. This is performed by measuring blood-temperature, injectate temperature, injectate volume and area under the thermodilution curve (4). By measuring the down slope time the volume of the largest compartment (pulmonary thermal volume) may also be measured. Derived from these measurements the global end diastolic blood-volume (GEDV), intra thoracic blood volume (ITBV) and extra vascular lung water (EVLW) can be estimated.

Comparison with other techniques
TTT have been compared with various other methods, both more and less invasive, in order to evaluate circulatory function. It has been reported to correlate with traditional methods like PAC (5), Echocardiography (6) and the double indicator techniques (7).

Practical use
In order to perform measurements it is necessary to use an artery catheter with a theremistor (to measure Δ T = temperature changes) and a dedicated central venous line ending in the superior vena cava for fluid injection. Usually 15–20 ml fluid is used, either cold or with room temperature. A special computer (Pulsion Medical Systems) or additional equipment to a multiparameter monitor (Philips) is mandatory to perform the calculations. In critically ill patients most ICU would use an arterial and central venous line in any case, so in that context there is really no extra monitoring catheters necessary to be inserted, in contrast to the PAC. Hence additional morbidity or mortality by inserting a separate catheter is eliminated. The computer measure and calculate a number of data, of which many are familiar to most...
anaesthesiologists (CO, CI, SVR) and some more unfamiliar. Intra thoracic blood volume (ITBV) has been shown to be a better measure on volume-status that CVP and PCWP (8). This is obvious since preload is a volume, not pressure. Stroke volume variation (SVV) is perhaps the best indicator on volume status (9) and is displayed as a continuous parameter. Perhaps the most unfamiliar measurements for many is the EVLW. This is simply an estimate on water content in the lungs, outside the pulmonary artery and venous system. Typically the normal values are 3–7 ml/kg, with values above 10 to be considered to be outside normal range. EVLW have been correlated to mortality, and in a recent study was found to be of prognostic value in critically ill patients (10). When < 7 ml/kg mortality was 30% and above 21 ml/kg more than 60% of patients died.

Will the TTT technique make the PAC obsolete? In our ICU TTT is used in approximately 80% in the clinical settings where we previously would have used the PAC. Still PAC is used when it is necessary to measure pulmonary artery pressure, and when we find it necessary to measure mixed venous oxygen saturation (SvO2).

References

157

Partial CO2 rebreathing for cardiac output monitoring

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The partial CO2 rebreathing technique is based on Fick’s principle and the fact that, in the partial pressure region in question, the solubility of CO2 in blood is linearly increasing with increasing partial pressure. Fick’s formula is rearranged for CO2:

\[ C.O. = \frac{VCO_2 - (CvCO_2 - CaCO_2)}{CvCO_2 CaCO_2} \]

where VCO2 is the carbon dioxide excretion and CvCO2 and CaCO2 is the content of carbon dioxide in mixed venous blood and arterial blood. The VCO2 is measured by continuous integration of flow and CO2 concentration by spirometry and capnography at the y-piece of the breathing system. The arterial carbon dioxide content is determined from the end-tidal CO2 concentration and the CO2 dissociation curve. The mixed venous CO2 content can not be measured non-invasively, but this problem is circumvented in an easy way by increasing the end-tidal (and thus the arterial partial pressure) CO2 concentration by inserting an extra dead space for ~30 seconds every third minute. When the extra dead space is inserted the end-tidal CO2 increases and more CO2 will remain in the lung capillary blood and pass over to the left heart. As a consequence the output of CO2 will decrease as measured at the y-piece. The duration of the rebreathing is selected so that it is short enough not to cause recirculation of CO2, i.e. the CvCO2 is unchanged and only the arterial CO2 content and the VCO2 is changed. The decrease in output of CO2 is related to the degree of increase in CO2 tension and the amount of blood flowing through the ventilated part of the lungs. For a given increase in CO2 tension the decrease in VCO2 will be related directly to cardiac output.

Assuming that cardiac output is stable throughout the measurement period

\[ CO = \frac{VCO_2 n/(CvCO_2 n - CaCO_2 n)}{CvCO_2 r/(CvCO_2 r - CaCO_2 r)} \]

where n indicates normal dead space and r indicates extra dead space (rebreathing). Rearranging the formula gives a differential Fick equation:

\[ CO = \frac{(VCO_2 n - VCO_2 r)/((CvCO_2 n - CaCO_2 n) - (CvCO_2 r - CvCO_2 r))}{\Delta VCO_2/\Delta CaCO_2 \times \Delta FetCO_2} \]

where FetCO2 is the end-tidal carbon dioxide fraction.

There are two main uncertainties with this technique. Pro primo: is the difference in FetCO2 between normal and rebreathing conditions equal to the difference in PaCO2 between normal and rebreathing conditions? And pro secundo: what is the impact of right to left shunt (venous admixture)? If there is no alveolar dead space the changes in FetCO2 and PaCO2 are linearly correlated, but in the presence of an alveolar dead space the changes in FetCO2 will be smaller than the changes in PaCO2. This will lead to an overestimation of cardiac output but the problem is minimised by calibration with blood gas measurements. The second problem is related to the fact that this monitoring method is only measuring the part of cardiac output that passes ventilated lung. This problem is less easy to compensate for with great precision but by using shunt estimation algorithms and calibration with blood gas measurements and entry of inspiratory oxygen concentration this problem is not seriously affecting the precision of the method.

The overall precision of the method in clinical practice is such that is has a place in medium severe cases, where the need for cardiac output monitoring will give a rationale for hemodynamic therapeutic strategies. One prerequisite of the method is that the patient is under controlled ventilation without triggering, thus the best performance is in the muscle relaxed patient during anesthesia. In most validation studies where the technique is compared to thermo dilution measurements the bias is quite small but in some studies, which has been performed after cardiac surgery result are less impressive. However, these less good results may be explained by the instability of VCO2 during changing body temperature and also changing solubility with changing temperature. In cases where pulmonary artery pressures are of importance this method should not be used.

References
Rocco, Spadetta, Morelli, Dell’Utri, Porzi, Conti, Pietropaoli. A comparative evaluation of thermodilution and partial CO2


158

Transpulmonary lithium dilution calibrated pulse wave analysis cardiac output

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This is continuous stroke volume monitoring technique based on pulse wave analysis. In contrast to the pulse contour methods, where the waveform is analysed, the LIDCO monitor makes an arterial pressure transformation into a volume-time by using an algorithm based on compliance measurements of human aorta. This makes the pulse wave analysis insensitive to where the arterial pressure line is inserted – a radial cannula works as well as a more centrally placed cannula.

When starting up the monitor, using arterial pressure signal from a blood pressure monitor the stroke volume and cardiac output values are uncalibrated. The measurement is then calibrated with a transpulmonary lithium dilution technique. A very small amount of lithium indicator is injected in a peripheral or central vein and the dilution curve is analysed by a lithium sensitive sensor placed at a side port of the arterial line. Arterial blood is sampled by a pump pumping the arterial blood at a low steady flow through the sensor. In a number of studies the transpulmonary lithium dilution technique has been compared with pulmonary artery catheter thermo dilution measurements of cardiac output and correlation has been shown to be very good. Comparisons have been performed in adults and children as well as in different medium size animals (dogs and pigs) with equally good results. In patients on lithium therapy the lithium calibration can not be used because of increased baseline levels of lithium and in patients where muscle relaxants are used, the calibration may be affected.

The monitor offers a number of derived variables like systolic pressure variation, pulse pressure variation and stroke volume variation which can be used for estimation of pre- and afterload with reasonable accuracy.

Also, the monitor can give continuous oxygen delivery values and systemic vascular resistance, SVR. However, the SVR is based on intermittent manual input of central venous pressure, which limits the usefulness of this parameter.

The LIDCO can be calibrated by other cardiac output measurements, such as thermo dilution measurements. As the lithium calibration is very expensive and not totally easy to handle thermo dilution calibration is an alternative in patients with a PA catheter, where the LIDCO monitor will add on continuous stroke volume measurements, which is of importance in patients with highly unstable circulation.

References


159

Haemodynamic monitoring in routine paediatric anaesthesia

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Contrary to the various techniques available for haemodynamic monitoring in adults the options for assessment of vital circulatory parameters in neonates and infants are quite limited. The reasons primarily responsible for this are both the small size of the patients but also the small market share and, thus, very limited interest by the manufacturers to spend any time and money on this specific target group. Nevertheless monitoring of the circulation is of vital importance also in children as in older patients.

Blood samples:

1. Blood gas analysis (arterial & central venous)/BE/Lactate
2. Calcium
3. Haemoglobin/Haematocrit

Basic parameters:

1. ECG
2. Pulse oximetry
3. Non-invasive blood pressure (NIBP)
4. Invasive blood pressure
5. Central venous pressure
6. Urinary output
7. Capillary refill
8. Central-peripheral temperature difference
9. End-tidal CO₂

More advanced options:

1. Echocardiography, trans-thoracic/trans-oesophageal
2. Thermodilution, PA-catheter

The presentation will deal with various aspects of the above-mentioned monitoring options. Apart from the specific circumstances associated with paediatric cardiac surgery the following set of parameters are suggested for the normal healthy child for minor surgery or the sick baby undergoing more major surgery:

Basic haemodynamic monitoring:

1. ECG
2. Pulse oximetry
3. Non-invasive blood pressure (NIBP)
4. End-tidal CO₂
5. Capillary refill

Advanced monitoring:

1. All parameters listed under Blood samples and Basic parameters listed above.
2. Pre- and postoperative transthoracic echocardiography or preferably if patient size permits continuous transoesophageal echocardiography.

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The incidence of explicit recall after surgery

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GA to facilitate a surgical procedure was for the first time successfully demonstrated in 1846 by Morton, although this may not be entirely fair to other pioneering work. This was a great leap forward, although the patient, Gilbert Abbot, had memories from his surgery, but had felt no pain. Thus, this was not only the first demonstration of successful GA, it was also the first case of awareness during anaesthesia.

In 1942, curare was added to the anaesthesiological armamentarium in order to attenuate the muscle tone, and this allowed for lower and less cardiorespiratory depressant doses of the primary anaesthetic. However, when mechanical ventilation was introduced and the doses of curare were increased to complete paralysis, it became possible to be aware during surgery with no possibility to alert the attending staff by voluntary movement.

In the first study on the incidence of awareness published in 1960, 1.2% of patients were found to have memories from their surgery (1). The current incidence of awareness in a general surgical population seems to be 0.1–0.2% when all traditional measures including monitoring of end tidal anaesthetic gas concentrations (no neuromonitoring) are used to ensure adequate anaesthesia (2,3).

However, the incidence of awareness may differ in various situations. Cardiac, Caesarean section and trauma surgery have been associated with higher incidences of awareness. Other conditions such as intravenous anaesthesia, monitoring of end-tidal anaesthetic gas concentration, administration of benzodiazepines and educational efforts may also affect the incidence of awareness.

Recently, two studies, one non-randomized study in a general surgical population (4), and one randomised trial in a population considered to be at increased risk for awareness (5) both identified an 80 percent reduced risk for awareness when BIS (Bispectral index) monitoring was used. Both these studies can be regarded as having been done in a "real-world" setting which is illustrated by the fact that 3 of the totally 4 BIS monitored awareness cases in these two studies were aware at a BIS above 60, and, thus, potentially avoidable.

Awareness during paediatric anaesthesia was recently investigated by Davidson (6). Among 864 children aged 5–12 y, an incidence of 0.8% was found. Only 12% of the patients in this study received neuromuscular blockers and only 1 of the eight children with awareness had been paralysed. No aware child reported distress. Further studies have been done indicating more severe suffering from relaxed anaesthesia and additional peer reviewed papers are awaited.

References

Monitoring depth of anaesthesia

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Auditory evoked potential

Whereas most modes of anaesthetic depth monitoring register spontaneous activity from the cortex, the auditory evoked potential (AEP) tests the brain stem response after a standardized signal of stimulation, i.e. sound stimuli. This principle of measuring the brain stems electrical expression in the EEG to a stimulus has been used for decades by neurologists in order to classify states of coma or brain damage, the stimulus being either cutaneous tactile or electrical stimulation (somatosensory evoked potential) or auditory stimulation. The auditory mode has some attractive features: it is fairly easy to standardize and does not cause any structural or cellular damage provided the sound is within reasonable limits of strength. Further, whereas lack of response to most sensory stimulation is a major feature of coma and adequate anaesthesia, the central nervous systems will still recognize and process an auditory stimulus, even during deep levels of coma. Although the AEP response from the brain stem is a very weak electrical signal, it is specific and may be described without the use of complex computer algorithms which is a pre-requisite for other, newer concepts.

Many groups have worked with the AEP for anaesthesia depth monitoring. Kenny et al. have used the AEP for titrating total intravenous anaesthesia and sedation with propofol together with opioid (1), and even described a closed-loop system which is in clinical use (2). As with other EEG based methods, the monitoring do not seem to be reliable when nitrous oxide, ketamine or high dose opioids are used for anaesthesia. Although the signal may be disturbed by ongoing muscle activity in the EMG range, this problem seems to be less with AEP when compared with the methods of passive EEG registration. However, with AEP a somewhat cumbersome device is needed to create ear-clicks and a possible concern about hearing damage from the clicks is present. The latter has been tested not to be any problem, as the level of sound needed for stimulation is less than the threshold for causing any harm. Still, some patients (and anaesthetists) think it is a little annoying and inappropriate to have these continuous ear-clicks when you are supposed to go gently into sleep. Delayed monitor output, due to need of sampling responses from at least 30–60 s of clicking for a stable signal, was solved by an advanced computerized mathematical method developed by Litvan and Weber-Jensen et al (3). By their algorithm a stable value is produced within 5 seconds. This made way for the first and only commercial AEP-monitor, the Alaris A-line monitor, now marketed by Datex-Ohmeda. The monitor costs about 10 000 € but is cheap to run, as different electrodes can be used, provided they are prepared for giving a good signal. The A-line have proved to give a fast, sensitive and specific monitoring of the awake – asleep distinction; comparable and faster than the BIS. However, although some good clinical studies have been published, the device is not very extensive documented and has not been tested in clinical studies of awareness yet. A further limitation has been with artifacts, ongoing signal production during decoupling and with use for detection of different levels of anaesthesia. Whether the problem of interfering EMG signals are similar or less than with the passive EEG

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concepts, is disputed and also have to do with which software version of BIS we compare with.
As the A-line value during anaesthesia may fluctuate between 5 and 20, it has proven problematic to use the A-line for titration of anaesthetic drugs to different levels of hypnotic effect. This may be more easy to achieve with the conventional, slower AEP concept (4,5).

Cerebral state monitor (CSM)
This device is using EEG to produce a score between 0 and 100 for depth of hypnotic effect. It has many of the same characteristics and problems as the BIS; EMG interaction with the signal, delay of response and insensitivity to effects from nitrous oxide, ketamine and high dose opioids. The benefits compared with BIS are the accessibility to the algorithm, which is open; and the cost issue. The monitor will cost about 2800 €, and any cheap electrode may be used provided the signal is well produced. Further, the device is small and handy and easy to carry around. A problem, however, is the lack of proper scientific documentation so far. Whereas we know from clinical work that the device works well and comparable to BIS in most patients, there is an impression that the device seems to be unpredictable in some patients, for reasons we are not able to elucidate so far. Thus, there is a definite need for more and better documentation on this device and also probably some further development of the algorithm.

Cutaneous conduction or skin conductance (SC)
This is a principle totally different from the commercial modes of anaesthetic depth monitoring which are basically monitors of hypnotic depth (with the possible exception of the response entropy). Skin conductance is a measurement of the output in the sympathetic peripheral nerve system, and is more related to pain and physiological stress than to the sleep-awake distinction. The principle is well known from the use of “lie-detectors”, which are based on the assumption that lying creates stress and increased sympathetic outflow. Each time the peripheral sympathetic nervous system is activated, the palmar and plantar sweat glands are filled up, and the SC increases (i.e. the resistance to a small electrical current decreases) before the sweat rapidly (within msec) evaporates and the SC decreases again. During an outgoing sympathetic nervous this will be a repetitive process. Thus, with stronger stimulation more episodes of sweating will occur and with more sweat during each episode. Then both an increase in the amplitude of the change in conductance (AC) and the number of skin conductance fluctuations (NSCF) can be interpreted as increased activity in this part of the sympathetic nervous system. This method is specific for the stimuli that induce the stress response. NSCF have been used to evaluate pain response in preterm infants (6), and is correlated with perioperative stress (7). The pain or stress stimuli induce an immediate increase (within 1–2 s) in emotional sweating and NSCF, and when the pain stimuli terminate, NSCF immediately decrease. Haemodynamic variables, such as blood-pressure and heart rate, are used as the routine method of monitoring stress during clinical surgery and anaesthesia. However, as haemodynamic parameters vary individually, and also are highly influenced by changes in blood volume, they have low specificity as monitors of adequate anaesthesia or sedation. Sympathetic nerves has acetylcholine as a ganglionic transmitter and is not disturbed by circulatory changes, but will of course be quite useless during strong influence of anti-cholinergic drugs.

References


162
Monitoring depth of anaesthesia; Bispectral Index, Entropy
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Background
Anaesthesia is the net result of sedation/hypnosis, analgesia and stimulation. Anaesthetic depth should describe the level, balance between these variables in the patient monitored in real time.

There is no Gold Standard for measuring the exact degree of anaesthesia in an in dependent patient and there is no uniform definition of adequate/optimal degree of anaesthesia.

MAC
The MAC concept is well recognised but carries obvious limitations with regard to the individual subject. MAC describes the end tidal concentration at which 50 percent of patients don’t react with meaningful movements at incision. Similar MAC awake is the concentration where 50 of subject no longer respond to verbal command. These are a population related descriptions and do not describe the anaesthetic level in an individual patient.

MAC bar aloud to the surrogate endpoint haemodynamic stress, “blocking autonomic response” which more mimic accepted clinical standards, trying to keep heart rate and blood pressure within reasonable limits from base-line.

Target organ – the EEG
The central nervous system is the target organ for anaesthetics and the electro encephalogram is without doubt a possible measure of anaesthetic effects.
The EEG derived variables, such as BIS and Entropy creates an index that possibly could describe the anaesthetic plane in an independent patient in real time.

BIS
The BIS, Bispectral index (Aspect Medical System, Natwick, MA, USA) monitors electro cortical activity and compares it with a database to produce a number that reflects level of hypnosis. In effect, the technology is “reverse engineered” to compare data with a static dataset. By design, therefore, patterns not incorpor-
rdated into the data library will not be accurately reflected by the BIS algorithm.

**Entropy**

Entropy quantifies the probability density function of the distribution of values. Hypnotic drugs increase the electroencephalographic amplitude. The probability density function broadens and flattens, thereby changing from a skewed to a more uniform distribution. There are various ways to compute the entropy of a signal. In time domain, one may consider for example the approximate entropy or Shannon entropy. In frequency domain, spectral entropy may be computed. To optimize the speed at which information is derived from the signal, a combination of time and frequency domain is constructed. Such an algorithm is implemented in the Datex-Ohmeda EntropyTM module (5/5 Entropy-module, Datex-Ohmeda, Helsinki, Finland).

Status entropy (SE) and response entropy (RE) values are generated. SE measures EEG activity up to a frequency of 32 Hz and is considered a stable indicator of the effect of hypnotics on the cortex. RE includes frequencies up to 47 Hz, representing EEG and EMG activity.

These devices can be seen from at least two perspectives. Evaluated critically in order to define their absolute capacity, accuracy.

As tools that provides the clinician with a supportive measure to be added, incorporated, into the evaluation of the patient, not as an absolute independent value but to as a support in the evaluation of the patients in combination with basic vital signs, movements, measures of drug delivered (ETaa) or Tci.

**What is shown?**

A number of studies have documented dose-dependent changes in BIS as well as in Entropy for most commonly used hypnotics and anaesthetics. Clear changes in indices have also been shown as compared to decrees in the Observer Assessment of Alertness Scale (OAAS) (1–4). Both devices have been shown to be less sensitive to the effects of drugs such as nitrous oxide and opioids, drugs with preferential effects on deeper structures in clinical doses (5–7). Also the effects of ketamine and xenon are not well described by BIS (8).

Questions have also been raised as to whether or not BIS is linearly correlated to increasing levels of sevoflurane (9). It has also been questioned if different agents cause slightly different patterns of decrease in indices (10).

Both devices create indices between 100 and 0, and both show similar patterns and values for sedation, anaesthesia and "deep anaesthesia".

Awake state is presented by values of >90, sedation 70–85 and adequate anaesthesia 40–60. While <30 is deep anaesthesia (11).

The devices show most similar pattern for increasing dose of anaesthetics as opposite to the Auditory evoked response index that has a different value base (12,13).

**Outcome from brain monitoring!**

There are a number of studies that show improved anaesthesia performance from the use of EEG derived monitors. Decreased consumption of main anaesthetics, improved emergence and recovery on the one hand and decreased incidence of awareness and recall on the other (14–18). There are, however, papers that questions the usefulness of these devices (19).

One may argue that these are somewhat contradictory findings, on the one hand side, decreasing anaesthetic consumption and shortening emergence as an effect from a somewhat lighter level of anaesthesia and on the other hand decreasing the incidence of “to light anaesthesia”, awareness with recall.

However having in mind that these monitors “in the best of situations” should improve anaesthetic titration in the individual patient in real-time expressing the level of anaesthesia hypnosis, sedation, and analgesia and stimulation intensity thereby provide the clinician with guidance as to provide “tailor made anaesthesia”.

**Summary & conclusion**

The exact place for the monitors, creating a net index based on the passive EEG registration from one electro cortical lead placed on forehead is far from obvious.

BIS has, however, gained huge popularity and there are today at least 500 publications on BIS and slightly less than 100 about Entropy. Both devices, Entropy as well as BIS, are attractive in that they are easy to work with; none-invasive, easily applied, they are both based on passive registration of the EEG from one pre-prepared electrode place on the forehead and they are seemingly robust.

Comparisons, pair wise, have however raised major questions as indices read in parallel have shown some diversity and more profound disagreement in not entirely neglectable numbers (13,19).

The cost associated to their use, mostly related to the disposable self-adhesive electrode, is high and their cost-effectiveness have been questioned (20).

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163 Cost effectiveness and drug consumption

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**Definitions:** Efficacy means how well a treatment works in a clinical trial, whereas effectiveness means how well the treatment works in clinical routine. Thus, these notions do not take cost into consideration. Efficiency deals with the relation between effect and cost. Different technologies based on either of EEG, auditory evoked potentials or both have been developed to assess the hypnotic effect during general anaesthesia. Most published studies concerning efficacy have involved the use of bispectral index (BIS).

Efficacy: At least 15 clinical trials have found significantly reduced consumption of anaesthetic drugs when BIS was used to guide the anaesthesia. In these studies including both intravenous anaesthesia and volatile agents, 13–40% less drug was administered. Three studies have failed to show any significant difference, and in one study significantly more drug was used when titrated against BIS. If the risk that positive findings are more likely to be published than negative ones is disregarded, it seems that drug consumption can be reduced by using the BIS.

Effectiveness: However, the results above were obtained in studies with limited numbers of included patients, and the trials were done by dedicated investigators. The results, therefore, may differ from clinical routine. In a recent study (1) in which 1580 anaesthetics were done by 69 different anaesthesia providers, there was only a slight, clinically insignificant difference in ET sevoflurane concentration between BIS monitored and non-monitored cases. No difference was found concerning time to leave the OR after surgery, PACU stay or the time to reach an Aldrete score of 9–10. The average BIS among the monitored cases was 47, indicating that anaesthesia providers in clinical routine may choose not to “go to the edge”. In this study, the average number of monitored cases per each anaesthesia provider was only 11. Despite a 3 month period to get accustomed with the BIS before starting the study, this may not have allowed for sufficient experience to take full advantage of this monitoring. The learning effect was studied in 1709 BIS monitored anaesthesias conducted by 30 persons (2). Over the study period of 17 months the only significant change was that time with BIS >60 during the first 10 minutes of anaesthesia was reduced from 2±2.5 to 1.1±1.6 min. In a second part of this study another 360 cases with available or concealed BIS monitoring were studied. Taken together, experience from, on average, 128 BIS monitored cases was associated with markedly increased user approval, but only modest objective changes in the conduction of anaesthesia and no significant difference between open and concealed cases in BIS derived parameters or age corrected end tidal sevoflurane-N2O concentrations. Thus, data on efficacy and effectiveness indicate that drug delivery can be reduced with BIS monitoring, but dedicated efforts may be required to substantiate this possibility in clinical routine.

Efficiency: From the discussion above, it must first be determined if the neurophysiological monitoring is actually associated with reduced drug cost or not. Thereafter different costs and savings must be added in order to assess efficiency. The costs include sensors, monitor cost and perhaps also time for applying this monitoring. Savings from shorter or no PACU stay are very difficult to determine with accuracy. To make this even more complicated, a fair evaluation should take cost for compensation (settlement) in case of awareness and cost for reduced working capacity among awareness victims into account. Also these costs, in case of awareness, are very difficult to assess and they differ between countries. Furthermore, we do not yet know if both potential achievements from neurophysiological monitoring (reduced risk for awareness and reduced drug consumption) can be reached at the same time or if we have to give priority to the one or the other in the individual patient. Due to the lack of sufficient data, no definite calculation will be presented here. Instead results from three studies are given which give some impressions. Using the BIS Yli-Hankala found the break-even duration of anaesthesia (monitoring cost = drug savings) to be 282 min for sevoflurane and 704 min for propofol (3). In a meta analysis of 1380 day care surgical patients in 11 trials Liu found small, statistically, but probably not clinically significant reductions in PACU stay and the incidence of PONV to a net cost of 5.55 USD per patient (4). In patients at high risk for awareness Myles calculated the cost for avoiding 1 case of awareness by BIS monitoring (82% risk reduction) to 2200 USD.

Conclusion: Data to support that BIS monitoring reduces anaesthetic drug cost in clinical routine do not seem entirely convincing, but this may at least partly be due to that information from this technology is not (yet?) fully adhered to by non-dedicated hands. More data must be gained before fair efficiency calculations can be done, and finally, should reducing human suffering invariably have to be efficient?

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Monitoring depth of anaesthesia – pros and cons of different methods

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There are 4 commercially launched depth of anaesthesia monitors available in the Nordic countries:

- BIS® (Bispectral Index) from Aspect Medical
- Entropy® from GE
- CSM® (Cerebral State Monitor) from Danmeter
- A-line® from Danmeter

Two widespread monitors not marketed in Scandinavia are PSI® (Patient State Index) from Physiomatex, which is sold exclusively in the US, and Narcotrend®, which is used mainly in Germany.

BIS, Entropy and CSM include various frequencies in EEG and EMG in different algorithms for index calculations, while A-line also takes into account the response from the auditory nerve when actively stimulated (AEP). There is no general agreement whether any of these monitors has proved to be superior to the others. Besides, no consensus exists about how the performance of these various depth of anaesthesia monitors should be evaluated.

Several factors might influence the anaesthesiologists’ rating of sleep monitors. These include:

- sensitivity and specificity to make a clear distinction between asleep and awake
- speed in detecting transition from awake to asleep and vice versa
- stability in the signal during periods of stable hypnotic level
- drug independency
- reliable signals displayed in the presence of artefacts and external noise
- price and cost/efficacy
- user friendliness
- documentation and overall experience.

A major factor is the monitor’s ability to distinguish asleep from awake. The only “gold standard” measurement of hypnosis is the patient’s conscious response to a specified stimulus. In 1996, Smith and Dutton introduced the concept Prediction probability, Pₓ, as an appropriate measure for evaluating and comparing anaesthetic depth indicators.(1) This concept has later been widely used (2,3) The prediction probability combines the more familiar concept of specificity and sensitivity into one single measure in a scale from 0.0 to 1.0. If the monitor makes correct “prediction” of a patient being awake or asleep for every point examined, the Pₓ will be 1.0. On the other hand, if all the predictions are opposite of what they should be, the Pₓ will be 0.0. A complete random guess will give a Pₓ of 0.5.

Some concerns with this concept are obvious. The study design is crucial for the resulting Pₓ. If the study takes into account only periods during which the patient is fully awake or in really deep anaesthesia, the Pₓ will have a fair chance of being close to 1.0, even for the roughest monitor. Pₓ values for a single device are thus of very limited value, unless the context is well-known. On the other hand, comparing different monitors by measuring the PK-values obtained from the same data sets could give valuable information. Such comparisons can be done either by sampling and comparing the corresponding data simultaneously in a clinical or a volunteer setting, or by applying different monitors retrospectively on EEG data set offline. The latter approach raises two specific concerns: First, it is crucial to check that the retrospective analyses give the same output by applying the original monitor to the set offline. Secondly, one should bear in mind that several of the practical difficulties that can be experienced with a monitor in the OR, for instance missing signals due to disturbances or technical failure, might remain uncovered when comparisons are made offline.

Other ways of comparing sleep monitors have been suggested. Schneider (4) presented a poorly weak linear correlation between PSI and BIS in a clinical study of 57 patients undergoing various anaesthesia, with a correlation coefficient of approximately 0.65 even when fully awake values were included in the analysis. A straight linear correlation is – on the other hand – perhaps not expected, as the algorithms for calculating the index from the EEG differ. It is expected, though, that the signal of one monitor indicates the same level of anaesthesia as the other monitor within the windows of different states of the patient (e.g. fully awake – sedated – light anaesthesia – deep anaesthesia).

The troublesome phases are those between fully awake and deep anaesthesia. Speed in detection of these transitions is wanted. A frequently heard complaint about BIS is that the monitor displays these transitions with a certain delay, and that the monitor cannot predict reactions from the patient. In fact, no anaesthesia monitor exists, that can predict anything about the patient’s clinical condition whatsoever. Entropy, CSM and A-line respond slightly faster. On the other hand, BIS is a highly fluctuating signal, and EEG for a certain period of time is needed for calculations of a reasonably stable index.

Despite the various effects the different anaesthetic agents have on the EEG, all the monitors are said to be drug independent. The problems with nitrous oxide and ketamine are well known, though, and there is no reason to believe that these problems will appear principally different between the EEG monitors. The contribution of opioids to the sedative state is also unreliable, detected by the EEG monitors.

The bibliography for BIS is incredibly larger than for the other commercial monitors, due to the fact that this monitor was launched almost a decade earlier than the others. Frequent use has been limited partly by the relatively high costs of monitors and sensors. In 2004 CSM was launched as a low-cost sleep monitor. The question is now not only whether CSM is superior to the other monitors, but whether the performance is just as good as for the others.

The number of sleep monitors launched from various companies – small and unknown companies included – is expected to rise within short time. There is a challenge to set up scientific standards for clinical evaluation of present and forthcoming devices.

There is an increasing interest in the field of automatically controlled drug delivery systems in anaesthesia. Reliable monitors for measuring and quantifying the hypnotic component of anaesthesia are necessary for closing the loop. The interest in monitors for the nociceptive component of anaesthesia is also...
considerable, and some commercial attempts have been made – as the response entropy (RE) from GE is an example of. Further commercial attempts in the field of nociception monitors are expected in near future.

References

165 Pharmacological prophylaxis and treatment of preoperative myocardial ischaemia

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Ischaemic heart disease is a major cause of perioperative morbidity and mortality. In addition perioperative cardiac events are associated with a poor prognosis. For these reasons prevention of adverse cardiac outcome is essential. This includes detailed assessment of the patient’s cardiovascular status and, in selected cases, coronary revascularisation. In addition pharmacological prophylaxis and treatment of perioperative myocardial ischaemia are essential.

Active drug prevention of ischaemia

The prophylactic administration of drugs that decrease oxygen demand, make the circulation more stable, or improve coronary blood flow and its distribution should reduce the risk of ischaemia and its consequences. Several classes of drugs must be considered: calcium antagonists, adenosine modulators, alpha2-adrenoceptor agonists, ATP-dependent potassium channel openers, beta-blockers. In addition, because of their effects on inflammatory mediators, statins play an important role.

Calcium antagonists. The acute administration of calcium antagonists is of limited efficacy, even though calcium antagonists cause coronary vasodilatation, relieve exercise-induced vasoconstriction, reduce left ventricular afterload, and improve the oxygen balance.

Adenosine modulators. A meta-analysis of five trials of acadesine (an adenosine modulator) showed significant reduction of adverse cardiac outcomes. Unfortunately, by the time the meta-analysis was performed, the development of acadesine had stopped.

Alpha-adrenoceptor agonists. Alpha-adrenoceptor agonists decrease sympathetic activity by a central mechanism, improve haemodynamic stability and decrease the risk of ischaemia. In addition, there is sedation and reduction in anaesthetic and opioid requirements. A study of mivazerol showed significant reductions in myocardial infarction and cardiac death but only in vascular surgical patients. The development of this drug stopped. Clonidine reduces the risk of myocardial ischaemia. A prospective study showed short- and long-term protection against adverse outcome.

ATP-dependent potassium channel openers. The K+ATP channel opener nicorandil is used successfully in the management of angina, protects the heart against the effects of brief periods of ischaemia during angioplasty, and decreases perioperative ischaemia but not adverse outcome.

Beta-adrenoceptor blockers. In 1997 the American College of Physicians recommend the perioperative administration of atenolol to patients with coronary artery disease (or risk factors for this condition) presenting for major non-cardiac surgery. This was not surprising: beta-blockers are known to reduce myocardial oxygen consumption, decrease the effects of sympathetic activity, may reduce sympathetic outflow, redistribute coronary blood flow, and may decrease the release of inflammatory mediators. For more than 30 years, beta-blockers have been shown to minimise the risk of perioperative myocardial ischaemia and myocardial infarction and adverse cardiac outcome.

Further evidence of beneficial effects of perioperative beta-blockade was obtained by Poldermans and colleagues in high risk vascular surgical patients selected because of reversible ischaemia on dobutamine echocardiography. Beta-blockade started a week or more before surgery and continued for 30 days postoperatively. This treatment caused a large reduction in cardiac death (3.4% vs 17% in the control group) and non-fatal myocardial infarction (0% vs 17% in the control group). However all patients were at a particularly high risk for coronary events (34% combined incidence of cardiac death and non-fatal myocardial infarction in the conventional treatment group); therefore the efficacy of beta-blockade shown in this study cannot be extrapolated to patients at risk for coronary disease, rather than with demonstrably severe coronary artery disease.

Beta-blockade seems to be the logical answer to the perioperative drug management of patients with risk factors for, or with, coronary artery disease. Why are beta-blockers not used much more frequently? There are perceived risks to beta-blockade such as worsening of conduction disorders or airway obstruction in patients with reactive airway disease. There is also the risk of worsening of left ventricular dysfunction. Though beta-blockers are used successfully in the treatment of patients with heart failure, their introduction shortly before surgery may not be well tolerated (indeed treatment of cardiac failure with beta-blockers must start with extremely low doses, increased progressively over several weeks).

The POISE study (PeriOperative Ischaemic Evaluation study) has been designed to answer the question of safety and efficacy of perioperative beta-blockade in patients with risk factors for, or with coronary artery disease. With over 3000 patients already enrolled (of a planned total of 10,000), the study should provide a definitive answer to the efficacy of beta-blockade. The reason for the study is that while the studies by Poldermans and colleagues and by Mangano and colleagues showed important benefits, a meta-analysis of all randomised controlled trials of perioperative beta-blockade did not show statistically significant benefits. If the POISE study is positive, the case for perioperative beta-blockade will be considerably strengthened.

In order to avoid the risk of hypotension at induction of anaesthesia, it may be appropriate to start treatment a few days ahead of surgery rather than the day before surgery and to have protocols for omitting the drug in case of bradycardia and hypotension (heart rate less than 50 bpm and BP less than 100 mmHg).

If perioperative beta-blockade reduces the risk of adverse events, are patients on chronic beta-blockade protected? This is not the case in non-cardiac surgery. The incidence of perioperative silent myocardial ischaemia and perioperative mortality are not reduced in patients on chronic beta-blockade. A systematic review of observational studies of outcome in patients on long-term beta-blocker therapy did not show any benefit. This may be due to beta-adrenoceptor up-regulation or insufficient beta-blockade. To date there is no clear approach to the management of patients on chronic beta-blockers. It may be that doses of beta-blockers should be increased in order to make the circulation more stable.

Statins. Statins block the biosynthesis of cholesterol, improve endothelial function by up-regulating nitric oxide synthase, reduce the levels of inflammatory mediators, scavenge super-
oxides, shift the fibrinolytic balance toward fibrinolysis, stabilise atherosclerotic plaques, and inhibit vascular smooth muscle proliferation. Statins reduce the risk of cardiac events and stroke in patients with coronary heart disease or cerebrovascular disease.

Recent evidence shows that patients receiving long-term aspirin therapy have a reduced risk of postoperative cardiac events. The anti-inflammatory properties of statins may explain why these drugs protect against perioperative cardiac events even after treatment for only one week. Abruption withdrawal of statins can cause coronary events. It must be noted that statins may cause rhabdomyolysis after anaesthesia and surgery.

Aspirin. Aspirin is the prototype non-steroidal anti-inflammatory agent. Aspirin blocks the synthesis of thromboxane A\(_2\) (TxA\(_2\)) for the life time of the platelet (about 10 days) while the synthesis of PGI\(_2\) is quickly restored where low-dose aspirin is used. Long-term aspirin prophylaxis is protective in patients with coronary and cerebrovascular disease. Aspirin has been shown to reduce cardiac mortality after coronary artery bypass surgery.

Conclusion
The future of drug-based cardiac protection is likely to be multimodal including agents that minimise haemodynamic changes, protect the ischaemic myocardium, and reduce the release, or activity, of inflammatory mediators. However, the availability of protective drugs does not mean that thorough assessment of the patient and further investigations are no longer necessary.

References
thermodilution catheter. Intra-aortic balloon counterc pulsation (IABP) should be initiated early (1). IABP has the potential to increase coronary perfusion pressure and decrease myocardial oxygen consumption. Patients with cardiogenic shock should receive aspirin and full dose heparin. A fibrinolytic agent should be initiated in patients with ST-elevation AMI if the anticipated delay to angiography is more than two hours. Augmentation of blood pressure with an IABP may facilitate thrombolysis by increasing coronary perfusion pressure.

Continues positive airway pressure (CPAP) should be started early as it has the potential to improve left ventricular performance by decreasing preload and afterload. It has been shown that mechanical ventilation in conjunction with IABP improves the outcome of patients in profound cardiogenic shock (2).

**Early definition of coronary anatomy**

Patients in community hospitals should be emergently transferred to an experienced regional tertiary care facility. Prophylactic IABP placement is recommended before transfer. Cardiogenic shock is characterised by a high incidence of triple vessel disease, left main disease and impaired left ventricular function and the extent of ventricular dysfunction and haemodynamic instability should be correlated with coronary anatomy. Isolated circumflex or right coronary lesions should rarely manifest as shock in the absence of right ventricular infarction. In this situation it is important to exclude mechanical or other aetiologies of cardiogenic shock.

**Early revascularisation in cardiogenic shock**

Definition of anatomy should be followed rapidly by selection of mode of revascularisation. Percutaneous coronary intervention (PCI) will most often be the treatment of choice. Recently, the SHOCK trial demonstrated that early revascularisation (PCI or coronary artery bypass grafting) reduces 6 and 12 months mortality (3).

**Future directions**

Thyroxin has been shown to improve cardiac output in patients with severe cardiogenic shock with multiple organ failure (4). NO-synthetase (L-NMMA) is a selective nitric oxide inhibitor which increases blood pressure and urine output and may reduce 30-day mortality in cardiogenic shock (5, 6). There is also some experience with percutaneous venoarterial cardio pulmonary bypass for emergency circulatory support in cardiogenic shock (7). Long-term survival rates after this procedure are encouraging in patients with cardiocirculatory disease amenable to corrective intervention (angioplasty, surgery, transplantation).

**References**

The Scandinavian Critical Care Trials Group (SCCTG) is a part of the Scandinavian Society of Anaesthesia and Intensive Care Medicine (SSAI) and aims to provide a Scandinavian network for research in intensive care medicine. Membership of the SCCTG is free and open to all researchers interested in intensive care and related disciplines. The working format of the SCCTG is transparent and independent of commercial interests. An advisory board is formed based on suggestions from an election committee for three years periods. The advisory board consists of five members including one chairman and one secretary. Preferably, all Scandinavian countries should have representatives in the advisory board. At present, the position of a Finnish representative is vacant. The main tasks for the advisory board are to organise the biannual SCCTG meetings and to review and assist the presentation of all proposed research protocols.

The SCCTG meetings are usually held in early autumn and spring. The venue alternates between the Scandinavian countries. The meetings span over three days and comprise three sessions. The incubator session opens the meeting and is the informal forum for free presentations and discussions of relevant research in basic and clinical sciences. The educational session is organised to include distinguished lecturers within specific fields from Europe, Scandinavia and the respective organising country. The business session deals with submitted and ongoing research protocols. Protocol discussions are structured with a chairman and presenter(s). To date, eight SCCTG meetings have been organised.

At present, two major Scandinavian multicenter trials are running under the auspices of the SCCTG. The Northern Hypothermia Network aims to promote, investigate and evaluate hypothermic therapy for cardiac arrest patients. The Scandinavian multicenter glutamine trial is a prospective, double-blind, placebo-controlled study on the effects of intravenous glutamine supplementation in intensive care patients. The SCCTG has completed and published the results of two practice surveys on the use of vasopressor/inotropic drugs (Acta Anaesth Scand 2003;47:693–701) and the routines for sedation (Acta Anaesth Scand 2004;48:944–50).

An integral part of the SCCTG is the web-site www.scctg.org. This site contains all information relevant to the SCCTG including protocols, guidelines, organisation, lectures, meeting notes, an on-line discussion forum, web-links and a contact list for the SCCTG advisory board. The web-site is linked to from all Scandinavian societies for research in intensive care medicine and provides the main communication platform for the SCCTG. The web-site also links directly to the database for ongoing studies. The web-site provides the main communication platform for the SCCTG. The Northern hypothermia network

Introduction: Two randomized studies have shown that treatment with induced hypothermia protects from neurological sequelae and death after out-of-hospital cardiac arrest [1, 2]. An advisory statement from the International Liaison Committee on Resuscitation (ILCOR) supports the clinical use of therapeutic hypothermia [3]. We believe that it is imperative to implement these new recommendations in clinical practice under strict control of treatment safety and outcome. Therefore the Northern Hypothermia Network (NHN) was formed, a research network originating from the Scandinavian Critical Care Trials Group (SCCTG), with funding from the SSAI. Today, the NHN consists of a steering group and members from five participating countries: Denmark, Iceland, the Netherlands, Norway and Sweden. The NHN aims to become members of the network and get one vote for the steering group.

One purpose of the network is to stimulate and spread the use of therapeutic hypothermia of comatose patients after cardiac arrest by organizing meetings, workshops and through an updated homepage (www.scctg.org). Another purpose is to stimulate the joint registration and collection of data from treated patients in an internet-based database, the Northern Hypothermia Registry. All comatose patients, i.e., those who are treated with induced hypothermia and those who are not, are eligible for registration in the registry. Hence, participating hospitals are urged to register all cardiac arrest patients treated in the intensive care unit (ICU). A third purpose of the NHN is to account for epidemiologic research from the registry and to initiate and perform randomised trials.

Methods: Patient data and cardiac arrest characteristics are collected in the Utstein-style. Data on hypothermia treatment, safety aspects, clinical investigations and general intensive care parameters are registered. Outcome is documented as neurological score at ICU and hospital discharge and at six months using the Cerebral Performance Category (CPC) scale [4]; CPC 1–2 representing a good outcome and CPC 3–5 a bad outcome. Descriptive data of the preliminary analysis of the registered parameters are presented as proportions or medians and interquartile range.

Results: At present, hospitals from all five participating countries are represented in the registry and 32 centres have signed up for membership. The on-line registration has been open since October 2004. By May 2005, 230 patients were registered, of whom 220 were treated with hypothermia and 10 without hypothermia.

In the hypothermia group the median age was 63 (54–74) years, 69% were men and 85% had an out-of-hospital arrest. The initial rhythms were VT/VF 63%, asystole 30% and PEA 7%. Seventy-seven per cent of the arrests were judged to be of cardiac cause. Eighty-four per cent of the arrests were witnessed and in 36% of the cases bystander CPR was performed. Time from arrest to CPR by medical personnel was 6 (3–10) min and from arrest to return of spontaneous circulation 17 (10–29) min. Time from arrest to initiation of hypothermia treatment was 75 (60–115) min and from arrest to target temperature reached 220 (150–320) min. A target temperature of 33°C and a treatment
period of 24 hours was used in more than 95% of all cases. Sixty-seven per cent of all patients survived to ICU discharge. At hospital discharge 49% of the patients had a good outcome, 47% of the patients were dead (CPC 5), 0% were in coma (CPC 4) and 4% were conscious but with severe neurological disability (CPC 3). Data at 6 month is not yet sufficient for full evaluation but the trend is that those with good outcome at hospital discharge stay in the good outcome group. The Registry is continually updated.

Conclusion: The Northern Hypothermia Network is a network with an infrastructure that enables it to perform epidemiologic research and randomized trials. The Northern Hypothermia Registry provides an easy and powerful way of evaluating the safety and outcome aspects of therapeutic hypothermia after cardiac arrest. Furthermore, data from the registry will generate ideas on where and how to focus future clinical trials in the field of therapeutic hypothermia. Data from the initial 220 patients treated with induced hypothermia and entered into the database indicate that the results are similar to those from the two published randomized trials.

A decision has been taken to merge the Northern Hypothermia Registry with the Hypothermia After Cardiac Arrest Registry (ERCHACA-R). Together the two networks will form The Hypothermia Network with a joint registry, The Hypothermia Network Registry, constituting a pan-European collaboration.

References

169

Substance abuse

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Drugs

Substance abuse may be defined as self-administration of drugs that deviate from accepted medical or social use, which if sustained can lead to physical and psychological dependence (1).

The drug abusing patient presents for surgery with several problems; some are generally associated with any drug abuse, others are related to the abuse of specific drugs.

Preoperative evaluation

Intravenous access: If there is a suspicion of previous or ongoing intravenous drug abuse, one may expect difficulty in gaining intravenous access, due to previous thrombophlebitis. An assessment of the difficulties related to intravenous access should be performed at the pre-anæsthetic clinic. The placement of a preoperative central venous line should be considered.

Nutrition: Drug abusers often have significant social problems and are prone to malnutrition. A body mass index below 19 is associated with significant perioperative risk. A state of malnutrition may alter the effect of several anaesthetics, leading to haemodynamic instability and increased risk of postoperative complications, such as infections and impaired wound healing.

Immune system: Intravenous drug users may suffer from the combination of an impaired immune system and exposure to different life threatening infections such as: human immunodeficiency virus, hepatitis and tuberculosis.

Cocaine

Cocaine is highly addictive; casual use is not possible once addiction occurs, and life-threatening side effects accompany its use. Cocaine produces sympathetic nervous system stimulation by blocking presynaptic uptake of norepinephrine and dopamine, thereby increasing the postsynaptic concentrations of these neurotransmitters. Because of this blocking effect, dopamine remains in high concentrations in the synapses, producing the characteristic “coca high”. Cocaine can cause coronary vasospasm, myocardial ischaemia and myocardial infarction. Systemic hypertension and tachycardia further increase the myocardial oxygen requirement at a time when the effects of cocaine decrease coronary oxygen delivery (2). Patients who smoke cocaine have an increased risk of lung damage and pulmonary oedema. Chronic cocaine abuse is associated with nasal septal atrophy, agitated behaviour, paranoid thinking and heightened reflexes. Cocaine overdose results in sympathetic nervous system stimulation of the cardiovascular system, including coronary vasospasm, uncontrolled hypertension and platelet aggregation.

Anaesthesia: When administering anaesthesia to cocaine abusers, it is important to be aware that these patients are vulnerable to myocardial ischaemia and cardiac dysrhythmias. Nitroglycerin should be available for treatment of myocardial ischaemia associated with systemic hypertension. Thrombocytopenia may be present and contradict the use of regional anaesthesia.

Opioids

Opioids are highly addictive; addiction developing within a few weeks of abuse. The drugs can be abused orally, subcutaneously or intravenously to achieve euphoric and analgesic effects.

Medical problems associated with opioid abuse:

- Acquired immunodeficiency syndrome (AIDS)
- Hepatitis
- Skin abscesses
- Septic thrombophlebitis
- Tetanus
- Endocarditis with or without pulmonary emboli
- Aspiration pneumonitis
- Adrenal gland dysfunction
- Focal segmental glomerulosclerosis
- Malnutrition

Withdrawal Syndrome: The periorioperative period can be complicated by withdrawal symptoms from opioid addiction. Symptoms include manifestations of excess sympathetic nervous system activity (diaphoresis, mydriasis, hypertension, tachycardia), and craving for the drug followed by musculoskeletal discomfort, insomnia, abdominal cramps, and diarrhoea.

Anaesthesia: Opioid addicts should have opioids maintained during the periorioperative period. Due to the development of tolerance, opioid addicts must be expected to need not only more opioids than non-addicts, but also increased amounts of other types of anaesthetics, such as volatile anaesthetics, barbiturates and propofol. A tendency to hypotension must be expected due to inadequate intravascular fluid homeostasis and impaired adrenocortical function. Opioid addicts appear to suffer from exaggerated postoperative pain. To avoid administering large doses of short acting opioids, methadone (a long acting opioid) can be chosen or regional blockade considered (3).
Barbiturates

Barbiturates are highly addictive, but their abuse is not associated with major pathophysiological changes. Barbiturates are mostly abused orally to counter insomnia, and their abuse is often associated with the abuse of other drugs. Tolerance for the effects develops rapidly, but the lethal dose does not increase at the same rate, thus heightening the risk of mortality with time. Anaesthesia: Barbiturate abusers develop a tolerance for other anaesthetic drugs, so more anaesthetic is required. Chronic barbiturate abuse leads to induction of the hepatic microsomal enzymes, thus speeding up the breakdown of drugs, such as warfarin, digitalis, phenytoin and others.

Benzodiazepines

Addiction develops much more slowly than with barbiturates. Overdose is not likely to be fatal except if in combination with other drugs or alcohol. Anaesthesia: There are no specific anaesthesiological considerations. Hepatic microsomal enzymes may be slightly induced.

Amphetamines

Amphetamines stimulate the release of catecholamines, resulting in increased cortical alertness with associated appetite suppression and decreased need for sleep. Physiological dependence for amphetamines is profound. Chronic amphetamine abuse results in depletion of the body stores of catecholamines. The abuser may suffer from chronic hypertension, dysrhythmias and malnutrition. Anaesthesia: Acutely intoxicated patients needing emergency surgery may suffer from hypertension, tachycardia, raised body temperature and an increased need for anaesthetic drugs. There may be malregulation of the body temperature, so this should be monitored during the perioperative period. In contrast, chronic amphetamine abusers may need markedly decreased amounts of anaesthetic, probably due to catecholamine depletion in the central nervous system. Hypotension should be corrected with directly acting vasopressors, such as epinephrine.

Hallucinogens

Hallucinogens, such as lysergic acid diethylamine (LSD) and phencyclidine (PCP) are usually taken orally. Psychological dependence is usual, whereas physical dependence or withdrawal symptoms are unlikely. The effects of these drugs are: visual, auditory and tactile hallucinations, distortions of the surroundings and body images. Sympathetic nervous system stimulation is seen as mydriasis, increased body temperature, hypertension and tachycardia. Anaesthesia: LSD prolongs the analgesic and pulmonary ventilatory depressant effects of opioids. Exaggerated responses to sympathomimetic drugs seem likely, so these drugs should be used with care.

Alcohol misuse

Chronic alcohol abuse is associated with a wide range of medical conditions, these having an important impact on the perioperative period. As alcoholism and alcohol abuse are very common in western countries this is of major importance for the anaesthesiologist.

Medical problems associated with alcohol abuse:
- Fatty change of liver/cirrhosis
- Hepatitis
- Oesophageal varices
- Wernicke’s disease
- Cardiomyopathy
- Pancreatitis
- Polyneuropathy
- Malnutrition
- Smoking/COPD

Withdrawal symptoms: Alcohol withdrawal symptoms are not uncommon in the postoperative patient. The symptoms range from mild to life-threatening, and include: anxiety, irritability, depression, bad dreams, headache, sweating, nausea, vomiting, loss of appetite, insomnia, palpitations, clammy skin, tremor, hallucination, agitation, fever, convulsions. The risk should be assessed and the symptoms prevented by administration of benzodiazepines perioperatively. Anaesthesia: It is important to obtain information about weekly alcohol consumption at the preoperative evaluation. Patients with alcohol abuse may have induced enzymatic breakdown of anaesthetic agents and may need more of these than other patients. Alcohol abusers often have haemodynamic instability during anaesthesia and it can be difficult to estimate their anaesthetic needs. Surgical bleeding is often profuse and the patients are at risk of hypoglycaemia and hypothermia. They may emerge from anaesthesia in an agitated state. Apart from withdrawal symptoms, alcohol patients suffer from an increased risk of postoperative complications, such as: infections, cardiopulmonary complications and impaired wound healing. These postoperative complications can be significantly reduced by 4 weeks of alcohol abstinence before surgery (4).

Tobacco

Smoking is related to a great number of medical problems. About one third of patients presenting for surgery are smokers.

Medical problems associated with smoking:
- Chronic obstructive pulmonary disease
- Emphysema
- Atherosclerosis
- Coronary artery disease
- Gastritis
- Gastric ulcers
- A wide range of smoking related cancers (lung, mouth and nose, bladder, renal, pancreas, cervix and others).
- Miscarriage
- Fetal malformations
- Premature birth

Anaesthesia: Smokers may suffer from reduced pulmonary function and haemodynamic instability during anaesthesia (Schwilk). Induced microsomal enzymes increase the breakdown rate of anaesthetic agents. Smokers have a significantly increased risk of postoperative complications such as: impaired wound healing, wound infection, anastomotic dehiscence, severe cardiopulmonary complications with intensive care admittance and secondary surgery. Smoking intervention 6 to 8 weeks before surgery reduces the risk of pulmonary and infectious complications, whereas wound healing improves after only 4 weeks of abstinence (5,6). The effect of a shorter term of abstinence on perioperative complications is unknown.

References

170
Herbal medicines and anaesthesia

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Aims: The purpose of this lecture is to describe the effects of herbal medicines on anaesthesia and surgery.

Methods: The use of herbs for the medicinal purpose has been present for thousands of years in different cultures and in different forms. There is a strong belief in people that "natural remedy is safe and without harmful effects". The number of people using herbal medicines is huge and increasing in USA and Europe. The patients usually do not disclose the use unless specifically asked. It is a concern to the anaesthesiologists and to the surgeons as well because of the adverse reactions these medicines can cause intra- and postoperatively. The money spent on these preparations is astronomical. In 2003, European countries spent almost $5 billion on over-the-counter herbal medicines. There are no standards regarding production, collection methods and impurities. So also strict trials and research are rather uncommon which can be due to the fact that herbal medicines cannot be patented. Unexpected outcomes can occur if the uses of these medicines go unnoticed preoperatively.

Results: The common drugs used are Echinacea, Garlic, Ginseng, Gingko biloba, St John’s wort, Valerian, Ephedra, Ginger, Kava kava and many others. Various investigations and case reports suggest that the effects of these medicines can be dangerous perioperatively. The effects are on the cardiovascular system, coagulation, blood sugar and drug interaction with the anaesthetics and other drugs used perioperatively.

Some of the major adverse effects of herbal medicines:

1. Adverse cardiovascular effects: echinacea, garlice, goldenseal, ginseng
2. Coagulation disturbances: Garlic, ginger, gingko, ginseng, feverfew
3. Prolongation of anesthesia: St John’s wort, kaka-kava, valerian
4. Adverse immunological effects: echinacea
5. Blood sugar lowering effect: gingko, ginger, garlic
6. Blood sugar increasing effect: Ephedra, licorice
7. Improvement of sugar tolerance: karela

Some of the major drug-interactions are as follows:

<table>
<thead>
<tr>
<th>Herbal drug</th>
<th>Nonherbal drug</th>
<th>Adverse effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ginseng</td>
<td>Estrogen, Barbiturates</td>
<td>Additive effects, Exces. sedation</td>
</tr>
<tr>
<td>Baldrian</td>
<td>Anticonvulsants, Alprazolam</td>
<td>Lower threshold, coma</td>
</tr>
<tr>
<td>Primrose oil</td>
<td>Spironolactone</td>
<td>Spironolactone less effective</td>
</tr>
<tr>
<td>Kava</td>
<td>NSAIDs</td>
<td>Feverfew less effective, Less absorption of iron</td>
</tr>
<tr>
<td>LICORICE</td>
<td>Cilostazol, sodium, lignocaine, calc channel blockers, dogoxygenine</td>
<td></td>
</tr>
<tr>
<td>Feverfew glibra</td>
<td>Cilostazol, sodium, lignocaine, calc channel blockers, dogoxygenine</td>
<td></td>
</tr>
<tr>
<td>St John’s wort</td>
<td>Sodium, flunitrazepam, midazolam, lignocaine, calc channel blockers, dogoxygenine</td>
<td></td>
</tr>
</tbody>
</table>

The list of drugs which should be used with extreme caution while the patient is on St John’s wort is pretty long one.

Conclusions: The herbal medicines have been used for thousands of years and have been effective without doubt. However, modern surgery and anaesthesia is new to the use of herbal medicines. In order that the old and new can work together is to gather more information, do more research and record the adverse effects which seem to occur. It is important to discuss this aspect of the herbal medicines with the health professionals and the patients. Our knowledge of these drugs is far from complete. Specific questioning to the use of herbs should be made in the preoperative assessment. American Society of Anesthesiology has suggested that patients discontinue herbal medications 2 weeks prior to surgery which is practicable and easy to follow. A definitive approach is suggested by some authors for the specific drugs. However, as often the patients take more than one medication prior to surgery which may complicate the matter. Apart from that a consensus has to be made and discussed openly with the consumers and media and to the health professionals in order to prevent the adverse effects these drugs can cause.

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171
From acute to chronic pain

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The incidence of chronic pain following otherwise uncomplicated surgery depends on the surgical procedure, but varies between 10–60% in the literature. Development of persistent non-nociceptive pain following surgery is a major health problem and a challenge for the surgical and the anesthesiological profession. The pathophysiology underlying the transition from acute to chronic pain is not known in detail. Animal experiments indicate that excitotoxic damage in the dorsal horn of the spinal cord may follow an intense afferent barrage. This may cause an exaggerated and prolonged sensitization of the central nociceptive pathways leading to chronic pain. An alternative (not mutually exclusive) explanation is that the accompanying disability, i.e. postoperative immobilization, fatigue, depression, semistarvation, may lead to physical deconditioning with incomplete recovery and development of a chronic pain state.
A number of predictors in development of chronic pain have been recognized. They may be grouped into three categories: the perceived intensity of acute pain, the emotional state and cognitive processes. The severity of the injury, combined with various individual biological, psychological and sociological factors determine the risk of developing chronic pain. Treatment strategies should focus upon attenuation of the nociceptive barrage during the acute pain episode, the use of antihyperalgesic agents (NMDA-blocking agents, alfa_2-agonists) and early rehabilitative measures.

References

172 Pharmacologic management of non-cancer chronic pain

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Introduction
The treatment of non-malignant chronic pain can be one of the most challenging tasks in modern medicine. Some tools, like the WHO analgesic ladder, have been devised to help clinicians choose appropriate drugs for different patients. Such tools have limited value in complicated cases of chronic pain.

A large proportion of chronic pain is of neuropathic nature meaning that is related to injury to the peripheral or central nervous system. Currently the classification of neuropathic pain syndromes is mainly based on etiological considerations. In physicians’ training causal treatment, where possible, is considered the gold standard. In situations where the cause of pain cannot be eliminated second best would be to institute a treatment based on a known pathophysiological mechanism of pain. Through research different pain mechanisms are being mapped but, with a few exceptions, we still have a long way to go from mechanisms toward a mechanism based pain treatment.

The cause of pain, especially when it’s chronic, is not always obvious and may be multifactorial. In order to be effective the treatment may have to be multifactorial and multidisciplinary. When it comes to assessment of pain intensity things can be quite complicated. The amount of nociception may be minimal but nevertheless the patient is in pain, suffering and showing pain behaviour. The usual analgesic drugs may not be very effective.

Some drug combinations may be partly effective and interventions may be ineffective or partly effective. This is where a multidisciplinary approach is needed combining pharmacological and nonpharmacological methods for the patients’ benefit.

Nociceptive pain
For nociceptive pain including acute pain two categories of drugs are mostly effective namely the non-opioids and the opioids. Paracetamol, traditional NSAIDs and the COX-2 selective inhibitors constitute the non-opioid group of analgesic drugs and the opioids are divided into the subgroups of weak and strong opioids.

Neuropathic pain
Most of the drugs currently available to treat neuropathic pain belong to the following groups.

1. Antidepressants (Serotonin-/NE-reuptake blockers)
2. Anticonvulsants
3. Opioids
4. NMDA-receptor antagonists

Some of the best studied neuropathic pain models are postherpetic neuralgia and diabetic neuropathy and much of the evidence regarding the effectiveness of these drugs is derived from studies comparing the effect of the drug in question to placebo in these conditions. Up to 50% of patients presenting with persistent pain may have some degree of comorbid depression justifying the use of antidepressants in neuropathic pain medication. Tricyclic antidepressants (TCA) have the best documented effect of antidepressant drugs in neuropathic pain. Toxicity is a major issue with the use of TCA, and many of the anticonvulsants as well, but they seem to be more effective in relieving pain than the newer and better tolerated selective serotonin reuptake blockers. TCA have been first choice drugs for some neuropathic pain conditions for many years but newer anticonvulsants drugs like gabapentin and pregabalin with a more favorable side effects profile than the older ones have proved to be equally effective as the TCA and are increasingly becoming first choice drugs.

The use of opioids for neuropathic pain is controversial. Neuropathic pain has traditionally been considered opioid resistant. However, in recent clinical studies opioids were shown to be effective in the treatment of neuropathic pain, provided an adequate dose can be reached that provides analgesia without excess side effects. Some opioids have non-opioid effects, like a weak NMDA-receptor antagonizing effect, that may increase the effectiveness of the drug in neuropathic pain.

NMDA-receptor activation is associated with windup, hyperalgesia and reduced opioid sensitivity. Two commercially available NMDA-receptor antagonists are ketamine and dextromethorphan. At therapeutic doses, dextromethorphan is very sedating and clinical trials have been disappointing. Ketamine has a variety of neuropsychiatric side effects that limit its clinical usefulness but has been noted in many case reports in very small doses for severe neuropathic pain in patients with advanced cancer. Other adjuvant medications include corticosteroids, antihistamines, phenothiazines and the botulinum toxin.

The treatment of chronic non-cancer pain with opioids
During the last two to three decades the fact that opioids can relieve pain and improve mood and functioning in many patients with chronic pain has gained acceptance. This has led experts on pain to recommend that such patients not be denied opioids. This kind of treatment is not easy to handle and potentially hazardous. There are several questions to be asked before prescribing opioids for chronic non-malignant pain.
Management strategies and recommendations have been put together by pain specialists in various parts of the world and some of them may be found in the reference list below. Most of the recommendation protocols stress that strong opioids should not be used as monotherapy but in the context of a rehabilitation programme setting goals of improved physical and social function. All advocate the use of sustained-release opioids at regular intervals. The route of administration should be oral. The decision to initiate or terminate long-term opioid therapy should, ideally, involve a multidisciplinary pain clinic. Before start of treatment the patient’s pain level, quality of life and functional status should be carefully assessed. After a trial period agreed by the physician and the patient the same parameters should be reassessed and compared to baseline levels. If treatment goals are not met the opioid medication should be discontinued.

References

Cognitive behavioural approach and rehabilitation

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Background: Common psychological consequences of chronic pain are for example depression, anxiety, anger, catastrophizing and fear and avoidance behaviour. Chronic pain patients have also a tendency to become socially isolated. In Cognitive Behaviour Therapy (CBT) the fundamental assumption is that behaviour and emotions are influenced by interpretations of events, rather than solely by characteristics of the event itself (Philips & Rachman, 1996). Chronic pain commonly results in significant psychosocial problems for patients and can begin to dominate almost every aspect of their life (White, 2001). Pain management programmes must therefore have a team of a range of professionals, together addressing the various disabling effects of the chronic pain (Main & Spanowic, 2000). CBT has been extensively evaluated and shown to be effective in terms of its impact on a number of biopsychosocial variables in chronic pain (Linton, 2000). The pain clinic at Reykjalundur Rehabilitation Center offers an interdisciplinary pain management programme for 33 inpatients with chronic pain. The programme is a 6 weeks inpatient programme, the last 2 weeks often on a day care basis. The programme consists of education such as a stress management and relaxation programme, a back-school that addresses the nature of chronic pain and coping methods, nutrition, sleep, exercise and a healthy lifestyle. Pain relieving drugs are gradually withdrawn but anti-inflammatory drugs are used when indicated. Turk and Okifuji (1998) have demonstrated the cost-effectiveness of a multidisciplinary pain rehabilitation programme and found it up to 21 times more cost-effective than alternatives such as surgery. Olason (2004) studied the outcome of the interdisciplinary pain management programme in the rehabilitation setting at Reykjalundur over a three year period and concluded that although analgesic drugs were withdrawn, the pain level was significantly reduced. Anxiety and depression were treated with CBT and decreased significantly. A great majority of the patients returned to work and a survey carried out 3–6 years after completing the programme showed that about 50% of the patients were still working.

Purpose: In the present pilot study we studied the effect of the interdisciplinary pain management programme, including cognitive behaviour therapy, on some of the comorbid factors of chronic pain, i.e. depression, anxiety, automatic negative thoughts, general quality of life and the experience of pain.

Methods: Participants in this study were 23 inpatients, 19 females and 4 males who all participated in cognitive behaviour therapy (CBT) in addition to the interdisciplinary pain management programme. The CBT sessions were once or twice a week, for six to eight weeks, 50–60 minutes each time, for a total of 12 sessions. The CBT sessions were delivered by CBT trained health professionals; a psychologist, a social worker, nurses and occupational therapists using a standardized treatment manual. All the therapists were supervised by a CBT qualified psychologist. The main focus in the CBT sessions was on addressing activity levels, maladaptive thinking patterns concerning pain problems, as well as depressive symptoms and anxiety. Finally relapse prevention was addressed. Depressive symptoms (Beck Depression Inventory, BDI), anxiety (Beck Anxiety Inventory, BAI), automatic negative thoughts (Automatic Thoughts Questionnaire, ATQ), health related quality of life (Health Related Quality of Life Questionnaire, HL) and experience of pain (The West Haven-Yale Multidimensional Pain Inventory, WHYMPQ) were measured at the beginning and at the end of the programme with a follow up measure at 2–14 months after completion of therapy.

Results and discussion: The results show statistically and clinically significant differences in measures of depression (BDI), anxiety (BAI), automatic negative thoughts (ATQ) and health related quality of life (HL) as measured in the beginning and at the end of the treatment. The differences remained comparable in all of the follow-up measures and there was no correlation between the results and the number of months (2–14) that had passed from completion of therapy. However, the results did not show significant changes in the patients’ experience of pain from the beginning to the end of the treatment or in the follow-up measure. Due to the lack of a control group in this study, the question of the effectiveness of CBT alone needs further research.

Last year we started a randomized controlled study where the impact of CBT is specially evaluated.

Conclusion: The results provide valuable information in showing that the whole interdisciplinary pain management programme with CBT is effective in reducing symptoms of anxiety and
depression and in enhancing the quality of life for people with chronic pain.

References

174 Conventional ventilator therapy in ARDS
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Acute lung injury (ALI) with its most severe form acute respiratory distress syndrome (ARDS) is characterized by an acute inflammatory process in the lungs, either due to a direct injury, e.g., pneumonia or aspiration of gastric contents in the lungs (pulmonary ARDS), or an indirect injury due to a systemic inflammatory response syndrome (extrapulmonary ARDS). This inflammatory process will cause interstitial and alveolar edema in the lungs, either due to a direct injury, e.g., pneumonia or aspiration of gastric contents in the lungs (pulmonary ARDS), or an indirect injury due to a systemic inflammatory response syndrome (extrapulmonary ARDS). This inflammatory process will cause interstitial and alveolar edema in the lungs, either due to a direct injury, e.g., pneumonia or aspiration of gastric contents in the lungs (pulmonary ARDS), or an indirect injury due to a systemic inflammatory response syndrome (extrapulmonary ARDS).

Ventilator modes: In the majority of patients with ALI/ARDS invasive mechanical ventilation is needed. Despite many investigations there is no ventilator mode that has decisively been found to be superior. Modes that allow for spontaneous breathing, e.g., airway pressure release ventilation, have, however, some advantages by decreasing the need for sedation, improving circulation as well as improving oxygenation. Pulmonary and extra-pulmonary ARDS: Although it has not conclusively been shown in studies, it is highly probable that the optimal ventilator setting is dependent on the underlying lung condition, particularly whether it is an extrapulmonary or a pulmonary ARDS, and whether the patient is in the early or the late phase of the disease process (3). In the early phase of an extrapulmonary ARDS, the lung collapse is usually very easily recruitable, and lung recruitment maneuvers in combination with successive high PEEP may improve lung function dramatically (4,5,6). After some days, when the lung collapse is consolidated, lung recruitment maneuvers might be in vain and could even be harmful (4). In pulmonary ARDS, where the lung already initially is consolidated and the alveolar space is filled by inflammatory debris and edema, a lung recruitment maneuver may not be effective and the PEEP-level should usually, in my experience, be kept at a lower level than in extrapulmonary ARDS. Tidal volumes and airway pressures: The ARDS-net study showed that tidal volumes of 6 ml per predicted body weight were superior to 12 ml per predicted body weight in patients with ALI/ARDS (7). However, the major determinant of the mechanical stress caused by ventilation is theoretically the ratio between tidal volume and effective end-expiratory lung volume. Thus, a large tidal volume to a small lung will produce a high stress (tension) in the walls of the terminal airways and the alveoli according to Laplace law (the tension of a spherical structure wall is dependent on the pressure difference over the wall of the sphere, the volume of the sphere, as well as the wall-thickness and the mechanical properties). The effective end-expiratory lung volume is in the adult patient more dependent on the disease process (decreasing the active air-filled lung volume) than on the body weight. Therefore, the size of the tidal volumes has to be adjusted for the individual patient by considering the disease process in the lungs (and not only by the use of a formula based on the predicted body weight). The only common available clinical method today for this purpose is to measure quasi-static breath-by-breath respiratory compliance. This is, besides the size of the tidal volume, mainly dependent on the effective lung volume, the disease process and the compliance of the chest wall. We know that high end-inspiratory airway pressures may cause overinflation and overdystension of lung units and should be avoided. Thus, in patients with low compliance, very low tidal volumes should be used, but in patients with higher compliance, higher tidal volumes might be used safely. However, since it is the transpulmonary pressure and not the airway pressure per se distend the lung units, compliance of the chest wall has also to be taken in account. Many patients with ARDS have low chest wall compliance (usually due an increased intra-abdominal pressure) and therefore, higher airway pressures and larger tidal volumes may be tolerated without harming the lungs. In these patients, measurement of the intra-abdominal pressure is helpful when setting the ventilator. PEEP: There are no standards how to set PEEP in ALI/ARDS. Obtaining a pressure-volume (PV loop), and setting PEEP according to the lower inflection point (LIP) on the inspiratory curve and the maximum deflexion (MD) on the deflation curve (after a recruitment maneuver) have been proposed (6,8). However, using LIP has no physiological correlate and even if MD might be useful it is only one ventilator manufacturer which provides a software-tool for obtaining an expiratory PV curve (8). What presently can be used in all ICUs is, after performing a lung recruitment maneuver, setting PEEP high and then slowly decrease PEEP downwards from high to low levels until oxygenation decreases (8,9). The adequate PEEP is located 1–2 cmH2O above this pressure-level. In addition, PaCO2 and compliance should be equal or improved after this procedure if newly recruited lung regions are kept open. In my experience, 16–18 cmH2O is “optimal” in the initial phase of extrapulmonary ARDS, while in pulmonary ARDS, I seldom use higher PEEP levels than 10 cmH2O. Adequate PEEP, besides improving oxygenation, might prevent tidal opening/closing of lung units and thus reduce the risk for ventilator induced lung injury. The ALVEOLI-study, though, did not find that high PEEP was advantageous compared with low PEEP in ALI/ARDS (10). One of the major limitations with this study is that extrapulmonary and pulmonary ALI/ARDS were treated the same, and a possible positive effect of high PEEP in patients with early extrapulmonary ALI/ARDS might have been concealed by a possible negative effect in patients with primary ALI/ARDS. Thus, unfortunately, in my opinion, the ALVEOLI-study does not give any answer to how to set PEEP in ALI/ARDS. A PEEP-effect may be produced by using inverse ratio ventilation. In theory, however, this effect will mainly be found in lung units with long time constants (which already are expanded during expiration) but the lung units with short time constants (i.e. collapse prone lung units) will still have time to collapse during expiration. Conclusion: In ALI/ARDS the inflamed lung should be treated gently and the ventilator therapy should be individualised taking the underlying cause of ALI/ARDS, the phase of disease...
process and the chest wall compliance (intra-abdominal pressure) in consideration.

References

175 Lung volume measurements during ventilator therapy
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During the last thirty years probably less than 300 patients have had the Functional Residual Capacity, FRC, measured during ventilator treatment. The majority has been measured for research purposes. The lack of clinical methods for measurement of FRC has led to the use of surrogate measurements, such as blood gases or lung mechanics measurements. In 1992 Lachmann wrote an editorial: “Open up the lung and keep the lung open” which turned out to be the starting point of a new interest in lung volumes, recruitment manoeuvres, baro- and volotrauma and the development of methods for measuring the FRC at bed-side. Lung volume and not pressures was focused. However, there was a considerable time delay before a considerable amount of scientific articles with that same focus was seen.

In non-ventilator patients, i.e. patients breathing spontaneously and cooperating, the main methods for measurement of FRC have been the body plethysmograph, where the measurements are based on Boyle’s law: Pressure × volume = constant. This method is not applicable in the ICU setting.

Gas dilution methods
These techniques are based on the washin of a known volume of an inert gas into the lung. Measuring the resulting concentration of the gas gives the volume of the FRC:

\[ \text{FRC} = \frac{\text{Volume tracer gas/concentration of tracer gas}}{\left(\frac{N_2}{\text{concentration of tracer gas}} - \frac{N_2}{\text{concentration of tracer gas}}\right)} \]

There are certain problems with the nitrogen washout technique in the ICU: there are no nitrogen analysers for clinical use and in most patients inspiratory oxygen cannot be changed with 80%. The lack of nitrogen analysers has been circumvented by calculating the nitrogen concentration as the residual of oxygen and carbon dioxide concentrations. This approach, in turn, causes new problems, especially when breath-by-breath integration of nitrogen flow and concentration is used. In such a situation it is of utmost importance that the measurement of oxygen concentration and carbon dioxide concentration with ventilatory flow are continuously synchronised in a very precise manner. Such synchronisation has demanded the use of research flow meters and gas analysers which has limited the clinical use. When the method incorporates determination of oxygen consumption and carbon dioxide production high inspiratory oxygen concentrations make measurements inexact or even impossible at 100% oxygen.

Due to these problems other gases have been used as tracer gases: Helium and Sulphur hexafluoride, SF6. Helium has a very low solubility in blood and is thus a very suitable gas, but there are no fast response helium analysers which has impaired the use of helium in the ICU. To perform measurements the patients have had to be connected to a circle system of known volume with a known volume of helium. Then the patient has been ventilated with this circle system until helium concentration has reached a new steady state concentration. There are several drawbacks with this technique and it is cumbersome to use.

Sulphur hexafluoride, SF6, is detectable by infrared technique with very fast response and only needs to be administered with low volumes resulting in alveolar concentrations below one percent after a washin procedure. SF6 has all the properties needed for precise measurements at the bed-side, but the gas is not registered as a pharmaceutical. Thus, it can not be used as a tracer gas in routine clinical practice but is confined to remain a very qualified research method.

Development of the nitrogen washout method has led to the possibility to minimize the necessary change in inspiratory oxygen concentration to 10%, by avoiding the continuous integration of oxygen and carbon dioxide concentrations as a substitute for nitrogen concentration. The method is instead based on the inspiratory and end-tidal (alveolar) plateau concentrations of oxygen and carbon dioxide as identified by a standard gas monitor. This method has been evaluated in oxygen consuming lung model and in patients with acute respiratory failure. Precision and repeatability is very good. One of the most
Symposia

important advantages of the technique is that the little change in inspiratory oxygen needed, 10%, makes it possible to use also in patients on 100% oxygen, as lowering the oxygen to 90% for 3-4 minutes to achieve a washin of nitrogen only affects physically solved oxygen with a decrease in arterial oxygen content of less than 5 ml/L.

CT-methods
From spiral CT-scan of the lung the degree of aeration can be quantified. The total lung volume can then be subdivided according to Gattinoni, where attenuation levels between −1000 and −900 HU indicates overdistended lung, −900 to −500 HU represents well aerated lung, −500 to −100 indicates poorly aerated lung and −100 to +100 HU indicates non-aerated lung. This radiological method for determination of lung aeration has a superior topographic resolution and is an extremely useful research technique but also a good clinical method. From a clinical point of view the main drawbacks are the need for transport of critically ill patients and also, this is not a method for continuous monitoring of lung volumes.

Electric impedance tomography (EIT)
Sixteen standard ECG electrodes are placed around the chest wall. EIT data are generated by injection of electrical currents of 5 mA, 50 kHz with measurements of voltages differences between neighbouring electrode pairs in a sequential rotating process, where a scan is obtained every 77 msec. The scan slice has an estimated thickness of 5–10 cm. Global as well as regional impedance changes can be analysed. The image obtained has a much less precise geographical resolution than the CT-scan, but the resolution is good enough for separation of left and right lung as well as dividing the lung into several ventral – dorsal fields. The main advantage is that it is a continuous monitoring method and can easily be applied in a clinical setting. It is very well suited for evaluation of the effect of recruitment manoeuvres and endotracheal suctioning.

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Adjunct therapies in severe ALI/ARDS – ECMO/ECLS
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ECMO (Extra Corporeal Membrane Oxygenation) is a technique for oxygenation in patients with severe, lifethreatening, acute respiratory failure. Oxygenation of the patients blood is achieved through an artificial lung. The technique is today often called ECLS (ExtraCorporeal Life Support) and can then also include extracorporeal support of different organs, e.g. variations of pulmonary support (ECLA, ECCO2R), heart support and liver support (MARS) (1,2).
ECMO started in early 1970ies for treatment of neonatal acute respiratory disorders, e.g. meconiumaspiration and congenital diaphragmatic hernia and was soon widely used in the US and some places in Europe with encouraging results. Pediatric patients with pneumonia and aspiration soon became the next target for ECMO-treatment (1,2).
ECMO treatment in adult patients has been controversial for decades since the first randomized clinical trial showed no effect of ECMO compared to conventional intensive care (3). This trial has been questioned and is today more of historical interest. A new RCT has been difficult to perform from ethical aspects. However, a neonatal RCT from UK shows significantly better survival after ECMO than after conventional neonatal intensive care, for neonates with acute respiratory failure (4). There is a new study ongoing in the UK (CESAR-trial) in adults with acute respiratory failure randomized for ECMO or conventional intensive care (5).
The ECLS techniques for pulmonary support use a modified heart-lung machine designed for longterm treatment, from days to several weeks. Blood is drained from the right jugular and/or femoral vein, oxygenated extracorporeally in an oxygenator and then returned to the great veins or arteries depending on the severity of the respiratory failure. The variations of the pulmonary support and devices employed have developed over the last years. A continuus heparininfusion is used to inhibit coagulation in the ECLS system (plastic tubings, oxygenator, canulae).
During pulmonary support the patient is ventilated gently with low inspiratory pressure to give the lungs a possibility to “rest” and to avoid further ventilatory lung injuries (1). The treatment of the underlying disorder is intensified since ECMO/ECLS only gives the lungs “time for healing”. The patient is lightly sedated and as awake and aware as possible, which is advantageous in the nursing care of the patient and also for neurological monitoring (6). The sideeffects of ECMO/ECLS, such as cerebral haemorrhage, fungal infections and fibronolysis, increase with time. Many patients need renal replacement therapies and plasmapheresis during their time on ECMO.
Pneumonia (pneumococci, Legionella), aspiration and lung contusions after trauma are dominating among adult diagnoses. The main indication for ECMO/ECLS is when the patient deteriorates in spite of maximal support in the ICU. Contraindications are age over 65 years with underlying diseases, malignancies (except pediatric leukaemia), immunodeficiencies, bone-marrow transplanted patients and fulminating MOFS. Many patients who are ECMO/ECLS candidates are not in a state for
transportation, and have to be put on pulmonary support before the transport. The transport during ECMO can be performed safely and without negative effects (7). In Europe the only unit set up for transport on ECMO is in Stockholm (8). Today nearly 40% of the patients treated at the ECMO centre in Stockholm are transported on ECMO.

The worldwide ECLS register (ELSO) has nearly 30,000 patients reported to date, and the outcome, for pulmonary support, until discharged among the neonates is 77%, pediatric patients 56% and adult patients 66% (9). There are two follow-up studies in adult ECMO patients ongoing, one in Leicester, UK and one in Stockholm. Time to full recovery after ECMO is several months but the majority of the patients do recover completely, and can go back to school or work.

ECMO/ECLS is an expensive and resource consuming treatment modality and is highly dependent on the expertise, experience and dedication of the staff involved. The only viable option today is to concentrate ECMO/ECLS patients to larger centres with the knowledge and resources to offer long term pulmonary ECLS.

“The concept of extracorporeal life support (ECLS) is simple but the procedure itself is complex. ECLS is a cousin, not a twin to operating room cardiopulmonary bypass. ECLS specialists are not operating room perfusionists, and perfusionists are not competent to manage ECLS without specialized training.” Robert H Bartlett, 1995.

References

177

Preoperative assessment of the patient for aortic repair

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Cardiovascular complications of anaesthesia and surgery are common in patients suffering from ischaemic heart disease, left ventricular dysfunction, arterial hypertension, and/or valvular heart disease. Vascular surgery is associated with a considerable risk of cardiac complications, particularly surgery of the abdominal aorta. The risk of cardiac death ranges between 4.7 and 7.3%. This results from associated co-morbidity: coronary heart disease (40–60%), hypertensive heart disease (30–55%), cerebrovascular disease (6–34%), diabetes (7–10%), renal failure (3–10%), and, generally, smoking (90%). The risk associated with coronary heart disease is obvious: 50% of the deaths following vascular surgery are due to myocardial infarction. This review will focus on coronary heart disease.

The identification of high risk patients is based on medical history, physical examination, complemented by objective testing of coronary reserve and cardiac function.

Clinical features
High risk groups: Patients with unstable coronary syndromes (myocardial infarction less than 30 days) unstable, new or disabling angina, decompensated congestive cardiac failure, or major dysrhythmias or atrioventricular blocks, and severe valvular heart disease are at high risk for cardiac complications1. Intermediate risk groups: Intermediate predictors of risk include mild angina, prior uncomplicated myocardial infarction (more than one month without evidence of reversible ischaemia), renal functional impairment (creatinine >180 μmol/l), and diabetes mellitus or uncontrolled hypertension.

Angina: Stable, well controlled ischaemic heart disease is associated with a moderate increase in perioperative morbidity. Unstable and disabling angina are associated with high post-operative morbidity. In such patients coronary angiography is often necessary prior to major surgery. Coronary angioplasty/stent insertion or coronary artery bypass surgery may be necessary where indicated in their own right. When angina is less severe, prophylactic coronary artery revascularisation may reduce the risk of postoperative myocardial infarction but only in high risk surgery2.

Myocardial infarction (MI) less than 3 months before surgery was known to be associated with a very high risk of re-infarction. Progress in the management of acute myocardial infarction, in anaesthesia and perioperative care has reduced this risk. However, irrespective of the delay between infarction and surgery patients presenting for major abdominal or thoracic surgery, especially abdominal vascular surgery are at risk. Patients with acute or chronic left ventricular failure, or angina after infarction also remain at risk. The 2002 ACC/AHA guideline suggests that a delay of 6 weeks between acute myocardial infarction and surgery is adequate in uncomplicated MI without evidence of inducible ischaemia on an exercise test3. Silent myocardial ischaemia. Pre- and peri-operative silent myocardial ischaemia is associated with short- and long-term adverse outcome4,5. However, ambulatory monitoring of silent ischaemia is not an effective preoperative screening test for coronary heart disease.

Patients with previous coronary revascularisation
Coronary bypass surgery (CABG). The risk of postoperative myocardial infarction is low in patients who have undergone CABG some time in the past, provided they are not operated on less than 30 days (maybe six weeks) after coronary surgery6, and do not have other risk factors such as recurrence of angina (the grafts are no longer patent) or poor left ventricular function as poor left ventricular function is a predictor of adverse outcome7. Asymptomatic patients appear to be protected for at least five years. Angioplasty and stenting. The risk of postoperative cardiac complications appears to be reduced after 90 days of angioplasty8.

Routine tests
ECG. Extensive Q waves are likely to be associated with impaired cardiac function; dysrhythmias may increase the risk
of complications while conduction disorders may justify temporary pacing.

Chest X-ray. A large heart shadow (cardiothoracic ratio more than 50%) correlates with poor left ventricular function. Undiagnosed lung tumours may be detected, as well as presence of thoracic aeurysm or dilatation.

Renal functions. Impaired renal functions may indicate involvement of renal arteries (not necessarily diagnosed on abdominal ultrasound).

Further evaluation

Medical history alone and routine tests often underestimate the severity of coronary heart disease, and further evaluation including a stress test is often necessary. Tests available to determine the coronary reserve involve a physical stress (treadmill) or pharmacological challenge (dobutamine, dipyridamole, adenosine). The stress allows ischaemia that is not present at rest to be detected.

With stress ECG, reversible ischaemia is diagnosed as ST-segment depression. With stress echocardiography it is diagnosed by reduced ejection fraction and new wall motion abnormalities. Similarly, with radionuclide ventriculography (technetium, MUGA scan) reduced ejection fraction and new wall dysfunction can be observed. Myocardial scintigraphy (thallium, technetium 99m sestamibi) shows uptake by the well perfused myocardium and reduced uptake by the ischaemic myocardium. A reversible defect exists where an area of the myocardium takes up the isotope at rest but not during stress. With single positron emission computerised tomography (SPECT) perfusion and function can be assessed.

Stress echocardiography is more widely available than radionuclide ventriculography and myocardial scintigraphy, and allows relatively non-invasive screening for coronary artery disease and for impaired cardiac function.

The presence of reversible ischaemia is associated with greatly increased risk of cardiac events following anaesthesia and surgery. Presence of reversible ischaemia is an indication for coronary angiography, as a high proportion of vascular surgical patients have correctable coronary artery lesions. The indications for investigations of coronary artery disease have been defined in the 2002 ACC/AHA guideline.

Indications for coronary revascularisation. Because of the severity of coronary artery lesions, some patients will need CABG “in its own right” as lesions are life-threatening and coronary revascularisation is essential for the patient’s survival. Thus CABG must precede elective non-cardiac surgery. A small subset of patients may benefit from prophylactic coronary revascularisation because their coronary lesions are severe and they are presenting for high risk surgery (abdominal, thoracic, major vascular, and major head and neck procedures).

Patients with mild to moderate coronary lesions are unlikely to derive benefits from prophylactic coronary revascularisation. However, the long-term survival after repair of abdominal aortic aneurysm is considerably worse in patients with uncorrected coronary artery disease.

The optimal timing of surgery after coronary artery bypass surgery is unclear. The risk of major non-cardiac surgery less than 30 days after CABG is very high; a delay of six weeks is generally recommended. After coronary angioplasty, the risk of cardiac complications of non-cardiac surgery is lower after three months. Where stents are inserted and potent antiplatelet medication is given, there is risk of stent thrombosis if these drugs are discontinued to soon, and of massive bleeding if surgery occurs while they are still administered. In such patients surgery within 14 days is very dangerous. A delay of six weeks is now recommended. Clopidogrel should be stopped 7 days before surgery. There is no data on eluting stents.

The question of revascularisation has been addressed recently in a randomised study. It showed that prophylactic coronary revascularisation did not reduce the risk of postoperative cardiac complications of vascular surgery. However, this study excluded patients with severe coronary artery disease and those with poor cardiac function. Therefore its results are only applicable to patients who have been fully screened with decisions based on documented evidence of the severity of their disease.

Troponins

Serial postoperative troponin measurement is of considerable value in the assessment of postoperative cardiac damage. Their elevation correlates with short- and long-term outcome. Elevated troponins should be used to decide on aggressive postoperative management.

Conclusions

Vascular surgical patients are at risk for cardiovascular complications of anaesthesia, particularly those presenting for surgery of the abdominal aorta. As this is high risk surgery, evaluation of their cardiac function, including coronary reserve is important as the severity of coronary lesions is not always clinically apparent.

References


76 Symposia

178 Parental presence during the induction of anaesthesia in children
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While permitting parents to be present during the induction of their child’s anaesthetic is no longer a novel practice, controversy continues to surround how to whether such practice should be a matter of routine and what steps should be taken to assure that the experience is not a traumatic one for either the child or the parent.

The practice of allowing parents to be present during their child’s anaesthetic induction has been gaining popularity over the last 30 years. As early as 1961, “selected parents” were allowed to accompany their children during the induction of anaesthesia at Children’s Hospital National Medical Center (CHNMC) in Washington, DC. (1) By 1988 approximately 19% of hospitals with major pediatric services and 14% of general hospitals in the United States were allowing parents to accompany their children during the induction of anaesthesia. (2) An informal show of hands at the 1988 Society of Pediatric Anesthesia (SPA) annual meeting revealed that roughly half of the 150 anaesthesiologists present permitted parents to be present during induction. (1) Many hospitals are also now realizing that permitting parents to remain with their children during the induction of anaesthesia may be an effective marketing tool and may lead to enhanced consumer satisfaction. However, some anaesthesiologists continue to feel uncomfortable having a parent present during the induction period fearing that something may go wrong or that the parent may be critical of their work. Others are concerned about having to divide their attention between parent and child. The discomfort of the Anesthesiologist is a common reason for not allowing parents to be present during induction of anaesthesia in pediatric patients.

Hannallah et al (3) examined the attitudes of rotating anaesthesia residents at a pediatric hospital (CHNMC) that routinely allows parents to be present during induction. He found that the percentage of residents who viewed the practice favorably increased over time as they gained more experience with the technique. Most parents who have attended their child’s induction and the anaesthesiologists who performed the induction agree that the presence of a supportive parent actually makes the anaesthesiologist’s job easier. (4, 5).

All anaesthesiologists who frequently work with children have witnessed the all too familiar scene of an inadequately sedated, screaming and tearful child being forcefully separated from their parents and carried to the operating room for the induction of anaesthesia. Separation anxiety tends to be greatest for children under the age of six. (6) Younger children, especially when agitated, are at greater risk for arterial oxygen desaturation. (7) While sedative premedication can be used to avoid the trauma of separation, the increasing number of ambulatory surgical cases, the cost of sedative drugs and very short hospital stay times for many ambulatory cases may make the use of “heavy”, long-acting premedicants undesirable or impractical. Shorter acting sedatives must be carefully timed to assure their effectiveness. Predicting surgical starting times can be difficult and premedicants that are administered too late can cause delays while everyone waits for sedation to occur.

Advocates for parental presence during induction believe that this approach avoids the trauma of separation and facilitates the ease of induction of anaesthesia without having to rely on premedication. Studies have shown that most children do benefit from having a parent present during the induction of anaesthesia. Schulman et al (8) in 1967 examined the effects of a mother’s presence during the induction of anaesthesia upon 32 preschool children undergoing tonsillectomy. They found that children accompanied by a parent during induction were observed to be less upset than those children who were separated from their parents. Hannallah and Rosales (9) studied 100 unpremedicated children ages 1–5 years undergoing ambulatory surgical procedures. They found that the presence of a parent resulted in a significant decrease in the number of very upset and turbulent children during the pre-induction and induction periods when compared to a control group that was induced without the parents’ participation. However, they noted no significant difference in the behavior of the two groups in either the recovery room or at home after surgery.

On the other hand, several other investigators have found that a parent’s presence during induction may not always be beneficial. Yemen et al (10) studied 62 children, ages 4–10 years, undergoing ambulatory surgery. They observed that unpremedicated children with no prior surgical experience did NOT demonstrate any less anxiety during a halothane mask induction with a parent present than did the children in the control group who did not have the support of a parent. However, 55/56 children interviewed postoperatively said that they would prefer to have their parent present during a future anesthetic induction. Unfortunately, the Yemen study has never been published in a peer reviewed journal. In a more recent study, Bevan et al (11) studied 134 children, ages 2–10 years, undergoing ambulatory surgery. Parents were divided into two groups, “calm” and “anxious”, based on the parent’s self report. They found that children of “calm” parents did not differ in their mood as a result of having a parent accompany them during the induction of anaesthesia, while children of “anxious” parents were significantly more upset by having an anxious parent present at the induction. In addition, “calm” parents were less anxious after being present at their child’s induction than were anxious parents. Some “anxious” parents actually reported that separation from their child after the induction of anaesthesia helped them to relieve their own anxiety.

The different outcomes in these studies suggest that perhaps other factors, in addition to the mere parental presence, may influence how children respond to the stress of induction. Schulman et al (8) noted a significant difference between the results of the individual anaesthesiologists who performed the inductions in his study; however, this aspect of the investigation was not studied in detail. He noted that the most important factor appeared to be the anaesthesiologist’s ability to establish rapport with the child during the first few minutes prior to induction. Interestingly, studies that indicate parental presence may be beneficial for the children tend to come from institutions where this approach is common practice and studies that do not show a benefit come from centers where they have limited experience with this practice (12). It is quite possible that one of the factors that may influence how parents and children
respond to the stress of anesthesia induction is how comfortable or anxious we, their anesthesiologists, are during this very stressful period.

Several other studies also support the premise that a child’s conduct during induction may be influenced by the behavior of their parents. (11) Bush et al (13) evaluated how a mother’s behavior influenced her child’s ability to tolerate medical experiences. He found that when mothers used distraction, did not ignore their children, and provided information about the hospital environment, children exhibited fewer signs of distress and were more likely to explore their environment, which is indicative of low child distress. When mothers reassured their children or were overtly agitated the child exhibited maladaptive responses. Mothers who were high in trait anxiety or who were agitated tended to ignore their children more and provided them with less information. This study supports the emotional contagion theory; when a parent is anxious and upset; their child is more likely to be anxious and upset. Parents who appear to be overly anxious may NOT be good candidates for accompanying their children during the induction of anesthesia. Many parents believe that they should accompany their child out of a sense of parental duty. (14) Parents should be reassured that they are not being a “bad” parent, if they choose to not accompany their child during induction. Parents must be calm enough to support their child’s emotional needs during the induction of anesthesia.

While many parents find some aspect of accompanying their child during the induction of anesthesia to be a stressful or unpleasant event, the vast majority feel that their presence is of benefit to their child and that they would prefer to be present if their child were to require a future anesthetic. (4)(5)(15)(16) In fact, 58% of parents reported that they believed that being with their child during induction was one of the most important aspects of their child’s surgical experience. (17)

Things that parents frequently find to be upsetting or unpleasant about attending an induction are: (4) (16)

1. How quickly their child goes to sleep
2. Witnessing their child’s distress prior to induction
3. Separation from their child after induction
4. Seeing and feeling their child go limp during induction
5. The appearance of the child’s eyes
6. Not feeling adequately prepared for the experience.

Vessey and colleagues (16) in their now classic 1994 study further clarified the group of parents at most risk for being upset by participating in the induction of their child’s anesthetic. Mothers reported a higher degree of upset than fathers ($P < 0.05$). The magnitude of upset was greatest in mothers who had only one child, followed by parents who were employed in health care (23% mothers and 18% fathers). Three common emotional themes or conditions were also reported by parents: a sense of helplessness, a lack of psychological support and a loss of control. The loss of control was the prevalent theme reported by parents who served as controls ($P < 0.05$). Similarly, skin conductance levels in ALL PARENTS increased from baseline until the induction of anesthesia was completed or separation from their child had occurred ($P = 0.009$). No rhythm abnormalities were detected on any of the parent Holter monitor data strips. Heart rates and skin conductance returned to baseline levels in all three groups in about three minutes following separation from their child irrespective of whether induction separation occurred.

A parent’s stress level can be decreased by assuring that they are provided with adequate information and emotional support prior to, during and after the induction of anesthesia (22). Parents need to be well informed about what to expect and what their child will experience. They do not intuitively know what they should do to help. Ideally, parents should receive some very basic information to thoroughly prepare them for their participation in the induction of anesthesia prior to the morning of surgery, when they may already be experiencing information overload. A hospital preoperative tour is an excellent venue for allowing both parent and child to become familiar with some of the equipment they will encounter on the day of surgery and how it is used to painlessly induce anesthesia. It is imperative that the anesthesiologist explain to that parent exactly what will happen; and how they can best help support their child’s emotional needs, and reduce their level of fear and anxiety. We should show them where to stand or sit so that they will not feel that they are in the way. We should encourage them to touch and talk to their children during the early phase of induction in order to help their child remain calm. We should explain the sequence of events during the induction of anesthesia; so that, parents know what to expect and can answer their child’s questions. Once the child is anesthetized and the parent is told that their child is safe, the parent may need both emotional support and physical assistance to safely exit the induction/operating room. This is a very emotional time for parents. Ideally someone should be available to direct them to the waiting area. Finally, Vessey and colleagues (16) reported that “staff rudeness/insensitivity” was on several occasions the most distressing feature reported by parents during their participation in the induction process. These reactions occurred primarily when staff members were discussing their own personal lives and did not appear to be concerned with the care they were providing to their child or support they should have been studied three groups of parents and children ($n = 88$). The group I children received oral midazolam 0.5 mg/kg and were separated from their parents prior to entry into the operating room. Group II children were accompanied by their parents during the induction of anesthesia and group III children acted as controls (no premed and no parental presence). Parental anxiety scores as judged by a self-reported anxiety instrument were significantly lower in the midazolam group at the time of separation when compared to the control and parental presence groups ($43 \pm 12$ vs. $47 \pm 10$ vs. $50 \pm 10$, $P = 0.048$). However, in a more recent study of similar design Kain and associates (20) showed that when the anxiety levels of parents of premedicated children were compared with the parents of children who were also premedicated with midazolam but were accompanied by their parents to the operating room for induction, the anxiety levels in the later group of parents were significantly lower ($P = 0.037$). The most recent Kain study looking at parental anxiety levels is very well designed (21). In this study they continuously monitored the heart rates and skin resistance of parents during the pre to post-induction period. The children of these parents were randomized to the same three treatment groups that were used in previous Kain studies (parental presence, parental presence plus midazolam and a control group). At several standardized time points parents in the two parental presence groups had significantly higher heart rates than did parents of children who served as controls ($P < 0.05$). Similarly, skin conductance levels in ALL PARENTS increased from baseline until the induction of anesthesia was completed or separation from their child had occurred ($P = 0.009$). No rhythm abnormalities were detected on any of the parent Holter monitor data strips. Heart rates and skin conductance returned to baseline levels in all three groups in about three minutes following separation from their child irrespective of whether induction separation occurred.

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rendering to the parent during this stressful time. There is no substitute for common courtesy. Parents should be encouraged to meet their own needs in addition to those of their child. It is not uncommon for parents to go without eating or drinking on the day of their child’s surgery. In a survey of parents who were bringing their children to the hospital for surgery Vessey (16) found that 40% of parents were fasting and 24% had only coffee for breakfast as a show of empathy/support for their child’s NPO status. While it is a rare event, parents have been known to faint during the induction of their child’s anesthesia and this troublesome event is more likely to occur in dehydrated, fasting parents.

A common belief among anesthesiologists is that there is some inherent benefit to parents and children when the induction which is performed in an induction room rather than in an operating room. By using an induction room, parents do not have to be separated from their child while they change into operating room attire; parents look like “mommy” or “daddy”, not a doctor. Also, induction rooms are not as distracting for parents and children since they contain far less “scary” equipment. However, to date, no study has been published that demonstrates whether there are any psychological or emotional advantages to using an induction room over the operating room.

The use of an induction room may require more set up time than an induction performed in the operating room. Kateria (23) has shown that an induction room induction does take approximately two minutes longer to perform; however, this does not mean that using an induction room is any less efficient than using the operating room for the induction. In fact, it has been this author’s experience that when there are several short, rapid turnover cases done in the same operating room, it is more efficient to use an induction room, because the child can be induced while the operating room is being cleaned and set up for the next case, which actually saves valuable operating room time.

If an induction room is to be used, certain guidelines should be followed. Most importantly, not all parents are suitable candidates to accompany their children during the induction of anesthesia in either an induction room or the operating room. Likewise, not all children are suitable candidates for having a parent present during their induction. Healthy, ASA I and II, children over one year of age who are scheduled for outpatient surgery are the most appropriate candidates. The induction room must be equipped with all of the essential anesthesia equipment, monitors and supplies that would normally be found in the operating room. Finally, parents must agree that if they are asked to leave the room at any time during the induction, they will do so.

In Summary, parental presence can be a positive experience for the child, the parent, and the members of the anesthesia care team. However, it is important that we, the members of the anesthesia care team, carefully evaluate each family unit and ascertain their suitability for parental presence during induction. The accompanying parent must be calm and capable of supporting their child’s emotional needs during this potentially stressful experience. The parent must be adequately prepared so that they know exactly what to expect and what they need to do to help their child during the induction.

References

Intraoperative glucose infusions to babies and infants – solution or problem?

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In adults glucose containing solutions are still quite widely used (e.g. 2.5% glucose with 70 mmol/L sodium chloride) although many centres have changed to glucose-free alternatives (e.g. Ringer solutions). Since neonates and infants have a considerably higher basic metabolic rate and also have a substantially higher need for glucose compared to adults it has for a long time been seen as best practice to give glucose containing infusions to this patients group intraoperatively. This concept has been challenged during recent years but still there is no established consensus regarding this everyday issue.

A quite considerable literature now exist showing that most small infants can safely be managed without intraoperative glucose administration. However, a number of different risk categories are present and needs to be taken into serious considerations. The issue of intraoperative glucose solutions can be summarized in three important questions:

1. What are the risks of transient hyperglycemia intra- and immediately postoperatively?
2. Is intraoperative hypoglycemia an issue?
3. Is potential hyponatremia a potential problem if glucose containing solutions are used?

Hyperglycemia is clearly associated with a worse outcome in situations with focal or global cerebral ischemia. However, apart from cardiac by-pass surgery and certain types of neurosurgery, significant cerebral ischemia is very unlikely during regular pediatric anaesthesia and in the vast majority of paediatric cases this is, thus, not a clinical issue. Osmotic diuresis due to hyperglycemia is also very rarely a problem of a clinically significant magnitude during paediatric anaesthesia. With the clear exceptions of cardiac by-pass surgery and some neurosurgical operations the risk of mild-moderate hyperglycemia intra- and immediately postoperatively is not a clinical concern in the authors opinion.

Although glucose-free solutions can safely be used in the vast majority of infants there are a number of risk categories that can develop dangerous hypoglycemia intraoperatively. Some of these risk categories are:

1. Premature infants with limited glycogen reserves.
2. The sick neonate.
3. Children on total parenteral nutrition or high glucose infusions preoperatively.
4. Children with significant liver or other metabolic diseases.
5. Insulin dependent diabetes mellitus.

Intraoperative hypoglycemia can in these risk categories develop surprisingly fast and will not cause any noticeable symptoms due to the anaesthetic and can, thus, result in devastating effects. A safeguard against unnoticed intraoperative hypoglycemia would be frequent intraoperative blood glucose sampling but in the authors experience this is very rarely part of routine practice at any hospital despite being recommended in major textbooks. Since the possible consequences of unnoticed intraoperative hypoglycemia are substantial and that it is more difficult to remember all risk categories compared to exclude glucose from cardiac by-pass surgery and certain types of neurosurgery it appears wise to allow for some intraoperative glucose administration as the routine option in the authors opinion. Based on the literature a glucose concentration of 1% appears maybe to be the best alternative but 2.5% glucose solutions can also be regarded as clinically acceptable. Higher concentrations should, however, not be used since such solutions are associated with more significant hyperglycemia.

Maybe an equally important issue as hyper-/hypoglycemia in this context is the question concerning the risks for significant hyponatremia. It is a routine observation that patients handled intraoperatively with for example 2.5% glucose with 70 mmol/L sodium chloride will have a slight degree of hyponatremia immediately postoperatively. However, this does not cause any clinically relevant problems. If this type of glucose solution is not only used for normal maintenance requirements a much more dangerous situation can occur. It is very tempting and convenient for the anaesthesiologist to use the same glucose containing solution that is used for maintenance requirements also for the intraoperative treatment of intravascular volume replacement. Despite being an isotonic solution in the IV bag the above mentioned example would rapidly become significantly hypotonic when the infused glucose has left the intravascular space. This can subsequently lead to very severe hyponatremia. Currently a number of such cases are under investigation in the UK where for example one paediatric patient, operated for appendectomy, died postoperatively due to very pronounced hyponatremia!

Based on the above a relevant routine practice would be the following in the authors’ personal opinion:

1. Do not use glucose containing solutions as standard for paediatric cardiac by-pass surgery or certain types of neurosurgery. Instead check blood glucose frequently.
2. For other babies and infants use a 1.0–2.5% glucose solution (with approx. 70 mmol/L sodium) for normal maintenance requirements (4–5 ml kg⁻¹ h⁻¹).
3. To replace ongoing losses (e.g. increased evaporative losses or third spacing) in excess of 4–5 ml kg⁻¹ h⁻¹ or to treat the need for further intravascular volume expansion use adequate amount of Ringer solutions.
4. Following longer or more major surgery repeatedly check glucose and sodium levels both intraoperatively and immediately postop.

Paediatric epidural analgesia – where are we?

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Central epidural blockade has been used for anaesthesia and analgesia in children for more than 50 years, but really didn’t take off until the 1980’s (1). In the past 15 years, the technique has gained increased popularity for many reasons: an increase in the attention to the requirements for effective analgesia in children, a realisation that the postoperative course may be favourably affected by a dense afferent block, and the development and availability of equipment of appropriate size, i.e. small gauge epidural needles and catheters (1,2). Despite the obvious popularity of epidural analgesia conclusive evidence of the superiority of this method of pain relief over other allegedly simpler and safer forms of analgesia for children has not been clearly established (3). In adults there is substantial evidence of the efficacy and safety of epidural analgesia, however in children, although there is substantial literature on the subject, there are relatively few objective studies available (3). Particularly, there are no systematic reviews, which can help and guide us in our clinical practice and there have only been few randomized and controlled trials (2,3). Unfortunately, the vast
The majority of publications are descriptive, observational or audit in nature with very limited reliable data in relation to efficacy, safety, advantages, disadvantages, outcome, morbidity and mortality. This lack of properly conducted studies on epidural analgesia in children has lead to a considerable diversity in clinical practice, making evaluations difficult and discouraging the adoption of a consensus of “best practice” or the emergence of standards upon which to base future comparisons (2,3). Today, the issue of informed consent has forced the paediatric anaesthetist to come up with a clear and balanced view to parents about the risk-benefit ratios of various methods of post-operative pain relief available and their implications for their child’s postoperative course. Unfortunately, at present, we are not properly informed to do so in relation to epidural anaesthesia in children.

**Indication:** Epidural analgesia using administration of local anaesthetics with or without additives (most often opioids) is used for intra-operative anaesthesia as an adjunct to general anaesthesia, and for postoperative analgesia for thoracic and abdominal procedures, spinal fusion and major pelvic and lower extremity surgery (1,2).

This may be particularly useful in high risk cases, e.g. children with gastro-oesophageal reflux undergoing fundoplication, children with respiratory disabilities undergoing major abdominal surgery, neonates undergoing repair of oesophageal atresia. Occasionally, the technique may also be used as the sole anaesthetic for ex-premature infants undergoing lower abdominal procedures (1,2,4).

**Anatomy:** The posterior epidural space may be divided into right and left dorsolateral compartments by the dural plica mediana; these are further subdivided into anterior and posterior compartments by a transverse membrane. These structures have been accused for being a problem when failure of insertion of a catheter or lateralisation of the epidural block occurs.

**Physiology:** Epidural blocks in children <6–8 years of age are generally associated with cardiovascular stability, whereas children >6–8 years behave more like adults and exhibit a variable decrease in both heart rate and arterial blood pressure. This is believed to be due to physiological differences between adults and small children. Small children have a reduced sympathetic system distance (in children aged 1/2-10 years) has been estimated to be approximately 1 in 200.000 epidurals in adults. Serious complications with epidural analgesia is also unknown, but has been estimated to be approximately 1 in 200.000 epidurals in adults. Serious complications resulting in permanent neurological deficit or even death in children are rare, with an estimated incidence of the former in the order of 1 in 5000. Risk factors are: multiple traumatic attempts at epidural cannulation, age less than 3 months of age the duration should probably not exceed 36–48 hours.

**Complications:** A number of complications have been described in children. Difficulty in identifying the epidural space, dural taps, hypotension, convulsions and arrhythmias. Technical problems with the epidural catheters are quite common and may result in premature discontinuation of epidural analgesia: leakage at the site of entry of the catheter through the skin, misplaced catheter, catheter occlusion, catheter connector disconnection and cracking of the filter. These problems are more common with the smaller catheters (23 G and 24 G). Specific and potential side-effects are: leg weakness, urinary retention, IV injection of local anaesthetics, subarachnoid injection, heel blisters or pressure sores, epidural haematomas or abscesses. Epidural abscesses associated with the use of short-term post-operative epidural analgesia for acute pain relief in children have not yet been reported. The actual incidence in children of epidural abscesses associated with epidural catheters is unknown, although an estimation of 15 per million epidurals has been made. The incidence of epidural haematoma associated with epidural analgesia is also unknown, but has been estimated to be approximately 1 in 200.000 epidurals in adults. Serious complications resulting in permanent neurological deficit or even death in children are rare, with an estimated incidence of the former in the order of 1 in 5000. Risk factors are: multiple traumatic attempts at epidural cannulation, age less than 3 months of age and the use of LOR with air to identify the epidural space (7,8).

**Conclusions:** Although epidural analgesia in children is a well-established method of pain relief, there is no agreed consensus on many aspects of the technique. Thus, concern remains over the lack of evidence supporting the benefits of epidural analgesia over other methods of pain relief. Future controlled multi-centre outcome studies are required, in which safety is weighed against efficacy in specific populations and the most common method used to identify the epidural space. Newer methods e.g. LOR to CO2, micro drip infusion, electrical stimulation guidance or ultrasound have not yet gained widespread use. Several studies have estimated the distance from the skin to epidural space using complicated formulas. However, a practical rule of thumb for the skin to epidural space distance (in children aged 6–8 years) has been estimated to be 1 mm/kg. The use of a test dose remains controversial for many reasons, e.g. all children are anaesthetized prior to the block.

**Dosages:** No reliable formula predicting the volume requirement of local anaesthetic requirement have been described for single shot epidural analgesia or intermittent top-ups. For continuous infusions the infusion rates stated in Table 1 have been shown to be "safe".

Several additives have been added to epidural solutions of LA. Opioids are particularly popular, either morphine (5–10 µg/kg/hour) or fentanyl (0.1–0.5 µg/kg/hour), however opioids induced side effects will occur, e.g. PONV, pruritus and respiratory depression. Clonidine has become a popular alternative to opioids (0.3–0.6 µg/kg/hour) because it is devoid of the afore-mentioned side effects (1,2). The duration of treatment is usually 48–72 hours depending of the age of the child and the type of procedure, occasionally longer. In infants less than 6 months of age the duration should probably not exceed 36–48 hours.

### Table 1. Recommended infusion rates of 2 local anaesthetics most commonly used in paediatrics (4–6).

<table>
<thead>
<tr>
<th></th>
<th>Bupivacaine 0.1%</th>
<th>Ropivacaine 0.2%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates</td>
<td>0.2–0.25 ml/kg/hour</td>
<td>No data</td>
</tr>
<tr>
<td>Children</td>
<td>0.4–0.45 ml/kg/hour</td>
<td>0.2 ml/kg/hour</td>
</tr>
</tbody>
</table>

82 Symposia

surgical procedures. However, the exact same studies are also required for all the alternative methods of analgesia, e.g. continuous morphine infusion in infants with an unprotected airway.

References

181 Practical Echocardiography I
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Routine cases
TOE examination especially in the OR and ICU is often undertaken under time limited and stressed circumstances. Nevertheless, as a routine and if the circumstances permit so, the whole heart including the pericardium should be examined in each case. With training and in most patients it does not take more than approximately 5 minutes for an overview. Therefore it is important to acquire and use a routine for the procedure and report.

Advantages
- Less risk of missing important information
- You learn more with documentation and report

A pathologic finding should always be examined in several views otherwise there is a considerable risk for misinterpretation. With the regular 2D image it should be kept in mind that structures are seen in one plane only. The technical development in the 3 dimensional echocardiography will facilitate correct assessments but so far it has not been developed in clinical practice. Still the investigator has to build a three-dimensional picture in the mind. With the new multiplane probes it is easy to obtain numerous images/views from the same position of the probe by just rotating the crystal (fig 1). Try to place the focus of interest in the middle of the image (the dotted line) which enables multiple views of the object you want to study in detail.

For the beginner this is one of the main obstacles in the beginning of the learning process. The best way to learn how the anatomy of the heart is pictured in the different standard TOE views is during a wet lab situation. To overcome the confusions in TOE terminology for the views the ASE (American Society of Echocardiography) and SCA (Society of Cardiothoracic Anesthesiologists) have agreed to the standards as in figure 3.
With each view also the rotation of the crystal is shown. To obtain these views with this rotation/angle of the crystal the starting-point is a horizontal plane of the crystal window which has to be lined with the horizontal plane of the patient. Of course, for example to find the optimal ME 4 chamber view the rotation of the crystal has to be slightly modified from patient to patient. Therefore in most textbooks on TOE images a considerable range in the rotation of the crystal is mentioned. Most used views/standard views/“starting views” (For real images see end of this abstract).

ME = mid esophageal, LAX = long-axis, TG = transgastric, SAX = short-axis
84 Symposia

These views are standards because the LV is often the focus of interest and they are usually easily obtained. Moreover for example from the ME four chamber view it is easy to make an assumption about what is wrong. The depth in the esophagus is not mentioned in the summaries below because it varies considerably between patients. However the ME views are mostly found in the range of 25–30 cm from teeth.

In regular 2D mode (ordinary grayscale imaging) the morphology/dimensions/function of the LV can be assessed both visually and by direct measures. For a more detailed analysis of LV systolic and diastolic function the transmitral flow Doppler is used. With the advanced tissue Doppler analysis further evaluation of regional wall motion has become a useful tool in ischemic heart disease and the cardiac resynchronization therapy (CRT).

Moreover the effect of mitral and aortic valvular disease upon the LV and left atrium (LA) can be evident. After long standing mitral regurgitation the enlargement of the LA is often evident with the concomitant risk for atrial fibrillation. In long-standing mitral valve stenosis (MS) the LV can be small but the LA enormous.

In aortic valve stenosis (AS) the concentric thickening of the LV with decreased sized LV cavity is a typical feature. With severe aortic valve insufficiency (AI) the LV becomes dilated.

To further improve diagnosis more images are important. The standard images above must often be supplemented with more views to answer the basic questions also in routine cases. The next set of images extends the examination of the LV, mitral- and aortic valves.

In the TG basal SAX and ME mitral commissural views assessment of mitral valve function is useful and especially to localize the mitral insufficiency with 2D + color. The ME AV SAX gives a good view of the normally tricuspid aortic valve and sometimes also the pulmonary valve. Doppler flow measures through the mitral valve can be performed in the ME mitral commissural view.

In aortic valve stenosis (AS) the concentric thickening of the LV with decreased sized LV cavity is a typical feature. With severe aortic valve insufficiency (AI) the LV becomes dilated.

Moreover it is not taken for granted that a perfect 2D image is a guarantee for an optimal lining.

More images are needed to examine the RV in more detail and also the aorta and the pulmonary artery.
2D/Mmode + color
RV, tricuspid and pulmonary valve morphology, dimension and function. Ascending aorta and pulmonary artery (including the bifurcation and right pulmonary artery) morphology and dimension. The left pulmonary artery is difficult to see because of airway interference.

Doppler
Tricuspid valve and pulmonary artery flow. The following images are focused on the aorta

UE = upper esophagus

2D/Mmode + color
Aortic and left subclavian entry, morphology and dimension.

Doppler
Usually of no use.

All presented views should be regarded as standard views and all cardiothoracic anesthesiologists should be familiar with how to find and interpret them. Once this skill and knowledge are acquired every view could be modified to optimize the examination. With the multiplane probes any structure could be investigated from 0 to 360 degrees by rotating both the probe and the crystal. However the image could be lost especially with a rotation of the probe because of lost contact with the surrounding structures. Therefore some investigators prefer larger probes for improved image quality. However, introducing a large size probe into the esophagus means increased risk for hurting the patient. Modern TOE probes have become smaller but still with improved image quality.

The beginner should as soon as possible focus on the image and not how far into the esophagus the probe is positioned and how much the crystal is rotated. The standard views are used as reference. Also if you are lost- always rotate the crystal to 0 degrees and face the window of the probe ventral/anterior.

Unusual cases
Most likely the number of patients with unusual heart abnormalities is low in general anesthesia. Anyhow, the variation in heart morphology and the central great vessels varies even in a population regarded as normal. There are some categories of heart and pericardial pathologies which certainly challenge the echocardiography.

• Congenital abnormalities represent a great variety of diagnoses from a "simple" coarctation of the aorta to complicated heart valve abnormalities.
• Diseases involving the pericardium is another challenge where it could be extremely difficult to distinguish a regular postoperative hematoma from pericardial cysts or pericardial fat or tumor.
• To differentiate intracardiac tumors from thrombi is another difficult issue.
• Miscellaneous

Congenital abnormalities
It is crucial to use the routine examination in these cases. The reason is that it is common with several abnormalities and the risk to miss all of them is obvious. One example is the bicuspid aortic valve and the combination with coarctation of the descending aorta distal of the left subclavian artery.

With the examination all capabilities of echocardiography must be used i.e. 2D, 2D + color, Mmode dimensions and Doppler flow are combined for a reliable diagnosis. Also the echocardiographer must be familiar with all standard TOE views and how they could be modified for a maximum visualization of the pathologies.

Pericardium
In processes involving the pericardium a correct diagnosis can be very difficult. After cardiac operations hematoma are not uncommon and usually they are easily diagnosed. However in other circumstances it is sometimes almost impossible to distinguish whether the finding is located in the pericardial sack or intracavitary for example in the right atrium or the right ventricle. Moreover if the abnormality is originated from the pericardial sack or the myocardium.

Intracardiac tumors
Intracardiac tumors is another difficult topic in echocardiography. If they are located in the trabecular parts of the myocardium they have to be of a considerable size in order to be found. Much effort has been made with iv contrast for more correct and easy diagnosis but the results are not encouraging.

Miscellaneous
This includes postoperative valve replacement complications as paravalvular or valvular leakage, placement of endovascular grafts and much more.

In summary
In recent years several papers have been published on guidelines for echocardiography examination of heart valves and heart function. These together with reviews on more specific topics cover the field of echocardiography for the interested reader. Numerous books with excellent figures and CD rooms with cine loops are available on the market.

Because of the evolving echocardiography techniques new options and possibilities seem to be a never ending story and the accuracy of ultrasound based diagnosis is continuously improving.

H
The standard views

ME 4CH normal
abnormal (LV enlarged)

ME 2CH normal
abnormal (LV spherical/dil)

ME 2CH LAX normal LV but abnormal (LV spherical/dil)

pericardial fat

TG SAX normal
abnormal (LV hypertrophy)

Inhaled therapies in postoperative pulmonary hypertension and right ventricular failure
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Acute pulmonary hypertension may cause right ventricular (RV) failure with a decrease in RV output and a decrease in left ventricular preload. The increased volume of the failing RV may also directly shift the septum towards the left ventricle with a consequent decrease in left ventricular distensibility, which will further decrease left ventricular preload. This will in turn decrease cardiac output and cause systemic hypotension with a decrease in RV coronary perfusion pressure, which may further impair RV function. What are then the therapeutic options in pulmonary hypertension and RV failure? Various intravenous vasodilators, nitrates, prostaglandins or adenosine, have been tried. They all cause a decrease in systemic vascular resistance...
and a decrease in arterial pressure (1), which might further jeopardize the perfusion of the RV.

Inhaled nitric oxide has gained an established place in the management of pulmonary hypertension after cardiac surgery (2). Inhaled NO induces a decrease in pulmonary vascular resistance (PVR) with no change in systemic vascular resistance or mean arterial pressure (1). However, cost, potential toxicity, and the lack of positive outcome data with inhaled nitric oxide therapy has generated interest in alternative inhaled, selective pulmonary vasodilators (3).

In recent years there is an increasing interest in the use of inhaled aerosolised prostacyclin (PGI2) for treatment of pulmonary hypertension after cardiac surgery (3). In a pharmacodynamic study (4), inhaled PGI2 (10 µg/ml) induced a dose-dependent decrease in PVR and transpulmonary pressure gradient (which decreased by ~29% and ~26%, respectively). Inhaled PGI2 also improved RV performance with no effect on systemic vascular resistance. An ideal pulmonary vasodilator should act on the post-capillary resistance section, which will decrease pulmonary capillary pressure (PCP) and improve capillary absorption of pulmonary interstitial fluid. In a preliminary study, we have evaluated the effects of inhaled PGI2 on PCP in patients with pulmonary hypertension after cardiac surgery. Inhaled PGI2 (10 µg/ml) decreased significantly the post capillary resistance by 40%, which was accompanied by a decrease in PCP (unpublished observations).

The effects of inhaled NO (40 ppm) vs. those of inhaled PGI2 (10 µg/ml) was compared in 10 heart transplant candidates, with high PVR, undergoing diagnostic heart catheterization. In all patients, both PVR and the transpulmonary pressure gradient decreased with both NO and inhaled PGI2, to a similar extent (5). Interestingly, in all patients, both NO and inhaled PGI2 induced an increase in pulmonary capillary wedge pressure. In other words, in patients with severe left ventricular dysfunction, inhaled NO or inhaled PGI2 might cause an aggravation of left ventricular failure due to the pulmonary vasodilatation which will increase left ventricular end-diastolic volume. Inhaled NO or inhaled PGI2 should therefore be used only in patients with isolated right ventricular failure.

PGI2, when administered intravenously, is a very potent inhibitor of platelet aggregation. It is therefore important to know the effects of inhaled PGI2 on platelet function after cardiac surgery and cardiopulmonary bypass. The effects of 6 hours postoperative inhalation of PGI2 (5 and 10 µg/ml) and placebo on platelet aggregation in vitro, bleeding time, chest tube drainage and systemic 6-keto PGF2α were investigated after uncomplicated coronary artery bypass surgery (6). There were no differences between the groups with respect to bleeding time or chest tube drainage. Furthermore, there was no increase in the stable metabolite of PGI2 (6-keto PGF2α) indicating that there is no spill-over of PGI2 into the systemic circulation during inhalation. However, there was a significant inhibitory effect on platelet aggregation, in vitro, after 6 hours of inhalation with 5 or 10 µg/ml of PGI2.

Milrinone is a potent both systemic and pulmonary vasodilator when given intravenously. Can inhaled nebulised milrinone also be used for treatment of pulmonary hypertension after cardiac surgery? Inhaled milrinone, at the concentration of 1 mg/ml, induces a selective pulmonary vasodilatation in patients with pulmonary hypertension after cardiac surgery (7). PGI2 increases the concentration of cyclic AMP while the phosphodiesterase inhibitor milrinone inhibit the conversion of cyclic AMP back to ATP. It is therefore reasonable that inhaled milrinone might have additive pulmonary vasodilatory effects when combined with inhaled PGI2. In patients undergoing cardiac surgery or heart transplantation with postoperative pulmonary hypertension, the effects of combined inhalation with PGI2 and milrinone were evaluated. As shown previously, inhaled PGI2 caused a significant decrease in PVR, which was further decreased when combined with inhaled milrinone (7). Twenty minutes after termination of inhalation there was still a significant decrease in PVR indicating that combined inhalation of the two agents prolong the duration of pulmonary vasodilatation as compared to the effect duration of each agent alone. Combined inhalation of PGI2 and milrinone had no effects on systemic vascular resistance.

Other potentially interesting inhaled alternatives for treatment of postoperative pulmonary hypertension in the future are the nitric oxide donor drugs nitroglycerin and nitroprusside, as suggested by some animal studies on experimental pulmonary hypertension (8,9). Compounds formed by reacting NO with various nucleophiles release NO spontaneously in physiologic solutions and have the potential to function as an aqueous slow-release form of NO. It has been demonstrated that inhalation of nebulised nucleophile-NO solution selectively decreases PVR in a porcine acute lung injury model with pulmonary hypertension (10). Clinical studies on the use of inhaled nitric oxide donor drugs in pulmonary hypertension are lacking.

Another treatment strategy would be to combine inhaled NO with a phosphodiesterase type V inhibitor e.g. sildenafil (oral, intravenous or inhaled) which prevents the degradation of cGMP and might therefore have additive effects to inhaled NO (11).

References

Practical echocardiography II: Valvular heart disease – is the repair good enough?

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In recent years the interest for valvular repair has increased considerably and in fact a repair is supposedly favorable compared with valve replacement. Most interest has been focused to the mitral valve but also the repair of the aortic valve has become an option. The question is which factors have been contributing to this change. Unquestionable the use of echocardiography in the intraoperative setting as a useful supplement to the preoperative diagnosis, has played and plays a key role. The intraoperative and real time assessment of the morphology/function/dynamics of the valve both before and after repair is crucial. However, one often mentioned obstacle to this assessment is that the patient is anesthetized which dramatically could change the pre- and afterload levels and consequently jeopardize the importance of the examination. This taken into consideration sometimes makes the decision making of the echocardiographer difficult – is the repair good or not?

There are some crucial questions to be asked before any repair should be considered. Even if the preoperative assessment propose a repair the intraoperative echo examination might not or vice versa. In my opinion the intraoperative echocardiographer should not be aware or have read the preoperative work up echo. It must always be kept in mind that echocardiography is a visual medium and it is easy to be biased from earlier examinations.

Some considerations
What is the mechanism for valvular function?
Coaptation problems
Primarily or secondary
Leaflet/cusp changes
Calcification
Ruptures
Rheumatoid

Leaflet/cusp morphology
Is there enough leaflet/cusp tissue for repair and how will the repair change the flow mechanics?

Pre- and afterload
What pre- and afterload should be applied to control the quality of the repair.

Ischemic time/another extra corporal run
The risk of insufficient repair with residual valve dysfunction and another extracorporeal period of perfusion must be considered in elderly patients with impaired myocardial function.

First the question of coaptation. One example is that the coaptation area of the anterior and posterior leaflet of the mitral valve should be at least 5 mm on the left atrial side of the valve.

Evidently the causes could be both leaflet/cusp pathology but also secondary to other changes for example a dilated left ventricle (LV) and a secondary mitral valve insufficiency (see figure below).
In secondary MR as result of LV ischemia the question is whether coronary artery bypass surgery will improve LV function and thereby decrease the MR. Unfortunately this is seldom the case and additive surgery a an annular ring could make the MR less pronounced.

With replacing an aneurysmatic ascending aorta with a graft from the sinotubular junction up to the truncus brachiocephalicus aortic regurgitation could be cured. However, it requires normal cusp morphology.

**Mitral valve repair in mitral regurgitation**

The most common (80%) cause in MR is an abnormality located to the middle (p2 segment) of the posterior (the mural) mitral leaflet. It is better to refer to the mitral valve apparatus when MR is discussed. The apparatus consists of: the two leaflets, the annulus, the primary and secondary chords and the left ventricle myocardium. All parts must be normal for optimal valvular function.

In cases like this a quadrangular resection of a part of the p2 segment is performed (valvuloplasty) and an annular ring (closed or open) is sutured to the base of the posterior leaflet and the annulus and all the way to the base of the anterior leaflet and its part of the mitral annulus.

This type of valvulo- and annuloplasty is regarded as easy and the results are good. However, studies have shown that the incidence of immediate failure is not negligible. Another option in a pure p2 prolaps (of the middle part of the segment) without chordal ruptures and a flailed part of the leaflet is the Alfieri stitch where the opposing p2 and a2 segments are sutured together (figure 4). However, the stitch must be absolutely correct placed to make the valve competent.

Any mitral valvular apparatus pathology located close to the posteromedial or anterolateral commissure is more difficult to repair with increased incidence of residual MR after repair. Moreover as shown in figure 5 after a p2 valvulo- and annulo-
plasty, there is still some MR located at the p3/a3 part of the valve. There are many surgical techniques described in repair as prolongation of chordae, new artificial chordae, sliding and transferring techniques.

There are always difficulties when leaflets show restrictive motion caused by rheumatic disease, calcification or thickening. Also the height of the different segments of the leaflets is important. In short the mitral valve opening area is decreased with this operation but a stenotic flow pattern is a rare complication.

The aortic valve – reparable or not?
The tricuspid aortic valve often becomes calcified with ageing. Not only the cusps become calcified but also the annulus and the sinus Valsalva. Consequently repairs of the aortic valve for aortic regurgitation (AR) is not as common compared with mitral valve repair for MR. However, if the cusps are morphologically normal or close to normal but dysfunctional because of lack of coaptation or apposition the AR could be surgically corrected. It must also be kept in mind that the configuration of the mitral leaflets and the aortic cusps is totally different. In short the tissue and the amount of leaflet material in the mitral valve leaflets are more forgiving than the aortic valve.

Is the repair good or not?
There are several important steps to take in assessing the result of valvular repair.

- Transvalvular flow pattern
- Velocity
- Preload level
- Afterload level
- Heart dysfunction
- Age

It is quite obvious that the final decision if the repair is good or not must be decided after weaning from cardiopulmonary bypass. When still on partial bypass a preliminary evaluation is reasonable and if the MR still is more than grade 2 the repair has failed and the discussion must be if further repair is possible or not. It has been shown that a residual MR of grade 2 or more worsen the postoperative prognosis. In patients without concomitant ischemic heart disease with a non-stunned myocardium and uncomplicated surgical/anesthetic procedure the function is usually easy to assess both before and coming off bypass.

Because all the constituents of the mitral valve apparatus are involved in its function the pre- and afterload levels must be accurate. Especially after a long history of MR with left atrial (LA) enlargement and eventually atrial fibrillation the pre- and afterload levels are crucial in assessing the result of the repair. A guideline in all cases is that the post weaning pressures should be similar to the levels with the patient awake.

When a repair of the mitral valve is combined with aorto coronar bypass for coronary heart disease the issue is how much LV dysfunction contributes to the MR. It has been shown that once the shape of the LV becomes more spherical as in advanced ischemic heart disease there is no use with annuloplasty. This makes sense because the malcoaptation of the leaflets is caused by the tethering force on the leaflet from the dilated LV.

Age and operative risk must be involved in the final decision. In young patients with active living the goal should be no residual regurgitation after repair. Also the mitral valve opening area must be sufficient for increased cardiac performance. In older patients a prolonged surgical repair or a second pump run for further repair increase the risk and therefore the acceptance of a mild (1–2 of 4) is acceptable.

Still the evaluation of the degree of residual MR or AR after repair represents a true challenge to the echocardiographer but the responsibility to immediately report unacceptable results is evident. The decision must be made based on a thorough examination of all important constituents in regurgitation and face the surgical team with your decision. After a team discussion the final decision is made – further repair or valve replacement.

References

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LV AD for destination treatment: heart transplantation seem safe and highly beneficial for terminal normalization of pulmonary pressures, making these periods of LVAD pumping leads to a progressive decrease of PVR. These patients mean systolic pulmonary pressure dropped to normal values, and is becoming increasingly important as left ventricular assist devices (LVADs) are being used for longer periods as a bridge to transplantation (period lengthening due to donor shortage) or recovery, or as destination therapy. However, its incidence and clinical management have not been widely studied. In one study the cumulative probability of device failure was 6%, 12%, 27% and 64% at 6 months, 1 year, 18 months and 2 years, respectively. Major failure occurred in 8 (7.8%) patients. Life-threatening mechanical device failure seems not uncommon and increases with time, but can be managed successfully in most patients. Improvements in design and manufacture should further enhance outcome with LVADs.

LV AD and its effect: Left ventricular assist device (LVAD) seem reverse remodelling independent of hemodynamic factors and would primarily depend upon normalization of the neurohormonal milieu. The relative contributions of LVAD-induced hemodynamic unloading (provided to the left ventricle [LV]) and normalized neurohormonal milieu (provided to LV and right ventricle [RV]) to reverse remodelling are not understood. Improved beta-adrenergic responsiveness, normalization of the Protein kinase A (PKA) hyperphosphorylation, and increased beta-adrenergic receptor density in LV and RV after LVAD support suggest a primary role of neurohormonal environment in determining reverse remodelling of the beta-adrenergic pathway. 

LV AD and Right heart failure: Pulmonary hypertension (PH) and elevated pulmonary vascular resistance (PVR) lead to poor outcome after heart transplantation due to postoperative failure of the non-conditioned right ventricle. Elevated PVR and severe PH were both previously considered as contraindication for heart transplantation. The role of LVAD support in the reduction of elevated PVR was evaluated in a series of clinical implants. In these patients mean systemic pulmonary pressure dropped to normal and PVR decreased to normal values under LVAD support. Clinical improvement was significant in all patients. A period of LVAD pumping leads to a progressive decrease of PVR and normalization of pulmonary pressures, making these patients amenable for heart transplantation. LVAD as bridge to heart transplantation seem safe and highly beneficial for terminal heart failure patients with severe PH.

LV AD for destination treatment: The REMATCH trial enrolled patients with more advanced heart failure and high prevalence of intravenous isotropic therapy. Patients undergoing isotropic infusions at randomization derived major LVAD survival benefit with improved quality of life. Patients’ not undergoing isotropic infusions had higher survival rates both with and without LVAD, but differences did not reach significance. Future studies should prospectively analyse isotropic and other therapies to determine how disease severity and parallel medical treatment influence the benefits offered by mechanical circulatory support. LVADs improved survival throughout follow-up for patients undergoing baseline isotropic infusions.

LV AD and infections: Significant infection rates have been reported among LVAD recipients. LVAD-related infection is common and may require antimicrobial therapy before, during, and after transplantation, but it does not prevent successful transplantation. However, patients with LVAD-related infection appear to be at increased risk for invasive vancomycin-resistant Enterococcus faecium (VREF) infection, which may contribute to early mortality after transplantation.

Device failure: Mechanical device failure can be life-threatening and is becoming increasingly important as left ventricular assist devices (LVADs) are being used for longer periods as a bridge to transplantation (period lengthening due to donor shortage) or recovery, or as destination therapy. However, its incidence and clinical management have not been widely studied. In one study the cumulative probability of device failure was 6%, 12%, 27% and 64% at 6 months, 1 year, 18 months and 2 years, respectively. Major failure occurred in 8 (7.8%) patients. Life-threatening mechanical device failure seems not uncommon and increases with time, but can be managed successfully in most patients. Improvements in design and manufacture should further enhance outcome with LVADs.

185 Is parenteral nutrition really that risky in the ICU?
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Enteral nutrition (EN) is the mainstay of nutrition delivery within intensive care but there has developed a blind faith in its benefits and a disregard of its risks. Some commentators even believe that parenteral nutrition (PN) is no longer required and that it is fraught with risks to the patients (1). This has never been the case and a robust defence of PN within ICU nutrition support is published (2). Sadly the indiscriminate use of PN or use of incomplete or unbalanced high glucose formulations particularly in North America was less a feature of practice in Europe where in addition we have used stable all-in-one formulations for decades.

A greater appreciation of the failings and risks of enteral nutrition delivery (3) combined with improvements in PN formulation and use help explain why PN is not as risky as some have believed. There is only one level one study that correctly addresses the question of the choice in those patients where uncertainty exists over gastro-intestinal tolerance. This study suggests that EN may even carry a higher mortality risk (4) and contributes to meta-analyses and guidelines that have implied there was no overall difference in mortality rates (5). A new detailed intention-to-treat analysis from nine studies comparing EN v PN used a component based approach to investigate the effect of trial quality (6). This has shown a significant mortality benefit in favour of the use of PN (odds ratio, OR 0.51, 95% CI 0.37–0.79; P = 0.04) confirming what this author has been saying (7). This is despite EN use being associated with a significant reduction in infectious complications. The difference was less evident when the start of nutrition support was not delayed. Since EN is generally cheaper recommendations agree that EN is preferred where the gastrointestinal tract is intact and practical but the important decision is also to decide when it is safe. When EN is necessary (as demonstrated by gastrointestinal failure or complete intolerance of enteral nutrition delivery) the best evidence available recommends the use of glutamine containing PN formulations as real outcome benefits have been described (8,9). The use of PN in combination with EN understandably remains controversial since there is a paucity of data but there appears no harm. What studies exist have given PN from the outset and not started it once clear EN failure has been documented. The latter is the accepted clinical position and means that PN should be considered depending upon the patient’s nutritional status and circumstances after 3 to 5 days once strategies to optimise EN have been exhausted.

Parenteral nutrition remains a valuable yet challenging weapon in our therapeutic armoury in the presence of gastrointestinal feed intolerance or failure. However it should be used
wisely and not indiscriminately since the majority of ICU patients with a fully functional gastro-intestinal tract may usually be fed safely with enteral nutrition.

**References**


**Perioperative glycemic control and therapy**

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The development of perioperative hyperglycemia, whether it occurs in the OR, ward, high dependency unit or ICU is common in adult patients. The role of blood glucose as a marker of inflammation/stress, potential role of glucose levels and insulin requirements as a herald of outcome, and the benefit of normal or near normal glucose control during the perioperative period with resultant enhancement of long-term patient outcome continues to be investigated. Many groups increasingly advocate the aggressive treatment of hyperglycemia with insulin infusion for diabetics and non-diabetics during the perioperative phase of care, but questions remain about universal application of tight control intraoperatorively, about the ideal glucose goal, about the true incidence and effects of resultant hypoglycemia and the mechanisms of benefit.

**Scope of the problem**

Diabetes mellitus (DM) is the most commonly encountered perioperative endocrinopathy (see table 1). Type 2 diabetes continues to dramatically increase in incidence. It is projected to affect 30–40% of Americans born after 2000. Diabetics require hospitalization and procedural interventions more frequently and have greater in-hospital and post-operative morbidity and mortality than their non-diabetic counterparts. Diabetes is the sixth most common cause of death in the US. We may underestimate hyperglycemia related complications since they frequently develop on the ward or postoperatively, but this should not dissuade us from careful preoperative assessment, intraoperative management and postoperative care of diabetic or hyperglycemic non-diabetics.

Diabetics may have significant and progressive micro- and macrovascular disease including advanced cardiac pathology (ischemia/infarction, hypertension, CHF, diastolic dysfunction, other), renal compromise (DM remains the leading cause of end stage renal disease in developed nations), and vascular pathology along with diffuse neuropathy. End-organ pathology may be evolving or well advanced prior to the diagnosis of diabetes mellitus since upwards of a third to one half of diabetics are unaware of their condition at the time of hospitalization or surgery. Roughly a third of patients undergoing coronary artery surgery annually in the US are diabetic. Although reports vary, the incidence of ICU patients with known diabetes varies from about 8–30% depending on pathology and demographics. Diabetics, however, is only the tip of the dysglycemia iceberg. A significant number of patients undergoing major surgical intervention or sustaining acute injury or illness develop hyperglycemia. Some of these patients may be previously unrecognized diabetics that are unmasked with stress. Hyperglycemia in the perioperative patient is caused or exacerbated by stress hormone and cytokine-induced insulin resistance and increased glucose production. Recent data from a medical ICU study suggests the potential utility of measuring the Hgb A1c as a predictor of dysglycemia in the critically ill. The preoperative potential application of routine measurement of the Hgb A1c, particularly in higher risk, older, sedentary, obese patients as a perioperative diagnostic tool or for risk stratification awaits further evaluation. Furthermore, the degree of hyperglycemia and insulin required to control glucose may correlate to morbidity and mortality and may reflect the degree of inflammatory response of an individual. Multimodal modulation of excessive inflammation has been hypothesized to be beneficial in the perioperative patient.

**Rationale for glucose control**

Beyond the avoidance of neurologically compromising hypoglycemia, there is little reason to believe that any state other than euglycemia [80 mg/dL (4.5 mmol/L to 110 mg/dL (6.0 mmol/L) is advantageous to the perioperative patient. Over the past decade, a growing body of literature reports the benefits of glucose control in various acutely ill adult populations (diabetic or non-diabetic) including selected ICU patients, CT surgical patients, patients suffering acute myocardial ischemia/infarction, stroke patients, and parturients. The potential benefits of glucose regulation and insulin administration include decreased osmotic diuresis, enhanced innate immunity, improved endothelial function, and less impact on ischemic tissue. These benefits are hypothesized to occur because of diminished lipolysis and less generation of free fatty acids known to exacerbate myocardial ischemia and dysrhythmias; inhibition of deleterious growth factors (AP-1, EGRC-1); enhanced production of nitric oxide synthase; and inhibition of pro-inflammatory mediators including cytokines, chemokines, acute phase reactants and adhesion molecules.

Several relevant studies deserve comment (table 2). Van den Berghe and colleagues reported a highly significant benefit from euglycemic glucose control in a critically ill population that was dominated by CT surgical patients who were actively fed enterally or parenterally within 24h of post op ICU admission. Almost 100% of their treatment group required infusions of insulin to maintain blood glucose between 4.5 and 6.0 mmol/L (80–110 mg/dL), some question whether this was secondary to overly aggressive feeding. The incidence of hypoglycemia was
reported to be 5%, but without significant sequelae. There was a highly significant reduction in morbid events such as sepsis, renal failure, transfusion requirements, and development of critical illness polyneuropathy and mortality in study patients that was most marked in those requiring more than five days of mechanical ventilatory support. The overall mortality was higher in the Van Den Berghe study than others report for similar patient populations, however. Finney, et al reported similar benefits to those of Van Den Berghe but with less tight glucose control (90–140 mg/dL), less aggressive feeding, and reported worse outcome with high glucose levels as well as the need for greater insulin doses. In a longitudinal study in almost 5000 CT surgical patients managed over a 17 year period, The Portland Diabetic Project reported improved survival, fewer deep sternal infections, and shorter length of stay associated with the initiation of insulin infusions preoperatively and continued for 3 days post operatively in patients undergoing cardiac surgery. The therapeutic glucose goal was <150 mg/dL. In a study in non-cardiac patients from a University-affiliated, closed medical and surgical adult ICU, Krinsley retrospectively reported increased mortality associated with increased admission glucose, mean glucose, and highest glucose. This was followed by a look-back comparative study after initiation of a glucose control protocol that found a thirty two percent reduction in mortality in patients prospectively treated with insulin infusions with normalization of glucose.

Regulatory bodies in the US such as the JCAHO and VNA, and thought leaders such as the American College of Endocrinology are calling for maintenance of euglycemia in the perioperative period even in patients who are not known to be diabetic. www.aace.com/clin/guidelines/InpatientDiabetesPositionStatement.pdf

The implementation of such practices appears to be widespread, but we must await additional data from on-going prospective trials and future investigations to corroborate benefits and identify potential problems such as the true incidence and clinical impact of hypoglycemia if routine insulin infusions are used in the perioperative patient (see future data from the NICE trial from the Australian-New Zealand Critical Care Trials group and the Canadian SUGAR study).

Some simple take away points regarding perioperative glucose control
• All type 1 diabetics have an obligate need for insulin and require it to avoid conversion to lipid metabolism with keto genesis and potential for ketoacidosis.
• Some type 1 diabetics may be very sensitive to insulin and may be able to guide you in dosing, while many type 2 diabetics may be resistant to exogenous insulin to various degrees.
• Some type 2 diabetics who are well controlled with diet alone or diet and oral hypoglycemic agents may require insulin during the perioperative period.
• Discontinuation of oral hypoglycemics at least the day prior to surgery is commonly recommended as is not restarting metformin until adequate postoperative renal and hepatic function is established.
• There is no perfect means to dose insulin prior to surgery, and insulin regimes should be individualized based on patient history, anticipated procedure, length of surgery, likelihood of protracted NPO status, and overall stress.
• Historical recommendations are to have the diabetic patient be the first case of the day (frequently unrealistic) and to give one-half to two thirds of the patient’s normal intermediate or long acting insulin dose preop.
• Many suggest that regular and short acting insulins be held preoperatively.
• An alternative is to hold all insulin the day of surgery and start an insulin infusion with or without a dextrose infusion (advised in longer cases, glycogen depleted patients, and “brittle” type 1 diabetes) and supplemental potassium.
• Intraoperatively, insulin may be ideally administered intravenously as short acting regular guided by frequent (hourly or more often) glucose measurements.
• Post op sliding scale subcutaneous insulin use is now discouraged since the incidence of poor control and hypoglycemia appears greater than a regime that supplies a basal amount of insulin supplemented by a rapid onset insulin as needed such as regular, aspart, lispro, or apidra.
• Guidelines for the use of insulin infusions and protocolized administration orders for insulin infusion are well established for use in the operating room, ICU, or ward. Current recommendations are for multidisciplinary development of insulin protocols based on local expertise, patient characteristics, and needs.

Summary
Dysglycemia is commonly encountered in the operating room and ICU patient. This trend is likely to grow as the incidence of type 2 diabetes increases. Tighter glucose control is reported to improve outcome in hospitalized patients, in general, and CT surgical patients, stroke patients, and those with acute coronary ischemia/infarction, in particular. The role of insulin dose and outcome continue to be investigated as does the potential

Table 1. Current WHO classification of diabetes mellitus (DM)

<table>
<thead>
<tr>
<th>Type</th>
<th>Absolute deficiency of insulin (DM Type 1)</th>
<th>Relative insulin deficiency or resistance (DM Type 2)</th>
<th>Multiple etiologies (DM Type 3)</th>
<th>Gestational (DM Type 4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Often autoimmune</td>
<td>Usually present in adulthood</td>
<td>Genetic – beta cell dysfunction or defective insulin function</td>
<td>Placenta produces anti-insulin factors</td>
</tr>
<tr>
<td>Type 2</td>
<td>Usually present in childhood</td>
<td>Usually present in adulthood, but at increasingly younger age</td>
<td>Drug</td>
<td>Affects 3–10% of pregnancies, almost half develop type 2 within 20 years</td>
</tr>
<tr>
<td>Type 3</td>
<td>Often obese and sedentary</td>
<td></td>
<td>Other endocrinopathy</td>
<td></td>
</tr>
<tr>
<td>Type 4</td>
<td></td>
<td></td>
<td>Infection</td>
<td></td>
</tr>
</tbody>
</table>

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94 Symposia

Table 2. Recent clinical trials

<table>
<thead>
<tr>
<th>Study and Type</th>
<th>Population</th>
<th>Protocol</th>
<th>Outcome</th>
<th>Issues</th>
</tr>
</thead>
<tbody>
<tr>
<td>Van den Berghe et al. PRCT</td>
<td>1548 patients: surgical, 2/3 CT surgery</td>
<td>Control-start insulin infusion if blood glucose &gt;215 mg/dl, Study group-use insulin infusion to maintain blood glucose between 80 and 110 mg/dl</td>
<td>Improved outcome, particularly if longer duration in the ICU</td>
<td>Mainly CV surgery; No benefit in others; Few if any medical patients; All pts feed within 24 h of ICU entry</td>
</tr>
<tr>
<td>Finney et al. PRCT</td>
<td>523 surg pts (85% CT surg)</td>
<td>Treated with insulin infusions Stratified by level of glucose control and insulin infused</td>
<td>Lower glucose better outcome, but more insulin worse outcome</td>
<td>Mainly CT surgery; No medical patients</td>
</tr>
<tr>
<td>Malmberg et al. PRCT</td>
<td>620 AMI pts</td>
<td>Randomized diabetics to tight blood glucose control with an initial insulin/glucose infusion or conventional therapy. Tight control group treated subsequently with aggressive subcutaneous insulin 4 times/day</td>
<td>Improved survival, most notable in pts with lowest risk and least previous insulin use</td>
<td>Only diabetics; Acute and chronic glycemic control beneficial</td>
</tr>
<tr>
<td>Furnary et al. Comparative</td>
<td>5000 cardiac surg pts</td>
<td>Done over 17 years. Initial study pts treated with subq insulin; second half treated with insulin infusion initiated on day of surgery &amp; now for 3 days afterward</td>
<td>Halved mortality rate in pts treated with prolonged continuous insulin infusion</td>
<td>Since comparative study, possibility of bias</td>
</tr>
<tr>
<td>Krinsley JS Retrospective</td>
<td>1826 ICU patients</td>
<td>Retrospective analysis of blood glucose levels vs. clinical outcome</td>
<td>Lowest in-hospital mortality in pts with glucose between 80–99 mg/dl; Progressive increase in mortality with increasing glycemia</td>
<td>Heterogeneous med-surg pt population in a Univ affiliated hospital</td>
</tr>
<tr>
<td>Krinsley JS Comparative</td>
<td>800 med-surg ICU pts</td>
<td>Prospective, non-randomized, compared to controls after initiation of glycemic control protocol</td>
<td>~30% reduction in mortality Less renal insufficiency No significant hypoglycemia</td>
<td>Heterogeneous population; No CT surg</td>
</tr>
</tbody>
</table>


beneficial mechanisms of euglycemia or near normalization of blood glucose in medical and general surgical patients. These mechanisms include favorable effect of glucose control on the inflammatory cascade, maintenance of innate immune function, and improved myocardial metabolism with limitation in free fatty acid generation, among others.

References


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187

Perioperative adrenal function and therapy

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The clinical introduction of cortisone in 1949 revolutionized modern medical practice by facilitating the treatment of patients with primary adrenal insufficiency (AI), autoimmune illnesses such as rheumatoid arthritis and systemic lupus erythematosus, and inflammatory processes such as asthma and inflammatory bowel disease. Corticosteroids also provided a pharmacologic basis for successful organ transplantation and various chemotherapeutic interventions. As with other major advances in medicine, benefits came at some expense. Deleterious effects included dose-related immunosuppression, hypertension, catabolism, glucose intolerance, bone demineralization, altered body habitus, and potential adrenal suppression and Addisonian crisis secondary to stressors such as critical illness or surgical intervention.

Endogenous cortisol action is integral to cellular homeostasis and metabolism. Cortisol modulates normal carbohydrate, protein, and lipid metabolism, cardiovascular function, wound healing and numerous other important homeostatic functions. Cortisol potentiates catecholamine production and regulates the synthesis, responsiveness, coupling and regulation of beta-adrenergic receptors. Recent reports describe adrenergic down-regulation and hyporesponsiveness in stressed critically ill patients even when they have normal cortisol levels. Additional data suggest recovery of adrenergic efficacy with the administration of physiologic doses of exogenous glucocorticoids. Glucocorticoid replacement use in the critically ill is increasingly administered, particularly to selected patients with sepsis induced hypotension or shock and various stressed perioperative patients.

We encounter patients routinely during the perioperative period that acutely or chronically receive glucocorticoids such as hydrocortisone, methylprednisolone, prednisone, betamethasone, and dexamethasone. Dose and duration dependent side effects such as adrenal suppression, immunosuppression, hyperglycemia, proteolysis, hypertension, and psychological alteration are perioperative concerns. Therefore the questions of AI and need for glucocorticoid supplementation arise routinely in steroid treated patients undergoing procedures that require anesthetic or critical care. Adrenal insufficiency may be primary (true Addison’s Disease with nonfunctional adrenal glands), secondary to pituitary or hypothalamic dysfunction, or tertiary (referred to as iatrogenic) from the administration of exogenous glucocorticoids. The latter is by far the most common cause of AI. Recently an entity of relative AI has been recognized in perioperative and critically ill. These patients may have relatively low, normal or supranormal cortisol levels during stress, but they do not respond normally to additional challenge as occurs with a cosyn tropin stimulation. They may also have glucocorticoid receptor down regulation. Judicious physiologic replacement in such patients may be beneficial.

Physiologic production

The body normally produces about 5–10 mg/m² of glucocorticoid per day, which is equivalent to 5–7 mg/d of prednisone or 20–30 mg/day of hydrocortisone. Various studies report the maximal stress production of glucocorticoids to be approximately 60–100 mg/m²/day. Therefore, there is no reason to supplement steroid treated patients with >150–200 mg of hydrocortisone or its equivalent in a 24 h period. Pharmacologic doses of glucocorticoids as used for inflammatory processes or acute spinal cord injury are frequently higher than maximal daily production, but physiologic replacement therapy should not be greater than 200–300 mg/d even in stressed critically ill patients. The choice of steroid replacement or supplementary agent should be based on need for glucocorticoid and/or mineralocorticoid effect, the biologic half-life and effect of the preparation, and the need to interrogate the hypothalamic-pituitary-adrenal (HPA) axis.

Current intraoperative guidelines and other uses

Questions remain about the appropriate dosing, need for supplementation in potentially steroid deficient or under-responsive patients with acute illness or those undergoing procedures, and utility of glucocorticoids in the treatment of a wide range of pathologies including community acquired pneumonia, acute respiratory distress syndrome (ARDS), sepsis, bacterial meningitis, acute spinal cord injury, and PCP pneumonia. Furthermore, some clinicians administer glucocorticoids prophylactically in a wide range of scenarios including prevention of nausea and vomiting in selected surgical or oncologic patients or to decrease airway edema after intubation.

Shortly after the introduction of glucocorticoids, several patients were reported to suffer catastrophic effects when they did not receive perioperative steroids supplementation. This lead to the subjective, one dose fits all perioperative replacement with hydrocortisone or its therapeutic equivalent. Sentinel work by Kehlet in the 1970s and others over the past two decades as well as an important review by Salem and colleagues in 1994, identified the variability in cortisol production during surgical procedures or critical illness, the impact of different steroid dosing on adrenal responsiveness, and the effect of the duration of steroid therapy on corticosteroid response. This work helped provide data for a rational supplementary dosing regimen based on the stress of illness or procedure. Appropriate physiologically based supplemental doses of glucocorticoids limit acute deleterious effects of unnecessarily excessive doses. Such effects include hyperglycemia, increased infection rate, delayed wound healing, electrolyte and fluid imbalance, and hypertension.

The key take away points about perioperative glucocorticoid supplementation are:

- Historically, excessive replacement doses of glucocorticoids were administered to patients taking exogenous corticosteroids.
- Dosing should be individualized for the patient in relation to the dose they chronically receive, duration of steroid therapy, and type of surgery.
96 Symposia

- Supplemental perioperative doses should be rapidly tapered to baseline doses.
- If the patient receives 5 mg or less of prednisone or its equivalent per day, he or she probably does not require supplemental therapy.
- If the patient has primary AI, he or she requires both mineralocorticoid and glucocorticoid replacement unless they receive a total daily dose of >50–75 mg of hydrocortisone, which provides adequate replacement mineralocorticoid effect. The patient with primary AI should receive steroid replacement equal to the degree of stress.
- If the patient has suspected AI, he or she can be treated with dexamethasone and undergo a cosyntropin stimulation to confirm the diagnosis of absolute or relative AI. Dexamethasone is not metabolized to plasma F (cortisol).
- Finally, you can always give more glucocorticoid.

ICU use of steroids

Over the past 40 years steroids have been administered at varying doses and duration to a wide variety of critically ill patients. Previously, supraphysiologic doses of glucocorticoids (~30 mg/kg of methylprednisolone) were administered to patients with septic shock or ARDS without benefits. Annane and colleagues recently reported the benefits in survival with treatment of physiologic replacement doses of gluco- and mineralocorticoids in a subset of patients with septic shock. Specifically, patients who had abnormal baseline as evidenced by an absolute level of <25 ng/dL and a cosyntropin stimulated increase of >9 ng/dL were treated with 50 mg qid of hydrocortisone and 50 microg daily of fludrocortisone per NG. This resulted in significant improvement in survival and an impressive need to treat response of 1 in 8 patients.

Several issues require further clarification about glucocorticoid use in critically ill patients: are we obtaining an accurate measure of cortisol availability; how prevalent is the use of etomidate, and its attendant adrenal suppression, to facilitate intubation in unstable critically ill patients; and is the routine cosyntropin stimulation test appropriate.

In a modest sized study, Meduri, et al reported benefits of physiologic replacement doses of glucocorticoids in patients with community acquired pneumonia. Previous studies by Meduri and colleagues laid the groundwork for a recently completed study by the ARDS Network where pharmacologic steroid treatment was administered to patients during the fibroproliferative phase of their ARDS http://www.ardsnet.org/lars.php. Preliminary data awaits final publication, but reported showed no overall benefit in survival.

Although debated by some, current recommendations are to infuse glucocorticoids as soon as possible after acute spinal cord injury (preferably within 8 h) for 24 to 48 hours after injury. A Dutch collaborative study reported the benefits of pulse glucocorticoids at the time of diagnosis of bacterial meningitis in adults just prior to infusion of antibiotics and continued every 6 h for 4 days.

Summary

Various therapeutic advances occurred with the clinical introduction of corticosteroids. Latrogenic adrenal insufficiency was recognized soon after the introduction of these potent agents. This was followed by recommendations for overly generous and prolonged perioperative and stress dosing of steroids. Current recommendations are to individualize such supplementation. Furthermore, steroids have been advocated in a wide range of life threatening illnesses. Although the optimal timing and dosing of glucocorticoids in selected populations of critically ill patients remains under investigation, there is increasing recognition of the entity of relative adrenal insufficiency in the acutely ill patient.

References


188

Anaesthesia for hip and knee arthroplasties

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The need for total knee (TKA) and total hip arthroplasties (THA) is increasing. The most common disorder needing arthroplasty is primary osteoarthritis, which affects about 20% of people over 70 years old. Risk of osteoarthritis is increased with obesity, heavy work and accidents. When the patient needs TKA or THA he is usually already elderly and has often several other diseases (cardiac, pulmonary, metabolic) which certainly affect the perioperative care.

Evidence supports the use of regional anaesthesia in these operations. A meta-analysis from several studies by Dr Rodgers et al. (1) showed that vascular events, blood loss and infections are decreased if the operations are performed on regional anaesthesia. Similar results were reported from a smaller TKA material where intubation anaesthesia caused more fluctuations in patients with severe sepsis and septic shock: a systematic review and meta-analysis. BMJ 2004;329(7464):480.

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of 1:3600 in females for TKA was calculated. The same frequency was 1:200,000 in obstetric patients (3). The patients with osteoarthritis and need for TKA or THA have often also other problems like spinal stenosis which still can increase the risk of epidural hematoma. Careful timing of the thrombosis prophylaxis and avoidance of other medication which affect blood coagulation prevent the risk (4).

The operation, where the bone marrows of femur and tibia are drilled and rods are inserted, causes release of fat and bone marrow cells and risk for pulmonary embolism even during the operation. In a study where transeosophageal echocardiography and pulmonary artery catheter were used during TKA 3/55 patients had pulmonary embolism (5). This was observed after tourniquet release when the pulmonary vascular resistance increased above 200 dyne/second/cm. At the same time venous emboli larger than 0.5 cm were observed in the echocardiography. The use of pulmonary catheter with a possibility to measure pulmonary vascular resistance has been recommended with bilateral operations.

The patient is commonly in the side position for THA. This can cause problems if the operation is long and if the patient has pain in the lower shoulder. Special mattresses and pillows have been designed to relieve the pressure in the lower shoulder (6).

There is always concern about blood loss. For THA hypotensive epidural anaesthesia by Sharrock has been introduced (7). The blood loss can be markedly decreased and the technique is safe. For knee arthroplasties the use of tranexamic acid has markedly decreased blood loss. It has also been used for THA (8).

The most reliable regional anaesthesia method is spinal anaesthesia, combined with epidural catheter. Bupivacaine and ropivacaine are most commonly used local anaesthetics. Small dose of clonidine provides longer anaesthesia and postoperative analgesia (9). It causes also relative hypotension and thus can be recommended especially for longer operations. Sciatic and lumbar plexus blocks have also been used, but they often need extra analgesia and combination of light general anaesthesia. For postoperative use neuraxial techniques and peripheral continuous blocks are recommended.

For TKA a tourniquet is used to provide bloodless field and facilitate the surgery. The operation can last up to two hours and during general anaesthesia, the tourniquet pressure leads to hypertension, which is very difficult to treat. This phenomenon is not observed during neuraxial anaesthesia (10).

**Conclusion:** The need for total knee and hip arthroplasties is increasing. The patients are usually old and have multiple problems. The active thrombosis prophylaxis increases the risk of epidural hematoma. The anaesthesia method should be safe and provide adequate pain relief also after the surgery.

**References**


**189**

**Analgesia for hip prosthesis surgery with comments on the PROSPECT project**

**Rawal N**

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Pain relief after surgery continues to be a major medical challenge. Unrelieved postoperative pain may delay discharge and recovery and result in an inability to participate in rehabilitation programmes leading to poor outcomes. Recent advances include better understanding of pain mechanisms, physiology, and pharmacology (1), publications of guidelines (2) establishment of acute pain services (3,4), initiatives such as “pain as the fifth vital sign”, and availability of multiple new drugs and devices. However, these advances have not led to any major improvements and undertreatment of postoperative pain continues to be a considerable problem worldwide (5,6). A variety of opioid and non-opioid-based analgesic modalities are available. It is well accepted that non-opioid analgesics and techniques be used as the first line of therapy and that opioids should be reserved for more severe pain.

**NNT or procedure specific treatment?**

In an effort to select appropriate analgesics for postoperative pain Oxford League Tables have been proposed. These tables are based on the concept of “number needed to treat” (NNT). Analgesic efficacy is expressed as the NNT, the number of patients who need to receive the active drug for one to achieve at least 50% pain relief compared with placebo over a 4–6 h treatment period (7,8). The League tables are derived from a variety of surgical procedures. Although it has been claimed that these data can be extrapolated to all types of surgery others have emphasized that this concept is not applicable to all types of surgery and that analgesic effects of drugs such as aspirin, paracetamol and NSAID’s may vary considerably between pain models and different surgical procedures (9). All pain management guidelines advocate generalized “one size fits all” recommendations for use of analgesic drugs and techniques. In clinical practice it is generally accepted that there is considerable difference in pain intensity and its consequences for example between thoracotomy versus hysterecetomy or hip replacement versus knee replacement. Thus, there is a need for surgical procedure specific guidelines. Two such initiatives are available on public Internet websites (10–12). The US Veterans Health Administration procedure specific guidelines can be accessed at www.oqp.med.va.gov/cpg/cpg.htm (10), however the website does not provide the background data or a complete list of references which allow the clinician can make choices based on local
conditions, regulatory issues and economic considerations. The more elaborate procedure specific guidelines are based on the recommendations from a group of European anaesthesiologists and surgeons (PROSPECT Working Group), which can be accessed at www.postoppain.org (11,12). The PROSPECT guidelines are based on systematic review of literature for a particular procedure using Cochrane Collaboration and include randomised studies that evaluate the role of analgesic drugs and techniques and also the role of anaesthetic and surgical techniques on postoperative pain. Furthermore qualitative and quantitative (meta-analyses) outcomes are generated. This procedure specific evidence, together with transferable evidence from a similar surgical procedure (where direct procedure specific evidence is not available in the literature), forms the basis of PROSPECT recommendations. The recommendations also take into consideration clinical routines and risk-benefit issues, for example the PROSPECT group does not recommend routine use of epidural analgesia for laparoscopic cholecystectomy although literature (limited) shows that the technique provides effective analgesia. Readers are presented with the available evidence and can make decisions, which can be adapted to their practice. Currently, PROSPECT recommendations are available for laparoscopic cholecystectomy, abdominal hysterectomy, and total hip arthroplasty. Within a few weeks the following surgical procedures will be on the website: colonic resection, total hip arthroplasty update and herniorrhaphy. Thoracotomy and breast surgery are expected to appear in 2006. It is proposed that about 15–20 of the most common surgical procedures will be included in due course. The recommendations will be updated regularly.

The PROSPECT recommendations for total hip arthroplasty are as follows: a) Regional techniques have superior analgesic efficacy and decrease postoperative morbidity compared with systemic regimens, b) On balance of risks and benefits, peripheral neural blocks are recommended for routine use, c) Spinal analgesia may also be used but urinary retention should be monitored, d) Epidural analgesia provides a less favourable risk/benefit profile in most patients but may be considered if the risk profile of the patient allows, e) Further comparative studies of regional techniques are warranted.

The PROSPECT recommendations for surgical techniques and perioperative procedures are as follows: a) It is recommended that surgical requirements rather than pain management should be the main consideration in choosing the surgical technique, b) The different surgical techniques tested in THA did not affect pain scores or function, c) In patients with a hip fracture, cemented prostheses had better long-term analgesic and mobility outcomes. However, factors such as patient age and comorbidities can influence the choice of the prosthesis type, d) Surgical drains are not recommended because they are associated with increased incidence of infection, a higher degree of patient discomfort and anxiety and in addition they do not confer a benefit for pain scores and function, e) Further developments in operative techniques for THA include the minimisation, which is being investigated for advantages over the conventional method including, less blood loss, less pain and shorter hospital stay.

The literature that forms the basis of these recommendations can be accessed on the website: www.postoppain.org.

References

190 Strategies to reduce homologous blood transfusions in orthopaedic surgery

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Bleeding in orthopaedic surgery is unavoidable, but the need for homologous transfusions may be kept reasonable by simple steps in an orthopaedic surgical unit.

In 1991 we introduced the collection of postoperative drained unwashed blood for autologous transfusion. This is a straightforward procedure that is easy to implement in a surgical unit. Later we introduced the perioperative Cellsaver device for retrieving and washing salvaged blood from the wound (1).

By organising these two procedures, we focused on blood loss, autologous and homologous transfusions. The discussion that followed included transfusion triggers. At that time we set the triggers to 7.0 g/dl for healthy youngsters and 9.0 g/dl for the aged and diseased patients. Transfusion triggers are vigorously debated. We still lack scientific evidence of beneficial measurable effects from homologous transfusions to patients with Hb between 6 g/dl and 10 g/dl (2).

The triggers we advocated and the focusing on blood loss was probably the main reason for our success in reducing homologous transfusions from a mean of 5 to 1.5 units pr. patient operated for thoracic scoliosis (1).

We argued for a clinical evaluation of the patient before postoperative homologous transfusions. But it was difficult to convince surgeons and the nurse staff that patients suffered fatigue from surgery itself more than blood loss with Hb ≥ 9.0 g/dl.

The day the surgeons included in quality criteria of surgery bloodloss and reoperation frequency, the use of homologous transfusions really decreased. They implemented new techniques like the use of argon diathermia. We introduced low-pressure anaesthesia systematically in major spine surgery with MAP = 60 mmHg as a target pressure in younger patients.

We kept the patients normothermic with warm-air blankets as hypothermic patients are coagulopathic by definition (3).
Preoperative autologous donation for perioperative transfusion was discussed with the bloodbank, but they refused. The quality of such blood cannot be guaranteed. The blood is only available for the donor and the logistics inherit the same possible faults as ordinary banked blood. Only 50% of such blood is used (Prof. B.G. Solheim, personal communication).

We systematically dilute the patient at induction of anaesthesia with 1L Ringer and 500ml plasma-expander. When 60% blood loss is reached, we give fibrinogen containing plasma products in order not to descend 1.0 g/L of plasma fibrinogen.

Reoperation has occurred due to misjudgement of blood loss and continuous postoperative bleeding. An acceptable Hb was kept due to recirculation of washed salvaged blood. But the fibrinogen level descended 1.0 g/dl (4).

We have demonstrated that there is a high level of fibrinolysis in the wound (4). Diluted tranexamic acid used for irrigation of the wound can thus prevent 50% of the blood loss (5). Tranexamic acid administered i.v. reduce blood loss in total knee joint arthroplasties (6) but not when administered at wound closure in hipjoint arthroplasties (7). Tranexamic acid has to be present at the time of fibrin formation to be fully active (8).

Biological and non-biological tissue sealants are available. Fibrin forms a matrix important for regeneration. Many biological tissue sealants are based on fibrinogen and the formation of fibrin when components are added. The inhibition of fibrinolysis is an important part of the components used. Which inhibitor of fibrinolysis to use is debated (9).

Our main strategy to minimize blood loss in orthopaedic surgery has been to focus on blood loss as a problem and to solve the problem together with the surgeons.

References

191
Critical illness neuropathy and myopathy and its impact on rehabilitation
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Muscle weakness is the most obvious and debilitating feature of recovery from critical illness. Intensive care clinicians recognise that muscle weakness contributes to prolonged mechanical ventilation, a prolonged ICU and hospital stay and adds considerably to the cost of caring for these patients (1). The last twenty-five years has brought a better understanding of the causes, the changing characteristics, the consequences and what might be done.

Inactivity is an abnormal, even “disease” state of muscle in man. Our genome developed over 10,000 years ago when it was associated with a cycle of hunting and rest, feasting and famine such that muscle is structured as a cyclical organ that is highly plastic to synthesis and degradation, storage and utilization. Found adaptations can occur over a matter of days that alter the structural and metabolic behaviour of muscle.

Initially early descriptions of the pathology by nature of their route of investigation tended to focus on either the electrophysiological (Critical illness polyneuropathy, CIP) (2) manifestations or, in our own group, the histological (Critical illness myopathy, CIM) (3). However time has shown that both coexist with a spectrum of tissue involvement to various extents (4,5,6). Key to appreciating the pathological changes has been the association with inflammatory states and the evidence of a vasculopathy with marked endothelial activation in both nerve (7) and muscle (8). Similarities with diabetic neuropathy has led to the exciting observation shown in the “Leuven” study that rigorous nutritional and tight glycaemic control in the critically ill not only improves survival but also reduces the incidence of neurological complications. In the very severely ill patient the catastrophic breakdown of muscle proteins shows losses of approaching 2% per day (9), and a daily decrease in the fibre area of 3% to 4% (10). The biopsies having the largest fibres show the greatest atrophy with early loss in the contractile myosin filaments with relative preservation of actin and the structural proteins. The systems involved in protein breakdown such as lysosomal and ubiquitin proteolysis is increased. The early loss of myosin with the retention of the structural proteins suggests that these fibres have the potential to recover. Immobility and absence of the normal stretch and stresses adds to this process since passive stretching alone in neuromuscularly paralysed ICU patients has been shown to reduce protein loss and maintain structure (11).

The length of stay on ICU (and days of ventilation) is the most important predictor of major physical mobility problems following intensive care and type of physical aids required (12). The recognition and management after ICU requires common sense (13). In the severest even safe swallowing may be impaired, let alone the ability to feed. The not uncommon clouding of consciousness, confusion and impaired cognitive function may confound clinical examination on the ward. Not until the tissue oedema has resolved can the true extent of muscle wasting be determined and muscle power correctly referenced to available muscle bulk. Co-existing joint stiffness may limit assessment of power. The most useful clinical assessments are those of body movement, rising from bed, chair, standing and walking. Even in the absence of obvious neurological impairment profound muscle wasting results in weakness of the postural muscles crucial for rescue when stumbling. It is for this reason that a most common complaint is difficulty walking over rough ground. The provision of a stick, especially in windy conditions can be of help. Similarly they must be warned when they go home that while they may have recovered sufficient strength to climb the stairs they may lack the strength for a confident and controlled descent. Alternatively they may only have sufficient strength to climb the stairs once in the day, making a stair assessment prior to hospital discharge of little practical use.

Physical therapy is the mainstay of fostering recovery and guidance on how to approach exercise and relate it to effort is important for rehabilitation (14). Many of the patients lacking any recall of their ICU experience fail to realise how weak they are while they are in hospital surrounded by nurses and phys-
iotherapists. They have falsely high expectations of their ability. Often it is only when they fall or go home that the extent of their weakness is apparent. Relatives must be made aware of the issues and difficulties and the time scales involved in recovery. In very long stay ICU patients electromyographic evidence of chronic denervation may be detected many years later. Despite initial profound weakness in these patients only a very few followed up 1–2 years later show clinical weakness or limitations in the activities of daily living (15). Occasionally some patients with CIP may still at 2 months show some sensory deficits; very few ICU patients remain troubled by this at six months. Anecdotally in follow up suggests the incidence of severe CIP nowadays appears to be reduced compared with the late ‘80s and early ‘90s and that today one rarely finds it a long term problem in all but a few.

Encouragingly the rebuilding of wasted muscle occurs over several months in most patients but since exercise is central to this other clinical conditions need to be optimised to foster mobility. Treatment of heart failure, angina, asthma, joint disease must be complimentary. Similarly psychological problems, especially those that affect adequate sleep must be adequately treated. The physical outcome of ICU patients is encouraging and any long term consequence of neuropathy and myopathy is rare.

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HRQOL can also be measured using more simple instruments. The EuroQol 5D is such a tool also being a non-disease specific questionnaire of HRQOL. This questionnaire is very easy to answer and consist of only five questions with three different levels of answers (table 1), and can also be applied during telephone interviews. It is also extensively tested and used in former ICU patients (6).

What is known about HRQOL after intensive care? Several European studies have been performed, mainly in UK, Portugal, Finland and Norway. Different instruments have been used, and most importantly, the time from discharge to measure of HRQOL differs. Only a few studies have investigated the same population more than once. There is obvious difficulties with obtaining status before critical illness, since most ICU stays are unplanned. Some investigators have tried to overcome this by asking survivors to answer forms in retrospect with regards to their pre ICU HRQOL, and some have asked proxies.

What is known from these studies are:

- HRQOL drops to very low values the first 3–6 months after ICU (7)
- HRQOL then increases in further survivors (5)
- HRQOL is probably less than the in the average population before admittance to the ICU (8)
- As long as 12 years after discharge, HRQOL still is lower than in the average population (9)
- Even in patients discharge from cardiac arrest, HRQOL is no different from other ICU patients (10)

References


193

Implications of sedation, delirium, amnesia for PTSD

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Intensive care brings patients through life threatening conditions despite profound metabolic and inflammatory disturbances that fifty years ago would have been impossible. Sedatives and analgesics in high doses are used for prolonged periods to facilitate mechanical ventilation. It is not surprising that a myriad of behavioural and psychiatric signs and symp-
toms have been observed and mistakenly called “the ICU syndrome or ICU psychosis”. However there is little evidence that collectively the aetiology is uniquely related to the intensive care unit but merely a feature of delirium. Increasingly, encephalopathy, drug toxicity, withdrawal are being recognised as aetiologi-
cal factors.

Delirium is characterised by a fluctuating mental status, inattention, disorganised thinking, and altered consciousness, agitation or passivity. Hallucinations may also be associated with delirium. The diagnostic criteria (1) include evidence of effects of a general medical condition, medicine or substance intoxication or withdrawal. The incidence of delirium has been described ranging from between 19% (2) to over 80% (3) within intensive care. Furthermore the presence and duration of delirium is a strong predictor of length of hospital stay after correct-
ing for severity of illness, age and days of sedative use. Not surprisingly the most frequent risk factor within ICU was benzodiazepine or narcotic use, while a history of smoking, alcohol and hypertension were predisposing factors. The Confusion Assessment Method for the ICU (CAM-ICU) (4) is a validated, practical and reliable assessment tool to diagnose delirium in ICU. It is recommended for routine use by the guide-
lines for sedation of the American Society of Critical Care Medicine (5).

In recent years the severity and extent of cerebral pathology that is occurring in the intensive care unit patient has been shown. Sensory evoked potentials (SEP) in severe sepsis show impairment in 84% of all patients and this was related to illness severity (6). Septic encephalopathy is a distinct feature inde-
pendent of any shock. The extent of ischaemic and apoptotic (programmed cell death) change is profound and is increased in septic and non-septic shock patients compared with those dying of sudden death (7).

Through “intensive Care aftercare” we have recognized a number of features associated with delirium. Patients have dif-
ferent kinds of hallucinations and delusions; some may be pleas-
ant and transitory others are unpleasant delusional experiences, firmly held beliefs and often persecutory or even life threaten-
ning (8). The behaviour of patients may be strongly influenced by the delusion they are experiencing but this may not be apparent to their carers, and could be for instance a passive acquiescence for fear of alien body invasion (9). Patients have difficult in remembering real events and can misinterpret events if suffi-
ciently aware. When patients remember real events this may enable them to orientate and explain any hallucination or delusional experience, even providing a feeling of security and safety. The nature of the delusional experience can be influenced by surrounding events or experiences immediately before the illness while its impact on the patient is determined by its mean-
ing to the patient. (10). Patients that are amnesic of any real ICU event may have all experience replaced by a strongly held delusional belief. If this is persecutory and in particular life threatening this memory is maintained and predisposes to developing post traumatic stress disorder (PTSD) (11). Relatives are also at risk of PTSD and will confound the support available to the patient (12).

How we use sedation within intensive care is now being called into question. Across Europe there is wide variation between chemical versus physical restraint to achieve compliance with procedures and ventilators. Practices are defended in terms of the patients’ comfort and to reduce anxiety while in ICU without consideration of longer term consequences. In a retrospective analysis of a study demonstrating that the waking of patients each day shortened ICU stay, the investigators examined whether later psychological distress was reduced (13). There was a trend towards those patients who were woken daily being less distressed and less likely to develop PTSD than those who were kept continuously sedated and only woken up once weaning of a ventilator commenced. Rehabilitation following severe illness requires a clear understanding by the patient as to what has occurred. Delirium and amnesia make this a challenge. Not only is there a duty of care by intensive care doctors to relate to patients what has happened while they were under their care, there is also the need to explain what happened (14). Our observation over more than 16 years of ICU follow up in a process we call “intensive care aftercare” confirm the benefit of rebuilding the autobiographical memory through careful discussion with patients and relatives by intensive care doctors or nurses (15), on the wards (16) and in clinics (17). In addition the added help of contemporaneously recorded diaries with pictures help patients come to terms with their illness and understand their rehabilitation (18). The therapeutic benefit of rebuilding the lost autobiographical experience of the patient is firmly realized and patient/relative diaries contribute to this process. Because patient recall may be absent or grossly distorted by delusional experience such piecing together of expe-
rience coupled with careful explanation must be done by those with direct experience of what has occurred within a support framework with access to psychological services. That close rela-
tives are also psychologically challenged means that follow-up care must be inclusive.

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194

Combined physical and psychological rehabilitation after intensive care

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Physical and psychological recovery from critical illness necessitating a stay in an Intensive Care Unit (ICU) may take a considerable length of time. A number of studies have shown that physical recovery can be prolonged, particularly following a long ICU stay, and may take up to a year, (1,2). Muscle wasting can be profound and it requires considerable effort on the part of the patient to rebuild this lost muscle. In addition many patients do not have a clear memory of their illness, particularly the ICU part, and consequently they may have unrealistic expectations of the speed of their recovery, thinking in terms of weeks rather than months. Intellectually patients may appear to understand when they are told how ill they have been but the lack of an autobiographical memory makes it hard for them to accept emotionally what they have been told.

An additional problem for some patients may be the recall of delusional memories, i.e. hallucinations, paranoid delusions and nightmares, from their time on ICU. These memories can be a potent trigger for the development of anxiety, panic attacks and symptoms of post traumatic stress disorder (PTSD) (3). Quality of life post critical illness can be poor with patients experiencing significant levels of anxiety, depression, panic attacks and a high incidence of symptoms of PTSD (4,5). Such psychological problems can become chronic and may be associated with comorbidities such as alcohol or drug abuse in an effort by the patient to control distressing symptoms (6).

There is, therefore, a real need for structured rehabilitation following ICU to encourage safe and sensible activity and exercise, and to give patients and their families advice and support with any psychological and physical problems they may be facing during recovery. The provision of a multi-modal rehabilitation programme, the ICU Recovery Manual (a patient-directed programme) in general ICU patients has been shown to accelerate physical recovery (7). However psychological recovery was not so easily influenced. There was a trend to a lower rate of depression at 2 months post ICU in the intervention patients (12% versus 25%), however this was not quite statistically significant. Perhaps most disappointingly there were no differences in levels of anxiety and PTSD-related symptoms between the intervention and control patients at 6 months post ICU. Those patients who could recall delusional memories from their time on ICU were more psychologically distressed than those without these memories, regardless of receiving the ICU Recovery Manual or not. Clearly patients who can recall delusional memories are at high risk of developing later psychological distress.

Rehabilitation services for critical care patients in the UK are at present fragmented. Intermediate rehabilitation beds are available for elderly patients, but are in short supply. Younger patients, below the age of 60, are very poorly provided for. The ideal would be to offer a streamlining service from admission to discharge and beyond. Rehabilitation should start once the patient is stable in ICU with early physical interventions involving passive movements and attention to joint positioning. Once sedation is stopped patients need frequent and short exercise sessions as they fatigue easily. The relatives should be involved at this stage so that they understand that it is safe for the patient to exercise.

If physical rehabilitation services post critical illness are poor in the UK, the recognition and treatment of psychological problems is, if anything, even worse. Waiting lists for counselling, psychotherapy or clinical psychology are long. Preventative strategies may, therefore, play an important role for ICU patients. Patient diaries are a useful early psychological strategy to help patients to come to terms with their illness and memories for ICU and hence reduce psychological distress. The diary records the patients’ ICU stay in everyday language and may be accompanied by photographs. In our unit the diaries are open to anyone involved in the patients care to write in and the family is also encouraged to contribute. The diary is gone through with the patient once they have left the ICU and any questions answered. Patient diaries with photographs have been used extensively in Sweden and their experience suggests that these are well received by patients (8).

Ideally patients who are not coping psychologically with their ICU experience should be recognised before their discharge home. Where a counsellor or psychologist is available support can be offered to patients who are very distressed by their ICU experience on the ward before hospital discharge. This should continue as an outpatient where necessary after hospital discharge. As our ICU follow-up service includes a qualified counsellor this allows patients to be assessed early and appropriate support to be offered in a timely fashion. Patients can also be reassessed in the dedicated ICU outpatient clinic and further support offered at this point for as long as is required.

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**195 Hemodynamic management of high risk patients: What is the Role of anaesthetics?**

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**Introduction**

It is generally stated that advances in anesthetic and surgical techniques and perioperative care have helped to reduce mortality in high risk patients, however, the role of anesthetic drugs remains controversial.

The predominant effect of anesthesia on the cardiovascular system results from its modulation of cardiovascular control centers in the brain. Modern anesthetics have mild to moderate direct influences on the heart and blood vessels and show more similarities than differences in their overall hemodynamic effects. Almost all anesthetics reduce sympathetic tone (the exception being ketamine) and as a consequence lower preload, afterload and inotropic state. In patients with normal cardiovascular reserve the resulting drop in arterial blood pressure is usually well tolerated and responds to fluid loading. Anesthesia induced arterial hypotension can be more dramatic however when pre-existing sympathetic tone in the conscious patient is high, when filling pressures are abnormally low or in the presence of diastolic dysfunction.

Despite the concomitant reduction in oxygen requirements, anesthesia-induced hypotension is poorly tolerated by patients with critical organ perfusion or by those with intra- and extracardiac obstructions such as cardiac tamponade, aortic stenosis, tetralogy of Fallot, or pulmonary hypertension. For such conditions, a proactive hemodynamic management based on adequate monitoring, a thorough understanding of the underlying cardiovascular disease and a complete comprehension of the effects of anesthesia (including mechanical ventilation) and surgical stress on the cardiovascular system is required. A discussion on the distinct principles of hemodynamic management for the diverse clinical conditions with increased cardiovascular risk is beyond the scope of this brief report. I will focus here primarily on the management of patients with ischemic heart disease.

This disease has the highest prevalence in the surgical population and remains the primary cause of mortality and morbidity in the perioperative setting. Most importantly, evolving insights in the pathophysiology of acute coronary syndromes are likely to have a major impact on future anesthesia management of such patients.

**Anesthetics and ischemic heart disease**

Concerns on the direct cardiodepressant effects of anesthetics are no longer a major issue to restrict their use in patients with ischemic heart disease. Except perhaps for the condition of severe left main coronary artery stenosis, the concomitant reduction in myocardial oxygen requirements usually outweighs the moderate decreases of coronary perfusion pressure induced by anesthetics. Theoretical concerns about coronary steal with anesthetic drugs that have mild coronary vasodilating properties have not been confirmed in experimental and clinical trials. In contrast, both experimental and clinical data show that volatile anesthetics have unique pharmacological properties which confer cellular protection against ischemia and reperfusion injury. The exciting topics of preconditioning and postconditioning will be addressed extensively in another report.

Historical studies comparing the effects of anesthetic drugs on outcome failed to show any difference between opioid based anesthetic techniques, volatile anesthetics and intravenous anesthetics. Nevertheless Slogoff and Keats reported more episodes of tachycardia and hypertension in an opioid-based anesthesia group while there were more episodes of hypotension in the volatile anesthetic groups. The most important observation in that particular study, however, was that the majority of ischemic events occurred in the absence of any hemodynamic disturbance. These data suggest that the pathophysiology of perioperative myocardial ischemia and infarction is more often related to distinct local events, i.e. acute coronary plaque rupture with subsequent thrombosis and vasospasm, rather than to imbalances in the hemodynamic determinants of myocardial oxygen supply and demand. This hypothesis is based on observations in the non-surgical setting where the composition and vulnerability of coronary artery lesions rather than the severity of stenosis are the most important determinants for the development of acute coronary syndromes. Indeed, plaque disruption with superimposed thrombosis appears to be the main cause of acute ischemic events.

Sympathetic neurohormonal activation (pain!) and inflammatory immune activation are considered the primary triggers for plaque rupture. Consequently, in addition to what has been the credo for years, i.e. the safeguarding of myocardial oxygen supply-demand balance, therapeutic efforts to prevent ischemic complications in the perioperative setting should focus much more on controlling sympathetic stress, inflammation and thrombosis. The beneficial effects of beta blockers, alpha 2 receptor agonists, aspirin and/or anticoagulants and statins on the short and long-term outcome of patients with ischemic heart disease are most likely due to an inhibition of triggers for plaque rupture and thrombosis, and support this hypothesis. Other perioperative strategies that have shown to lower mortality in cardiac surgery such as strict glycemia control may also operate through a protective effect on endothelial function and a modulation of the perioperative inflammatory response.

With this new paradigm for the pathophysiology of perioperative myocardial ischemia and infarction, any discussion about the potential role of anesthetics in the hemodynamic management of patients with ischemic heart disease should also address their effects on coronary plaque stability. In this respect, experimental studies suggest that volatile anesthetics may protect the vasculature during inflammation. Intravenous anesthetics have also been found to possess some anti-inflammatory and/or antithrombotic effects. However, most of these studies focus only on limited aspects of the complex inflammatory cascade and future studies are clearly needed to clarify whether such observations have clinical implications for the management of patients with ischemic heart disease. Finally, it should be noted that intriguing data from a recent clinical report suggest that the doses at which anesthetic drugs are administered and the resulting depth of anesthesia may also have an impact on long term outcome.

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first, the severity of ischaemia and of myocardial damage can be modulated by interventions before the onset of ischaemia, i.e., by preconditioning. The current concept is that very short periods of ischaemia (like during angina) trigger the strongest known endogenous cardioprotective mechanism, ischaemic preconditioning. Second, although ischaemic myocardial damage can only be salvaged by reperfusion, reperfusion itself can lead to additional cellular injury that further augments the ischaemic state of injury. During the initial phase of reperfusion, injury is mainly caused by the consequences of ischaemic calcium overload together with the re-supply of energy that triggers several critical intracellular events, including activation of cellular enzymes and over-activation of contractile apparatus. Later during the time course of reperfusion, injury is further augmented by leukocytes that become activated and release a variety of mediators including oxygen derived free radicals. Reperfusion injury may cause cell death and infarction (“lethal reperfusion injury”) or may only result in a delayed mechanical dysfunction of the myocardium (“stunning”).

While most previous research has focused on the modification of the ischemic conditions (e.g., by cooling or by using different cardioplegic solutions), the interaction of anesthetic drugs with the mechanisms of ischaemia-reperfusion injury is a relatively new topic. Anesthetic substances may interact with nearly all the above mentioned mechanisms and current research strongly suggests that these interactions may become clinically important for the anaesthesiologist.

Myocardial ischaemia: It was already described in 1969 that halothane – like all negative inotropic drugs – can reduce the severity of myocardial ischaemia. These findings of an (moderate) anti-ischaemic effect of inhalational anesthetics were confirmed in a variety of experimental models and ischaemic conditions (isolated hearts, isolated papillary muscle, coronary occlusions with and without reperfusion). Global myocardial ischaemia, cardioplegic arrest, hyperperfusion, cold storage of isolated hearts, demand ischaemia in patients etc.

Preconditioning (for review see (1,2)) was originally described as ischaemic preconditioning, i.e., very short periods of ischaemia that precede the main ischaemic period and offer substantial protection against ischemia-reperfusion injury. Several non-ischemic stimuli can precondition the heart, including pharmacological challenges by adenosine, opioids, and several halogenated inhalational anaesthetics cardioprotection lasts for some hours after the application of the stimulus. After ischaemic preconditioning, a second window of protection appears after 24 h lasting for about two days (late ischaemic preconditioning).

Cardioprotection by late ischaemic preconditioning can be further augmented by anaesthetic preconditioning: five min of sevoflurane inhalation before a prolonged ischaemia reduced infarct size by 50% in already late preconditioned (short myocardial ischaemia 24 h before) rabbit hearts. In addition to animal studies, some work points to the existence of preconditioning in human myocardium: Pre-administration of isoflurane 10 min before aortic cross-clamping and cardioplegic arrest during coronary artery bypass surgery has been shown to reduce myocardial damage in humans. In a recent study, patients receiving a volatile anaesthetic during cardiac surgery, had a better myocardial function and less myocardial damage (measured by troponin).

The protective effect of anaesthetic preconditioning is mediated by opening of the ATP regulated potassium channels of the mitochondrion, which also mediates the protective effect of ischaemic preconditioning. Ketamine can block this channel and prevent the cardioprotective effect of ischaemic preconditioning at clinically relevant concentrations. The effect is stereospecific for the R(−)-isomer and does not occur with S(+)-ketamine. Cardioprotection by late preconditioning is also blocked by a single

916

Cardiac safety of anesthetics: Cardioprotection and preservation of cardiac function

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The severity of myocardial ischaemia not only depends on the duration of ischaemia, but is also modified by the conditions of ischaemia (electrical activity, inotropic state, temperature etc). The last years have profoundly changed our understanding of myocardial injury during an ischaemic event: first, the severity of ischaemia and of myocardial damage can also be modified by interventions before the onset of ischaemia, i.e., by preconditioning. The current concept is that very short periods of ischaemia (like during angina) trigger the strongest known endogenous cardioprotective mechanism, ischaemic preconditioning. Second, although ischaemic myocardial damage can only be salvaged by reperfusion, reperfusion itself can lead to additional cellular injury that further augments the ischaemic state of injury. During the initial phase of reperfusion, injury is mainly caused by the consequences of ischaemic calcium overload together with the re-supply of energy that triggers several critical intracellular events, including activation of cellular enzymes and over-activation of contractile apparatus. Later during the time course of reperfusion, injury is further augmented by leukocytes that become activated and release a variety of mediators including oxygen derived free radicals. Reperfusion injury may cause cell death and infarction (“lethal reperfusion injury”) or may only result in a delayed mechanical dysfunction of the myocardium (“stunning”).

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bolus dose of racemic ketamine, but not by S(+)-ketamine. Barbiturates may also block the ATP regulated potassium channels, a blocking effect on preconditioning may only occur at supratherapeutic doses.

**Lethal reperfusion injury:** (for review see 3,4) It was found recently that cardioprotection by halothane was much more pronounced if the substance was given to isolated hearts only during reperfusion compared to the situation when it was given before or during ischaemia. In isolated cells, it was possible to identify the underlying protective mechanism which consisted of a suppression of reperfusion induced calcium oscillations that are responsible for immediate cell death at reperfusion. At the molecular level, we found that this mechanism is linked to an interaction of halothane with the sarcoplasmic reticulum ryanodine receptor of reperfused heart cells. In addition, halothane may also reduce secondary reperfusion injury caused by activated leukocytes. Even after cardioprotection by a cardioprotective solution, volatile anaesthetics confer additional protection during reperfusion. It was possible to confirm the protective effect of halothane against lethal reperfusion injury in vivo, where a marked reduction of infant size was seen if 1 MAC halothane was given for the first 15 min of reperfusion after coronary occlusion. The cardioprotective effects were also shown to be independent of the haemodynamic side effects. Cardioprotection against lethal reperfusion injury was also seen with desflurane, sevoflurane and enfurane in vitro and in vivo preparations, while surprisingly, no cardioprotective effect against lethal reperfusion injury was found for isoflurane, both in vitro and in vivo. After protection against ischaemia by cardioplectic arrest, all inhalational anesthetics were found to have an additional protective effect against reperfusion injury, but there were marked differences in the protective profile of the single substances and protection by some inhalational anaesthetics also depended on the composition of the cardioplectic solution.

**Stunning:** Some studies found a better functional recovery if isoflurane or halothane were given. However, from these studies it is not entirely clear whether the better functional recovery results from a direct effect on the stunned myocardium or is a secondary effect of a reduction of the severity of myocardial ischaemia because the substances were given already before and during ischaemia.

**Clinical perspective:** To summarise, there is a large amount of experimental evidence that inhalational anesthetics exert beneficial effects on different mechanisms of ischaemia-reperfusion injury. Given before ischaemia, they trigger the strongest known endogenous cardioprotective mechanisms: preconditioning. Given after ischaemia, they have specific actions against reperfusion injury – even after cardioplectic arrest. Very promising are the rapidly increasing number of studies which confirm the cardioprotective effects of sevoflurane in the clinical setting in patients. Most promising is that not only markers of myocardial damage like Troponin release after cardiac surgery are reduced (4,5), but also length of ICU and in hospital stay was found to be shorter after sevoflurane or desflurane anaesthesia for cardiac surgery with cardiopulmonary bypass (6,7) and one recent study could also demonstrate a better one-year outcome (8). Currently, it is unknown if anaesthetic preconditioning alone will give the full protective effect in the clinical setting and in addition, the optimal protocol of anaesthetic administration is for clinical preconditioning is still unknown. Therefore, it appears to be safest to give the volatile anaesthetic throughout the whole procedure (6). While on one side, the volatile anaesthetics have that strong protective action, on the other side, other intravenous anaesthetics like ketamine can block cardioprotection and may be harmful in ischaemia reperfusion situations.

References
It seems therefore that optimization of efficacy of treatments with a reduction in morbidity, mortality or hospital length of stay is a more efficient way to reduce costs related to the surgical intervention. Specific perioperative strategies may help to obtain these goals. For instance, the perioperative use of drugs such as β-blocking agents, α-adrenergic agonists, calcium antagonists and statins have been shown to reduce cardiovascular morbidity and mortality. The potential influence of anesthetic strategies on outcome and resource utilization is less obvious. A limited number of studies has identified the anesthesiologist as a potential risk factor for adverse outcome. However this appeared mainly related to the skills and experience in handling perioperative hemodynamic instability. The choice of the anesthetic regimen on the contrary seemed not to affect outcome but the introduction of early extubation anesthetic protocols has resulted in lower intensive care length of stay and hence lower costs per operation.

Recently, increasing experimental evidence is indicating that some volatile anesthetic agents exhibit cardioprotective effects. This organ protective profile might have implications with regard to postoperative morbidity, mortality and hospital length of stay. Until now, only a few studies have addressed this issue. Perioperative optimization of stroke volume significantly improves tissue perfusion, thereby reducing cardiac morbidity and intensive care unit length of stay. Compared to an intravenous anesthetic regimen, the perioperative use of a volatile anesthetic seems associated with a lower level of markers of organ damage and dysfunction and a better early recovery of myocardial function after ischemia. This organ protective profile has been associated with a lower intensive care unit and hospital length of stay and one study even claims that the use of a sevoflurane-preconditioning protocol would reduce the one-year incidence of postoperative cardiac events. However, at an intramoment, firm scientific evidence that the choice of the anesthetic regimen is able to affect perioperative morbidity or mortality is still lacking. Nevertheless, the observation that the use of a volatile anesthetic regimen seems to be associated in some pathologies with a decreased length of stay in the intensive care unit, may definitively have economical implications. Compared to the potential saving using certain drug mixtures, it is obvious that cost savings related to shorter length of stay will be significantly more important. It seems therefore that studies on the economic implications of the use of anesthetic cocktails should not be limited to a net calculation of costs but should also include the potential effects of organ protective properties on hospital length of stay.

References


198 How volume kinetics works

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Since 1997 my research team has worked on a model called volume kinetics, the purpose of which is to bridge the gap in pharmacokinetic fundamentals that characterizes present-day fluid therapy. Mathematical analysis plays an important role in volume kinetics, so in order to produce adequate computer programs, we have entered into a several years’ long collaboration with the Royal Institute of Technology in Stockholm. With their assistance, several volume kinetic programs have been developed and used in the approximately 30 papers based on this kinetic approach that have been published so far.

Volume kinetic theory differs from pharmacokinetics in that the infused fluid increases its own volume of distribution so that the meaning of such terms as clearance becomes changed and that the “concentration” of the fluid must be expressed as a dilution of substances in the blood, such as hemoglobin. Volume kinetics assumes that an infused fluid is distributed between one, two, or three functional fluid compartments in the body. A computer adapts mathematical expressions for these three models to serial measurements of dilution, and statistical methods are used to indicate which model is most suitable.

A volume kinetic analysis is performed on data collected during the infusion of the fluid and for 2–4 hours thereafter. Analyses during a shorter period require simultaneous urinary output measurements. The infusion whose kinetics are to be studied is introduced via a vein in the arm and the blood samples (3 ml) are taken from a contralateral brachial vein every
5 minutes during the infusion and 60 minutes thereafter, and then every 10 to 15 minutes. The analysis comprises B-Hb, B-RBC, and B-MCV which are used to form an expression of plasma dilution. A kinetic model are fitted to the serial data on this plasma dilution and the parameters are estimated by the computer program using a process called least-squares regression. The first figure to the left shows the basic volume kinetic model in which the program estimates the parameters $V_1$, $V_2$, $k_1$, and $k_r$. The second figure to the right shows the modeled dilution of $V_1$ and $V_2$ in the course of an infusion of brisk 30-min infusion of Ringer’s acetate in one volunteer. By this approach one can model the dilution of peripheral parts of the body, which cannot be done by alternative methods. Interestingly, the volume changes of $V_1$ and $V_2$ over time can be obtained by multiplying the respective dilution of these spaces by the estimated size of $V_1$ and $V_2$, respectively.

The parameter estimates can be used for computerized simulation of the dilution-time and volume-time curves with regard to experiments not performed, provided that linearity is demonstrated in the model. This makes it possible to construct nomograms showing how much fluid should be given at various times to obtain and to maintain a predetermined dilution.

It is not certain that the obtained volumes $V_1$ and $V_2$ represent known physiological volumes. As a rule, $V_1$ corresponds fairly well to the estimated plasma volume while $V_2$ will correspond to two-thirds of the interstitial space.

The first series of volume kinetic studies explored the kinetics of infusion fluids in volunteers with particular emphasis on Ringer’s acetate. Model linearity and the outcomes of repeated infusions with and without hypovolemia were explored [1–4]. A second phase included the analysis of fluids which affected a more remote intracellular fluid space, such as glucose solutions and hypertonic saline [5–7]. One study also used sodium and the accompanying natriuresis to estimate the kinetics of hypertonic saline [8]. A third series of studies were conducted on sheep in the US and compared animals that received fluid in the presence of isoflurane with those that were awake, and found that isoflurane promoted “third-space losses” of fluid [9–13]. Technically, this was demonstrated by observing that the model-predicted value of $k_r$, which is the renal clearance of the infused fluid, was much higher than the measured urinary excretion. Finally, a fourth series of studies focuses on fluid therapy in diseases and during surgery. For example, females with pre-eclampsia both distributes and eliminates Ringer’s solution much faster than controls, which results in a poor volume effect of infused fluid [14].

A finding of great interest to the anesthesiologist is the marked reduction of $k_r$ for crystalloid fluid that develops during anesthesia and surgery [15–17]. This is a reduction of the renal clearance of infused fluid, and implies that infusing fluid during surgery must be well balanced. Interestingly, it also implies a much reduced difference in the volume effect of a crystalloid fluid, like Ringer’s acetate, and a colloid like 4% albumin. The plasma volume expansion resulting from albumin is governed by the capillary leakage of albumin [18], and this is hardly reduced during surgery. The plot below is based on kinetic data obtained during thyroid surgery (Ewaldsson & Hahn, Anesthesiology in press) and also on kinetic data from healthy volunteers as provided in references 2 and 18. The result suggests that the difference in plasma dilution yielded by 4% albumin and Ringer’s solution is almost abolished during surgery.

Today, nomograms can be constructed which show how fast infusion fluids should be given to obtain and to maintain a predetermined plasma dilution during various conditions. The present challenge is to establish which degree of plasma dilution during anesthesia and surgery which is associated with optimal patient well-being and outcome.

References
The types of trauma encountered in each setting also differ. While military medical personnel most often have to deal with penetrating trauma, civilian health care professionals encounter both penetrating and blunt trauma. The importance of early intervention has been debated [1], but there is now widespread consensus to initially stabilize a traumatized victim by securing the airway, stabilizing the neck and stopping external bleeding. Present prehospital guidelines state that 1–2 L of crystalloids should be infused rapidly in shock provided the insertion of an intravenous cannula will not substantially delay transportation of the patient to definitive care. These guidelines follow conventional recommendations to immediately replace the lost intravascular volume [2]. The principle of massive and aggressive infusion of crystalloids comes from recommendations by Shires and co-workers [3] who advocated the replacement of extracellular deficits in addition to the lost intravascular volume. These principles were successfully implemented during the Vietnam war and subsequently implemented in the US. With the advent of rapid transportation systems and trauma centers, however, the type, volume, time of initiation and even the value of prehospital fluid resuscitation have been challenged in the past 20 years. The reluctance of certain providers to start intravenous fluid therapy in the field has been associated primarily with the lack of sufficient education among rescue personnel, the lack of benefit of such administration, the risk of rebleding [4] and the delay of transportation to definitive care sites. Existing trauma protocols are now scrutinized as regards to iv fluid therapy [2] [5].

Hypertonic solutions have been used in double blinded studies of patients who were hypotensive and had traumatic injuries [6]. A large number of patients have been included in these studies and criteria for entry have been measured that can be attained in the initial minutes of treatment such as presence of traumatic injuries, hypotension and determination of a trauma score (assessment of respiratory rate, blood pressure and cognitive function) [7]. Efficacy endpoint in those studies has been survival. The studies have contained a number of patients with traumatic injuries and hypotension, consequently involving an extremely heterogeneous population with a varying probability of survival. Although promising, these clinical trials have not provided definitive data as to the efficacy of hypertonic solutions [8] [9] [10]. This has been in part due to the limited numbers of enrolled patients and the diversity of the underlying trauma.

Wade and co-workers in 1997 conducted an extensive meta-analysis of all randomized prospective clinical trials using hypertonic 7.5% saline solutions to determine whether hypertonic solutions improved survival in patients in hypotension associated with traumatic injury [8]. They separated the analysis into two groups: the effects of a 250-mL bolus of hypertonic saline (HS) alone and or in combination with a colloid, hypertonic saline dextran (HSD). The two hypertonic groups were compared with matched groups receiving a 250-mL bolus of isotonic solution. In all cases, additional isotonic solution was administered to follow the hypertonic solution as needed. After a meticulous search for available studies, the authors found six eligible studies using HS and eight studies using HSD. A total of 615 patients were treated with HSD and 340 patients were treated with HS. All individual studies were randomized, included a control group, and had as endpoint survival at discharge or after 30 days. In the meta-analysis for studies using HS, no difference in outcome was found. For HSD, all studies except one showed an improvement in survival, but again, differences reached statistical significance in only one of the individual studies and as well as in specific subpopulations – patients with head injuries and those with penetrating injuries requiring surgery. The mean difference of survival calculated for all studies favoring treatment with HSD over controls was 3.5% (P = 0.07, one-tailed). The conclusion was that HSD may be beneficial in improving survival in patients with hypotension associated with traumatic injury. Subsequently, a meta-analysis using individual data from six of the eight studies containing data with HSD was performed [11], which showed a significantly lowered mortality for HSD in patients in which HSD was infused as the first fluid (in contrast to isotonic therapy).

Recently, a large randomized study in Melbourne containing trauma patients given hypertonic saline alone (without the added colloid) failed to show any improvements in neurological outcome for the hypertonic group [10].

The lesson to be learned from these studies is that the number of patients in individual trauma trials generally has been insufficient to establish statistically significant improved survival and that aggregate data from these trials are encouraging but not fully significant. Moreover, meta-analyses studies can be criticized [12] because there are difficulties associated with comparing the underlying studies. Since meta-analyses are not generally considered sufficient evidence for regulatory approval, HSD has not been approved for use in the United States. Interestingly, no other currently available volume expander has been required to go through randomized clinical studies or regulatory approvals in order to show improved survival and for that reason be used in the prehospital setting. Current fluids are used because they have shown volume-expansion properties. The lack of definitive proof of lowered mortality, coupled with concerns raised among surgeons when Bickell et al [13] reported that conventional fluid therapy might be inferior to delayed prehospital fluid resuscitation in hypertensive and penetrating trauma patients, resulted in a general reduction of interest in prehospital resuscitation with hypertonic solutions in the United States.

In Europe and other countries, however, the situation is different. In Austria, HS colloid solution has been in use since 1991. Austria and Brazil were the first countries in which this type of solution was used routinely for resuscitation from severe trauma and shock. In Austria, HS is mixed with hetastarch (Osmohes – 7.2% sodium chloride + 10% hetastarch 200/0.5 – now replaced by Hyperth (7.2% sodium chloride + 6% hydroxyethyl starch 200/0.62). In Sweden, Rescueflow® (7.5% sodium chloride + 6% dextran 70) has been registered since a few years [14]. Germany in 2000 approved HyperHES® (7.2% sodium chloride + 6% hetastarch 200/0.5) for prehospital use. The introduction of these solutions in prehospital protocols have encouraged some new
studies in Canada and the US. The US Army has a recommendation for the use of hypertonic solutions for the resuscitation of battlefield victims.

References
orthopaedic surgery less invasive and less expensive perineural techniques may be as effective as epidural technique (18,19). It is increasingly accepted that the epidural (and other) analgesic techniques should be integrated into multimodal postoperative rehabilitation fast-track protocols to improve outcome (20). The role of Acute Pain Services in implementing such protocols and evaluation of cost-effectiveness of analgesic techniques is crucial (21–23).

References


201 Enhancement of epidural analgesia by adjuvants in local anaesthetic solutions

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Many drugs are used, and many more are tested as adjuvants in epidural anaesthesia and analgesia because they may enhance and prolong the effects of local anaesthetics and opioids. They can lower the dose-requirements of local anaesthetics and opioids and thus reduce the risk of toxicity and side-effects. Such adjuvant drugs may also produce analgesia themselves. Opioids have already attained an integral role in epidural analgesia and are not specifically dealt with in this presentation.

Adrenaline

By its a1-adrenergic action, adrenaline causes vasoconstriction at the injection site and slows down drug absorption. Through its activation of a2-adrenergic receptors on the spinals, adrenaline may have an additive analgesic effect with other spinal analgesics (1).

Adrenaline 5 μg/ml is typically added to the solution of local anaesthetics which have short or medium duration of action (2), but a similar reduction of lidocaine uptake from the epidural line may have an additive analgesic effect with other spinal analgesics (1).

Clonidine

Clonidine intensifies the analgesic action of opioids and local anaesthetics at the spinal cord level through a2-adrenergic agonism (4). In order to produce epidural analgesia with clonidine alone, doses of 100–150 μg/h are needed (5) with sedation, hypotension and bradycardia as consequences. In combination with local anaesthetic and opioid, doses of 18.75 or 20 μg/ml/h of clonidine have been found to enhance the epidural analgesic effect, but still, hypotension and bradycardia may occur (6,7).

As low clonidine concentration as 2 μg/ml/h are needed (5) with sedation, hypotension and bradycardia as consequences. In combination with local anaesthetic and opioid, doses of 18.75 or 20 μg/ml/h of clonidine have been found to enhance the epidural analgesic effect, but still, hypotension and bradycardia may occur (6,7).

Ketamine

Ketamine has a central antinociceptive effect through N-methyl-D-aspartate (NMDA) receptor antagonism, but interaction with spinal opioid receptors and a1-adrenergic receptors has also been shown (9). Among eight epidural ketamine studies in adults,
Symposia

included in a recent systematic review (10), five reported a positive outcome. Hallusinogenic and sedative side-effects were rare. In children, epidural or caudal administration of ketamine for postoperative analgesia has attained routine status in some centers (11) despite the lack of studies on its nervous system toxicity.

Neostigmine

Neostigmine inhibits the breakdown of acetylcholine, the endogenous transmitter involved in the production of spinal analgesia. Addition of a small dose of neostigmine to either an epidurally administered opioid (12) or a local anaesthetic (13) has been found to enhance postoperative analgesia. Also in labouring women, a large dose of epidural neostigmine added to sufentanil, has been shown to produce good analgesia without motor block and nausea (14). More studies on its use in labour, e.g., to demonstrate its safety concerning the foetus and the uterine function, are needed.

Others

A large variety of drugs with experimentally proven spinal analgesic action, have also been administered epidurally in man, either alone or in combination with and opioid or local anaesthetic. Those studied for the use in postoperative pain include, e.g., midazolam and droperidol, and those for the control of chronic pain or cancer-related pain, e.g., corticosteroids, somatostatin, octreotide and calcitonin.

Warning

Many of the drugs that are already used clinically in human epidural analgesia, except adrenaline, morphine and sufentanil, are not officially registered for epidural administration. Their safety regarding spinal neurotoxicity has not been assessed properly.

References


202 Epidural analgesia: technical problems and how to solve them

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Epidural analgesia has shown to be an excellent method for pain relief with high patient satisfaction, first during labor and later in postoperative period. Therefore the anticipation and prevention of complications, along with their early diagnosis and treatment are utterly important. The technical problems/ complications of epidural analgesia are procedure or drug related and can occur at any time from insertion to removal of the epidural catheter.

1. Problems related to epidural puncture and insertion of the catheter: an individual learning curve

The methods mostly used for epidural puncture are the “hanging-drop” and “loss-of-resistance” technique either by median or paramedian approach. Literature supports not only analgesic superiority, but also decreased morbidity when using saline (vs air) as the medium for determining epidural space by loss of resistance technique (1). The most common technical problems are suboptimal placement of the epidural catheter in the epidural space, venous cannulation, incidence of paresthesia and inability to advance the catheter into the epidural space. Insertion of the catheter more than recommended (3–5 cm) into epidural space can result coiling and knotting of the catheter. The analgesia is more successful and venous cannulation rate is less, when the recommended depth is used (2). During attempted removal a radicular pain may indicate a knot around a nerve root. Further in parturients the risk of epidural vein cannulation is significant higher in sitting position (15.6%) compared with lateral position (3.7%;3). While the sitting position in thoracic region for epidural puncture allows a more symmetrical anatomy and the success rate of epidural puncture increases. Perioperative regional analgesia blockades as well as epidural catheter placement has been recommended to be inserted in awake patient because of a relative risk of the development of persistent paresthesia.

2. Differences of the epidural catheter: personal favourites

Desired advatanges of an epidural catheter seem to be multi- orifice, reinforced and soft tip catheter. Currently available catherers establish the range of bending stiffness that should not be exceeded, only optimized to clinical outcome. The reinforced arrow catheter has the advantage of ease of insertion...
and an infrequent incidence of associated paresthesias and epidural vein cannulation (4) The soft tip catheter is needed in risky situations i.e. as in cardiac surgery with fully heparinized patients or in the need of long-termed epidural analgesia (i.e. major abdominal/thoracic surgery) when the increased possibilities for intrathecal migration of the catheter or urination of vein in long-termed use exist. The tip of the FlexTipPlus catheter tends to stay at the level of insertion when inserted in the thoracic epidural space, especially in elderly patients.

3. Confirming the epidural catheter position: quality control
For the detection of epidural catheter location many different tests have been used including epinephrine, local anaesthetics, opioids, isotopenrenol and air. In obstetric population the sensitivity of epinephrine-containing epidural test dose has been shown 100%, the specificity 96%, the negative predictive value 100% and positive predictive value 63%. The overall accuracy of this test was 95.5% (5). Reasons to avoid epinephrine-containing test dose are preeclampsia/eclampsia, hypertension or cardiac disease. Nonpregnant population and patients with beta-blocking drugs may not respond to the cardiac chronotropic effect of epinephrine and alternative testing has to be used. During the thoracic approach to the epidural space, the control of the Tuohy needle is even more critical. Two different methods has been proposed i.e. epidural catheter confirmation with nerve stimulation (6) or epidural puncture guided by an acoustic signal (7). Multi-centre studies are still lacking of these methods.

4. The extension of sensory blockade: promoting analgesia
In extraduroscopic examination the amount of fatty tissue was reduced and extradural space became widely patent with increasing age (8) and this affects the spread of sensory blockade in epidural analgesia. Neither the level of epidural puncture nor catheter tip direction influences the extension of sensory blockade in thoracic epidural analgesia. In the low thoracic region the spread of sensory blockade is more cranial compared with the high thoracic region (9). When the epidural catheter tip position and distribution of intraepidural fluid is evaluated by computed tomography, it has been able to demonstrate extraordinary variability between patients but at the same time epidural space is a forgiving system and different sites of catheter tips and spread of injected solution are compatible with adequate anaesthesia.

5. Migration/fixedation of epidural catheter: tunnelling a long-term catheter
The incidences of epidurovasal (11.5%) and epiduro-subarachnoid (0.9%) malpositioning of epidural catheters have been reported (10). In thoracic epidurals, migration has shown to be common in patients operated in lateral position as well as related to the flexion and extension of the spine. Subcutaneous tunnelling has been shown to prevent clinically significant inwards and outwards movement of epidural catheters (11).

6. Infection (hematoma) after epidural space cannulation/removal: strict follow-up of guidelines
It can take up to 60 days after epidural catheterization before clinical signs of epidural abscess develop with a triad of symptoms: back pain, fever and variable neurological signs and symptoms (12). However contamination rarely leads to spinal epidural infection. A weak point for possible increasing risk to contamination is a disconnection between the epidural catheter and its luer lock connector which has reduced with FlexTipPlus catheter and its Snaploc adapter when compared with other catheters and their screw caps.

7. Technical failures of epidural analgesia in the postoperative period may reflect the quality of care and the standard of postoperative pain therapy: Acute Pain Service (APS)
Three most common technical problems in postoperative period are leakage, dislodgement and occlusion. The rate of technical failure has been reported as high as 18.7% in the first 72 h, but in a later review based on 165 papers the incidence of premature catheter dislodgement was 5.7 (4.0–7.4%) (13). Annual auditing of the technical epidural failures is one way of quality and safety assessment of the postoperative pain management. However there is no sequential studies available and because of limited information on equipment malfunctioning and human and system errors, the effect of introducing an Acute Pain Service on technical incidents cannot be assessed yet (14).

Conclusion
Epidural analgesia has been used more than 25 years and still there some basic technical problems to be solved i.e. to find an immediate catheter placement test, to understand the different way of spread of epidural blockade/analgesia in the lumbar and thoracic region and to permanently decrease the postoperative technical failure rate of epidural analgesia.

References
114  Symposia


203 Epidurals and thromboprophylaxis

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Epidural anaesthesia and analgesia conveys indisputable benefits to surgical patients. The principal gain is superior postoperative analgesia. In addition to the reduction of pulmonary complications the real outcome benefits have been difficult to demonstrate because they may be confined to specific patient groups undergoing specific procedures. The most scary complication of epidural analgesia is epidural hematoma which, although rare, results in persisting significant neurologic disability in most of the victims.

Without thromboprophylaxis deep vein thrombosis (DVT) complicates the postoperative course in about 50–60% of the patients with total hip replacement or hip fracture surgery. This can be reduced by a factor of five with modern state of the art thromboprophylaxis using low molecular weight heparin (LMWH) preparations. Again besides the reduction of venous thromboembolism observed by flobegraphy or scintigraphy the real meaningful clinical impact of thromboprophylaxis has been more difficult to demonstrate. The real challenge for us as anaesthesiologists is that LMWH thromboprophylaxis has been suggested to increase the risk of epidural hematoma 50-fold from 1/150 000 epidurals to 1/3000 epidurals (1,2).

Despite the troublesome figures above it is a viable clinical option to preserve the advantages of both epidural analgesia and thromboprophylaxis in a same patient. Currently the dose of LMWH as well synchronization of the timetable of administration and epidural catheter insertion and removal are important. Epidural instrumentation should be performed at a time window when anticoagulant effect is at its nadir and after the instrumentation time must be reserved for reparative clotting before next administration of LMWH. The implementation of this protocol has been shown to reduce the occurrence of epidural hematoma substantially and, if the guidelines are enforced, LMWH prophylaxis cannot be regarded as a contraindication of epidural analgesia (3).

The patients on chronic anticoagulation and anti-platelet therapies may pose more difficult treatment dilemmas. Usually they cannot be solved by protocols. Instead, in each such patient, treatment options should weighed in a preoperative clinic. The decision should be a consensus of the physicians involved in the care of the patient before and during the planned operation. Very often anticoagulation can be stopped preoperatively, perhaps in the coverage of LMWH prophylaxis, to allow the drug effect to wear off. In some cardiology patients, such as the patients with mechanical prosthesis in a mitral position and in a patients with recent intracoronary stents, this is not possible and in those situations the anaesthesiologists has to use alternative methods for analgesia and analgesia.

New drugs for thromboprophylaxis are being released to the market. A long acting Factor Xa inhibitor should prove to have an equal safety record as other LMWHs provided that 20–22 hours is allowed to dwell between drug administration and epidural instrumentation. It is too early to promote the use of epidural analgesia in patients receiving a direct thrombin inhibitor, ximelagatran. It is, however, important that anaesthesiologist are involved in at least Phase III trials with new antithrombotic drugs, because important data as regards to the use of epidural analgesia is produced in these large scale controlled clinical studies. In addition to dosage and administration time adjustment of antithrombotic agents a choice of epidural drugs is important. The patients should not be paralyzed because new muscle weakness is an important early sign of impending epidural haemorrhage. The patients should be regularly asked and assessed for possible symptoms and signs. This is most important after removal of the catheter. Implementation of this surveillance program is a responsibility of APS-service and it should work for 24 hours since epidural laminecromies must be performed within 6–8 hours from the start of symptoms.

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204 EBM – Do we need to care?

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The term evidence based medicine has been used intensively and increasingly over the last decade. The widespread use of the term has often led to confusion and misunderstandings. Therefore its very important to clarify what EBM really is, and explain some of the terms related to it.

The definition of EMB from David Sackett, one of the pioneers in the use of EBM used the following definition (1):

• “The conscientious, explicit, and judicious use of current best evidence. Neither alone is enough.”

Another way to say it is:

• “Good doctors use both individual clinical expertise and the best external evidence. Neither alone is enough.”

The practice of EBM

The essential steps in the practice of evidence-based medicine can be summarised as (2):

1. To convert our information needs into answerable questions
2. To track down evidence – searching for evidence, which may come from clinical examination, the laboratory, the published literature, electronic databases, or other sources
3. To appraise the evidence critically and assess its validity and usefulness or clinical applicability
4. To implement the results of this appraisal in clinical practice
5. To evaluated the process
Framing the clinical question: A clear clinical question contains three elements

- The patient. Who is the question about?
- The intervention and the comparison(s)
- The relevant clinical outcomes

Framing the question carefully not only helps clearing the mind, but also clarifies the target of the literature search and supplies some keywords.

Searching for evidence: Evidence can be found in a multitude of places.

- Asking colleagues
- Textbooks
- Journals
- Electronic databases

The electronic databases (3) will provided the widest range of information and are updated. More than 800 databases containing medical literature exist worldwide. The more useful ones include PubMed, Embase, Cochrane Library, Biosis, Cinahl, but many other can be sought according to the clinical question.

Critically appraising the evidence: Assessing the quality and the clinical applicability of the evidence: Critical appraisal is difficult and requires some practice and theoretical knowledge (4,5).

Some of the key points, however, are:

- Does this article focus the clinical problem? If not, it might as well be trashed straight away.
- Was study design appropriate?
- Were the methods used sensible?
- Were corrects statistics used?
- Are the results of the article valid?

Implementing the results in clinical practice (5): This process can be very difficult and the are several barriers to overcome. First thing is to consider whether the results can be applied to the patient(s) in question. Is our patient so different from those in the trial that its results cannot help you? How great would the potential benefit of therapy actually be for your individual patient? In order to use the EBM principles at a wider range it is necessary to work at many level:

- Policies and guidelines. These should be evidence based and well conducted
- Helping practitioners to recommend effective treatments
- Helping patients to follow effective treatments

Evaluating the process: How skilled are we in the practise of evidence-based medicine? Did we ask the right questions, and did we ask any questions at all? Did we find useful answers? Did we ask our colleagues about the evidence behind their decisions?

The practice of EBM can take time, be difficult and sometimes cumbersome. Sometimes no evidence is found, more often the relevant article all of very low quality, either not addressing the question in focus, or relying on surrogate outcomes. Trials are often heterogeneous and every trial performed differently on different patient groups. None the less, though EBM has many weak links in the chain and does not always supply us with a useful answer, no critic so far have given us a better way to improve clinical practice in the modern world.

References


205

Large randomised trials with factorial design will help clinicians

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Background. A recent viewpoint in Lancet (1), addressed concern, that many scientific articles are written just to get something published neglecting the clinician who would like the medical literature to guide their practice. Today evidence-based medicine is expected to help in clinical decision-making. It is believed that the strength of evidence from lowest to strongest is as follows: clinical experience, basic research (in vitro research and animal studies), observational studies, individual randomised controlled trials (RCTs), and systematic reviews of RCTs (of which a “quantitative systematic review” is often called a meta-analysis). Large randomised, controlled trials are also generally considered as the gold standard in evaluations of the efficacy of clinical practice plans. Actually, RCTs have been used for a long time to obtain data and evidence for clinicians.

Discrepancies between meta-analyses and large RCTs. It is worrying that the results of published meta-analyses have not always been confirmed in subsequent large RCT’s. Le Lorier et al (2) reported that there are discrepancies between meta-analyses and subsequent large randomised trials. They compared the results of large, randomised trials of 1000 patients or more that were published in four major peer-reviewed journals – New England Journal of Medicine, Lancet, Annals of Internal Medicine, and Journal of American Medical Association (JAMA) – with the results of meta-analyses published earlier on the same topics. They identified 12 large RCTs and 19 meta-analyses addressing the same questions and found that the outcomes of these large RCTs were not predicted accurately 35% of the time by previously published meta-analyses. If there had been no subsequent large RCT, the meta-analysis would have led to adoption of an ineffective treatment and to rejection of a useful treatment in 32% of cases. Publication bias and heterogeneity of the trials included in the meta-analysis may explain such discrepancies. Furthermore, concomitant therapies may have changed after some of the smaller RCTs included in meta-analysis were published. The authors recommend that if large, well-done RCTs have been conducted, practice guidelines should strongly be influenced by their results (2).

Factorial trial design. It has recently been demonstrated in IMPACT-study (3,4) that large RCTs using factorial design can be highly efficient because they can answer several clinical questions at the same time and offer the only systematic approach to investigate interaction of combinations in multi-modal approaches. When assessing the single and combined benefits of six interventions for the prevention of postoperative nausea and vomiting, IMPACT-study used a 2^6 factorial design.
Who should decide on our continuous professional development?

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Optimising education is a complex issue, but the question of who decides on what professional development is very clear. The main person responsible for the continuous professional development was the individual doctor, but time has come for a discussion of who actually should be involved in that decision. Beforehand the doctor decided what to be learned and how to do it. Often continuous professional development meant participating in a given course, where the method used primarily was lectures. A link between clinical responsibilities and the educational activities were not always present.

References


206

The patient

The most important team player is the patient. In the CanMEDS 2000 project a broad spectrum of competencies than mere medical expertise were described based on patients needs and demands (1). These aspects include physicians’ role as communicator, health advocate, collaborator, manager, scholar and issues of professionalism. The seven roles described here is no also included in the guidelines for postgraduate medical education in Denmark (2,3). Patient’s expectation to the health care system and doctors are that high quality of care is delivered.

They expect health care professions to have an updated knowledge of diagnostic and therapeutic procedures as well as the use of the latest new treatment. Today’s patients are unwilling to accept that young doctors are to start a given procedure for the first time on them, without the doctor being supervised by a senior doctor. Especially the young patients can be described as competent patients, who have been looking for information at the internet or asked other health care professions for a second opinion. The expert patient is a new approach to chronic disease management. This also expects new competencies of the doctor (4) as the patient and health professions make some sort of partnership.

The patient expects that the doctor is able to communicate with patients as well as the relatives in a respectful manner and share decision making. Patients are aware of the risk of critical incidents or error and expects to be informed and given an explanation as well as an apology after critical incidents or errors related to their treatment (5,6). This demands certain skills of the doctors.

One topic that often comes up, when the cause of a critical incident or error is being evaluated is communication failure – either communications with patients or communication between health care professions in the team or between departments (7).

In summary, the patient expects doctors to have a broad range of competencies. Older doctors may not have been trained and assessed in these competences, whereas these competencies are included in the education of residents.

The organisation

Organizational accreditation has some impact on the continuing competences of doctors through the standards imposed. One example is certification of advance cardiac life support skills. The IOM report focus on patient-centred care and interdisciplinary teams and suggests that organisation integrates core competencies into accreditation, and credentialing processes across professions (8). The goal is an outcome based educational system that better prepares clinicians to meet both the need of patients and the requirements of a changing health system (8). It recommends that all health professions educational boards should move toward requiring licensed health professions to demonstrate periodically their ability to deliver patient care.

At the organisational level one could start with a discussion of what is good patient care and whether good patient care is delivered in the department or organisation. The gap between what we do and what is good patient care should be described and also the activities necessary to close the gap. Some of these activities might be related to the knowledge, skills and attitudes of the doctor and imply that educational activities are needed. Thereby the department or the organisation might have a strong influence on a given doctors educational activities.

The doctor

From the doctor’s perspective, it is important to be able to provide good patient care within the area that the individual doctor is responsible for. The importance of being a life longer learner is obvious for most doctors and often the individual are well aware of the need for education and training and can plan...
relevant activities. Also the departmental needs are important and many departments have introduced appraisal, where new tasks or assignments are discussed, the need for further training or education discussed and a contract signed describing these plans. In summary, the core competencies needed are based on patients’ needs as well as the organisations needs, but also the individual doctor views and wishes should be taken into consideration.

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How to maintain and evaluate competence?
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This presentation has three points. The first illustrates the need for maintenance of competence and reviews the effect of traditional educational interventions. The second discuss a comprehensive concept of competence and the life long need for deliberate practise. The third addresses the challenges of selecting meaningful assessment strategies that support deliberate practise and at the same time serve as documentation of competence.

The need
The old assumption that years in practice and clinical experience enhance knowledge and skills probably doesn’t hold in times of fast turnover in medical technology. In a recent review Choudhry et al. found that years in practice was inversely related to knowledge of practice and quality of health care (1). Physicians who have been in practice for more years are more likely to possess less factual knowledge, less likely to adhere to appropriate standards of care, and may have poorer patient outcomes. For example anaesthesiologists’ and surgeons’ knowledge of the risks associated with and indications for the transfusion of blood products were negatively associated with the number of years in practice (2). Attending physicians had lower knowledge scores than did residents, however higher confidence in their knowledge. Residents’ transfusion decisions were strongly influenced by their attendings’ desires, resulting in inappropriate ordering of transfusions. The traditional focus of maintenance of competence has been on attending CME courses or conferences, workshops, rounds, journal clubs and the like. Davis et al. demonstrate in a review that the effect of these traditional methods regarding learning and change of practice is generally poor (3). Grimshaw et al. estimates that the overall absolute median effect size is approximately 10% improvement, suggesting modest although worthwhile benefits (4). However, in essence there is a general problem of routinely translating research findings into daily practice and a need for effective and efficient strategies of disseminating and implementing new medical technology and guidelines of good practice. A monocular focus on individual physicians’ knowledge and skills is not enough and a wider perspective on the concept of competence is needed as is the appreciation of the fact that most physicians are working in complex systems (5).

The concept of competence
There is an emerging consensus regarding adopting a broad and context-based concept of competence, which Epstein & Hundert define as “A habit of action – the habitual and judicious use of communication, knowledge, technical skills, clinical reasoning, emotions, values, and reflection in daily practice for the benefit of the individual and community being served” (6). Across jurisdictions this concept has been described as various aspects of competence necessary for effective medical practice (6). These aspects include the physician’s roles as medical experts and health advocates as well as the role as communicator, collaborator, manager, scholar, and professional. In short these aspects address the importance of physicians engaging in deliberate practise in terms of continuously assessing the quality of current practice (one’s own as well as that of the system and profession in general), and striving for improvement in the interest of the individual and the community (8). Undergraduate and graduate medical education are now requested to include all of these aspects of competence in their curricula, that is to formulate specific objectives, indicate teaching and learning strategies, and design assessment programmes accordingly. However, one could question how the present population of role models and teachers in the formal education – the current specialists – can be qualified to educate tomorrows doctors and specialists according to the new broad concept of competence. Another question is how to support the continuous development of practicing specialists and how to demonstrate accountability to the public.

Assessment strategies
Assessment of the physicians’ performance and quality of practice is in its infancy and much more research in this area is urgently needed. Numerous instruments have been suggested (6,9). However, the challenge is to select the appropriate ones and compiling programmes that are sufficiently valid without bureaucratic overloading of the physicians and administrators. Another challenge is to avoid instilling a shame and blame culture. The overall purpose of any assessment programme is fostering learning and ensuring good practice. Thus assessment instruments are means to meet that end and should be of help to the individual and the systems to monitor their performance and indicate areas in need for improvement.

References
Anesthesia for endovascular repair of cerebral aneurysms

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Cerebral vascular aneurysms have an important impact on community health. Ten to 30 persons in a population of 100,000 suffer from subarachnoid hemorrhage from a ruptured aneurysm every year. Of these, more than half will die, and fifty percent of the survivors will suffer permanent neurological damage. The main direct causes of death in the patients who reach the hospital are reperfusion and vascular spasm. Reperfusion is common during the first week following the initial hemorrhage. There may be a mortality of 60%. Medical therapy can reach the hospital are reperfusion and vascular spasm. Reperfusion is common during the first week following the initial hemorrhage. There may be a mortality of 60%. Medical therapy can

Endovascular therapy is an alternative to surgical clipping of the aneurysm. In this method, which was introduced several decades ago with moderate success (see e.g. [1]), the aneurysm is approached with a microcatheter through the lumen of its parent artery and filled with exogenous material. The currently favored technique, in which the lumen of the aneurysm is filled with detachable platinum “coils”, was described by Guglielmi in 1991 [2]. These coils ultimately cause endoluminal thrombosis and fibrotic obliteration. The patients presenting for endovascular therapy tend to be older and have more severe cardiovascular disease [3].

The International Subarachnoid Aneurysm Trial (ISAT) in over 2000 patients provided overwhelming evidence that endovascular coiling was superior to surgical clipping in the treatment of ruptured aneurysms [4]. Endovascular repair of ruptured aneurysms is thus ultimately bound to replace surgical treatment in the long run. These procedures are tedious, uncomfortable and potentially dangerous for the patient and require expert anesthesiological management that caters to the needs of the neuroradiologist while ensuring patient safety. The procedures, which last several hours, are usually carried out under general anesthesia (e.g. [3]), although there are reports that they can be performed fairly safely with conscious sedation if necessary [5].

Monitoring and anesthetic management standards in the radiology suite should not differ from those in the operating rooms, and the facilities must be evaluated with this in mind. The basic requirements for this workplace are a reliable oxygen supply, monitoring devices, an anesthesia machine, suction, and adequate equipment for airway management and for dealing with complications and emergencies.

The patient is premedicated with a short-acting benzodiazepine. A balanced anesthetic using an opioid combined with propofol or a low-solubility volatile as the hypnotic component is our method of choice. The absence of gas scavenging in the room will preclude the use of volatile anesthetics. The use of nitrous oxide is left to the discretion of the anesthetist, but we consider it unnecessary. Our opioid of choice is remifentanil, but others can also be used, seeing that the procedure is not painful and only small doses might be required. Rapid awakening allowing early neurological assessment, but without coughing, bucking or vomiting that can induce arterial blood pressure spikes is the primary goal.

A single peripheral venous cannula is used for uncomplicated cases. If complications are expected or the patient in poor clinical condition, a second peripheral cannula and perhaps a central venous catheter are inserted. If deliberate arterial hypotension is planned, arterial cannulation could be contemplated. Routine monitoring in our institution consists of 3-lead ECG, capnometry (and expired anesthetic gas concentration if this is used). Although large amounts of contrast medium are occasionally injected, we do not consider a urinary catheter to be a routine requirement.

The patient must remain immobile for the duration of the procedure since even slight movements will make it more difficult to place the tip of the catheter into the aneurysm. This is the indication for controlled ventilation versus spontaneous breathing. Continuous neuromuscular relaxation, on the other hand, is not essential if the level of anesthesia is sufficiently deep, since there are no painful stimuli that might elicit a motor response once the arterial catheters have been inserted.

There procedure carries a risk of intravascular thrombosis and the anesthetist should be prepared to provide anticoagulation. This point should be directly discussed with the neuroradiologist and explicit instructions requested.

There is no generally valid recommendation as to whether the patient should be hypo- or hyperventilated. We aim for mild hyperventilation, but too pronounced hypocapnia might critically reduce cerebral blood flow in a patient with only marginally adequate brain perfusion due to hemorrhage-associated vasospasm.

Blood pressure should be kept in the low to normal range with two exceptions: deliberate hypertension if there is evidence of intraoperative vasospasm, and deliberate hypotension if the aneurysm should rupture during the procedure.

These are two of the major complications of the procedure, which also include coil migration and embolism in more distal portions of the cerebral arterial system and unintended occlusion of the parent artery, either by thrombosis or by herniating coils.

After the procedure, the patient should be monitored for 24 hours for changes in mentation, state of consciousness and motor activity, which might indicate coil dislocation with
embolization, thrombotic occlusion of the parent artery, aneurysm rupture or vasospasm.

References

209 Resource utilization after subarachnoid haemorrhage – endovascular or surgical treatment
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Endovascular treatment has become a feasible option in the treatment of cerebral aneurysms. There is still no clear consensus on how the modality of treatment impacts the outcome of SAH patients, and so far no answer to the question, if either treatment strategy has a favorable impact on resource utilization. A recent prospective multicenter study suggested that subarachnoid hemorrhage (SAH) patients treated with endovascular coiling fared better than patients treated with surgical clipping (1). In contrast, a randomized study from Finland suggested that the outcome of patients with SAH may be most dependent on the severity of the initial bleeding, not on the modality of treatment (2,3). Intensive care unit (ICU) costs account for the largest proportion of total costs in the treatment of patients with SAH (4,5). Any therapy that reduces the use of ICU resources would probably result in considerable savings.

We studied in Kuopio University Hospital (KUH) whether there were differences between endovascular and surgical treatment of ruptured cerebral aneurysms in the utilization of ICU resources or in the length of hospital stay (6). Endovascular treatment has been a routine alternative for surgical therapy of ruptured intracranial aneurysms in KUH since September 1997. The study population consisted of 68 patients with endovascular and 103 patients with surgical treatment. The median lengths of stay in the ICU was 1.7 vs. 1.8 days and in the hospital 14.0 vs. 15.0 days, P = n.s., respectively. The accumulated TISS-points were also similar among patients with endovascular and surgical treatment (56 vs. 55, P = n.s.). Even when the patients were analyzed separately according to preoperative clinical status, no differences between the groups could be observed in the duration of ICU or hospital stay or intensity of ICU treatment. Among patients with endovascular treatment, there were 19 readmissions to the ICU, and among patients with surgical treatment there were 23 ICU readmissions related to the treatment procedure. In both groups, vasospasm and respiratory failure were most common reasons for readmission. Although the cumulative hospital patient days were similar in the treatment groups, patients with endovascular treatment had more frequent hospital visits for control angiographies (6).

Also a previous report from USA suggested that the induction of endovascular treatment option did not reduce the total ICU length of stay or hospital charges (7). However, it should be kept in mind that large multicenter studies about this issue are still missing, and that the this data present practices of a single institution. Furthermore, for a broad-based cost analysis, the costs of procedure itself, or the costs of coils, clips, operating room occupancy etc. should not be calculated.

The modality of treatment of patients with SAH may not have major impact on resource utilization. When choosing between endovascular or surgical treatment, both options are likely to require similar ICU resources at least for one year after the initial treatment.

References

210 The Laryngeal Mask Airway (LMA) – future developments
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The Laryngeal Mask Airway (LMA-ClassicTM) was invented by Dr AIJ Brain (1), and became available for clinical use, in the UK, in 1988. Over the next decade, the safe and successful use of this device in a wide variety of surgical procedures, in fasted patients (“elective surgery”), has been documented (2,3). The introduction of LMAClassic variants to the LMA-ClassicTM, LMA-FlexibleTM, LMA-UniqueTM and the Intubating-LMA-FastrachTM provided clinicians with a minimally invasive, safe and reliable alternative method to tracheal intubation (TI) for airway management during general anaesthesia in a wide range of surgical procedures. A review of airway management, during general anae-
the end of the last millennium, confirmed the LMA-
Classic™ and its variants, as the airway of choice, in a wide variety of elective surgical procedures (4). The successful use and misuse of the LMA™, and its variants, have been described in over 2500 clinical papers in peer reviewed journals, and in an excellent text-book (5) that underlines the impact the LMA™ and its variants have had on the practice and conduct of general anaesthesia, the management of the “Difficult Airway” and Cardiopulmonary Resuscitation. The success of the LMA™ and its variants, have resulted in a number of other “supraglottic” airway devices being introduced into clinical practice. The impact of these devices on airway management is being evaluated, and could not be dealt with within the scope of this lecture.

**LMA-Proseal™**

Despite the published evidence of the safety and efficacy of the LMA-Classic™, in over 250 million patients without mortality, many practising anaesthetists remained concerned about the risk of aspiration with the LMA™ and its variants. Concerns included use for Positive Pressure Ventilation (PPV), (6,7), in obese patients and those considered to be “at risk” due to delayed gastric emptying. This concern was addressed in 2000 (8), when Dr Brain introduced the LMA-Proseal™ into clinical practice. The LMA-Proseal™ is a modified LMA-Classic™, which makes 2 “end to end” anastomoses: one with the respiratory system (as in the LMA Classic™), and a second one with the gastro-intestinal(GI) tract. The separation of the Respiratory and GI tracts, and the addition of a posterior cuff increases “seal” pressure during assisted or PPV and allow the use of the LMA-Proseal™ in obese patients (9) and those with low pulmonary compliance. The addition of the drainage tube allows easy clinical diagnosis of correct positioning; as when improperly positioned, the LMA-Proseal™ seal around the larynx (first seal) is inadequate when tested with PPV, and if it is not inserted to the correct end point i.e. the upper oesophageal sphincter the anas-tomosis with the GI tract is incomplete (second seal) and gases escape through the drainage tube. O’Connor and Stix (10) have suggested an easily performed test to demonstrate correct positioning of the drainage tube. The drainage tube in the LMA-Proseal™ allows access to the GI tract and gastric contents are easily accessed with a suitable gastric tube. The success of this device with PPV has been documented (11). The LMA-Proseal™ increases the “comfort level” in a number of surgical procedures currently undertaken, by some workers, with the LMA-Classic™. These procedures include prolonged PPV, laparoscopic procedures, intra-abdominal procedures and in “non-supine” patient positioning during surgery. A majority of surgical procedures could be undertaken with PPV without muscle relaxants, and muscle relaxants need only be used if surgically requested. The use of the LMA-Proseal™ and PPV without muscle relaxants, minimizes the risk of “awareness” during anaesthesia and the need to monitor the patient to prevent this disastrous consequence of anaesthesia using muscle relaxants and TI. The LMA-Proseal™ requires meticulous attention to detail with the recommended insertion technique, whether inserted digitally or with the introducer tool, for optimum performance and effective use. Alternate insertion techniques, often successful with the LMA-Classic™, are not as successful with LMA-Proseal™ insertion. In the speaker’s opinion, the LMA-Proseal™ has replaced the LMA-Classic™ as the airway of choice in all procedures in which the LMA-Classic™ had been used and in many additional procedures.

**LMA-CTrach™**

The Intubating LMA-Fastrach™ was introduced into clinical practice by Dr Brain, as an airway device and as a device through which TI could be successfully achieved with a dedicated TT in patients known to be difficult to intubate (12). The success of this device has since been documented in 254 patients with difficult to manage airways (13). One of the concerns expressed by clinicians, was that this system could be considered as a “blind upon blind” technique and, may be undesirable if suspected or unknown “supraglottic” pathology existed. A view of the glottic aperture before TI, could be achieved with the ILMA-Fastrach™ by using a FOL passed through the dedicated TT13(13). Dr Brain in collaboration with M.Zocca developed this concept, which is now called the LMA-CTrach™. The LMA CTrach™ is a modified LMA Fastrach™, with an integrated fiberoptic system, which permits visualization of the anatomical structures immediately in front of the aperture of the mask and the passage of the dedicated tracheal tube (TT) through the vocal cords during TI. Visualization is achieved by connecting a detachable, portable, colour display, the LMA CTrach Viewer™, to the LMA CTrach™ airway after insertion. The viewer provides a high resolution, colour image of the larynx. When in position, the viewer is just above the patient’s chin, so that it is directly in line with the actual anatomy being displayed. Thus, for the first time, the user can ensure that the glottic aperture is aligned with the mask aperture prior to passing the ETT. However, unlike the view obtained using a laryngoscope, where the posterior margin of the glottis may be hidden from view by the tube itself during intubation, the LMA CTrach™ Viewer provides a view from the under side of the TT. Since this view allows the user to continuously view the arytenoids during intubation, the danger of accidental oesophageal intubation may be reduced. The findings of initial trials with this device will be presented.

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Airway management in pediatrics – recent developments

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The procedure of difficult airway management in pediatric patients is not new. It follows clear rules, has specific conditions and is more than a little bit different compared to adult patients. The Airway in children is characterized by several specific features. First there is the pediatric anatomy with a smaller trachea and a small omegashaped larynx, his higher position and the subglottic narrowest portion of the upper airway. Together with a higher oxygen consumption and reduced oxygen reserves, compared to adults, it varies with developmental changes depending on age. This is important to know. These pediatric conditions alone are often responsible for airway problems. In inconsiderable cases they are nevertheless combined with congenital errors or malformations and thus arises real airway problems. The knowledge of the unique pediatric anatomy, the combination of airway abnormalities and syndromes are necessary for pediatric anesthetic practice. To gain experience and skills in this field it is wise to know a stepwise approach to manage a difficult pediatric airway.

First step is to know the normal anatomical and physiological conditions of the child. Second step is to know the combination of syndromes or diseases and a difficult airway like Pierre Robin sequence or Franceschetti syndrome and other conditions like epiglottitis and stidor or other pitfalls. The third step is to have those materials available and prepared to apply to a difficult airway. An important peculiarity is that not all of the materials known and available in adults are also available in children. Examples are: Fast-Trach® or McCoy blades in small sizes. Not to mention the skills with these materials. The fourth step is to have an own algorithm for the situation of a difficult airway whatever its origin might be. It is a difference to manage a known situation well prepared or an emergency situation in an unknown case. The fifth step is to know and to guarantee, before any kind of manipulation is done, how to secure oxygenation. The time course of desaturation in children and especially in infants is very fast. Spontaneous breathing and no muscle relaxation is one indication. The patient is to be secured before the airway is intubated. The FS is by far the most versatile of the fiberoptic devices. Nowadays this transmission can be achieved via a camera at the tip of the device. In the following text the term "fiberoptic" covers both kinds of equipment.

Fiberoptical devices for airway management can be divided into different categories:

- The flexible scopes (FS), traditionally called "fiberscopes".
- Semi-flexible/malleable scopes with fiberoptic image transmission.
- Example: The Acutronic intubation stylet or the StyletScope (1)
- Rigid scopes.
- "See around the corner" – stylets. Example: The Bonfils intubation fiberscope.
- "See around the corner" – laryngoscopes. Example: The Bullard laryngoscope.
- "See around the corner" – Laryngeal mask airway, the C-trach LMA.

The FS is by far the most versatile of the fiberoptical devices. The FS comes in sizes from ultra thin that can pass to the trachea of premature children. The FS can be used for airway access both via the nose and via the mouth.

The purchase of a FS is expensive and due to its vulnerability, maintenance- and repair-cost may be high. The rigid and semi-flexible devices are less expensive and probably less fragile. Anticipated difficult airway: A case where you know or suspect mask-ventilation, intubation or extubation to be difficult or impossible. Fiberoptics can be employed in several stages of management of the anticipated difficult airway:

Preanaesthetic evaluation of the airway: The FS is by far the fiberoptic device that is best suited for this purpose. If pathology in the airway (tumor, infection, edema, foreign body . . .) is suspected a pre-anesthesia evaluation is often valuable. The finding can support the choice of airway-management during the following anaesthesia induction. For example the revelation of a very severe narrowing of the glottic opening may suggest that an awake tracheostomy is a wise choice. A fiberoptic airway evaluation can not stand alone but must be combined with an external evaluation (mouth opening, neck- and tongue-mobility) and cetera.

Intubation: In case of an anticipated difficult airway it is advisable to secure the airway while the patient is awake or at least breathing spontaneously (3). The FS is excellently suited for both awake intubation and for intubation in the anaesthetised patient (4) but, dependent on the anatomy, any of the fiberoptic devices may be used if only their limitations are taken into account (for...
example the LMA c-trach requires 2 cm’s of mouth opening). Naso-tracheal intubation over the FS causes severe bleeding in 1.3% of cases (4) which is an argument in favour of applying orotracheal intubation in cases where a nasotracheal intubation is not mandatory for other reasons.

Orotatal tracheal FS-intubation can be divided into two steps

Step one, Getting the tip of the FS to the lower trachea, is facilitated by the use of a dedicated fiberoptic-compatible oral airway (FOOA) that serves several purposes: It maintains the patency of the airway, it protects the FS from the bite of the patient and it facilitates the location of the vocal cords provide that the device is carefully selected to suite the type of pathology presented by the patient (5). If a FOOA is not used then lingual traction can facilitate the passage of the FS past the soft palate and jaw thrust can facilitate the passage of the FS between the epiglottis and the posterior pharyngeal wall (6).

Step two, Getting the tube into trachea passing it over the FS. The challenge is to prevent the tube from impinging on laryngeal structures, especially the arytenoid cartilages. This can be achieved by a) using a tube that is only slightly wider then the outer diameter of the FS, b) withdrawing the tube 5 cm’s followed by a 90 degrees counter-clockwise rotation and reinsertion (7), c) using a tube with a bevel that is shaped so that it is especially suited for the purpose7 or by combing these techniques.

When FS is applied after a failed conventional intubation it should be performed early in the course, not after multiple attempts at direct laryngoscopy that may induce oedema and bleeding rendering FS-intubation difficult or impossible (8).

Extubation: In a patient where the intubation was difficult or in whom surgery or airway management may have changed the airway anatomy or caused oedema the FS can be used for evaluation of the airway in order to decide whether it seem safe to extubate the trachea or not. However the predictive value of this examination may be low. The location and character of post-extubation stridor may be determined by FS-examination.

Placement of bronchial blockers: The FS is essential in the placement of bronchial blockers allowing lung-separation even in small children.

Control of correct placement of tube-tips, double lumen tubes, laryngeal mask airways, tracheal catheterisation (9) etcetera.

Limitations and drawbacks of fiberoptic techniques: All the fiberoptic techniques are dependant on vision, indicating that:

- The presence of blood or secretions may compromise its use.
- A lumen must be present in order to see anything, if tissue is bulging in from all sides this may be impossible.

References


213 Transtracheal catheterisation

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Transtracheal catheterization (TC) or cannula cricothyroidotomy involves the combination of insertion of a cannula through the cricothyroid membrane with high pressure ventilation, either with a jet ventilator or with a manually driven jet device. Besides LMA™ and surgical cricothyroidotomy, TC is an essential technique for management of the “cannot intubate – cannot ventilate” scenario (1), and is recommended by all national anaesthesia societies worldwide (2–7).

Several aspects are important for the safe use of this technique (1,8):

- If possible, the catheter should always be inserted via the cricothyroid membrane, because the ring-shaped cricoid reduces the possibility of unintentional penetration of the oesophagus.
- Injection of local anaesthetic into the trachea with a small gauge needle (e.g. 25), before inserting the cannula aids placement of the catheter.
- Verification of correct cannula placement by aspiration of air should always be performed before lung ventilation.
- High inflation pressures should only be used if a jet ventilator with a endexpiratory pressure control is available. The upper airway must always be kept open to verify deflation of the lungs and exhalation.

Besides the use of the TC in the “cannot intubate-cannot ventilate” scenario, transtracheal high frequency jet ventilation is an established technique in elective ENT procedures, for example, laser surgery of the vocal cords (9–13). In elective cases, catheter placement should always be performed under fiberoptic control (10). Fiberoptic guidance helps to prevent tangential and para-tracheal errors of positioning, as well as fatal rupture of vessels and damage to structures involved in voice production (14). It also enables optimization of the position of the distal end of the catheter, which is necessary for the correct functioning of jet ventilation.

A prophylactic insertion of a TC under local anaesthesia is indicated if the airway is regarded as “extremely” difficult – which is always a clinical decision – or if a fiberoptic intubation fails or cannot be performed, for example due to severe facial trauma (8). This procedure has two advantages. First, it decreases the chance of hypoxia, and second, it facilitates the subsequent definite protection of the airway, either conventional or fiberoptic intubation.

Provided that the placement of the TC is followed by this rigorous step by step approach and supervised by an experienced anaesthetist, adverse events are rare (10, 13). Even though there is only little or no experience performing this technique.
in many hospitals, we should become familiar with a potentially live saving technique (7). Nowadays, percutaneous as well as surgical cricothyroidotomy are part of many workshops and there is therefore no excuse for not having been exposed to it (15).

References

214 An update on prevention and treatment of postoperative nausea and vomiting
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Surgical patients want good prevention and prompt treatment of postoperative nausea and vomiting (PONV) (1). Although the pathophysiology of PONV is multifactorial we know quite well which factors will contribute to the incidence of PONV. Risk factors for PONV: Positive results with strong clinical impact are associated with female gender, non-smoking status, history of motion sickness or PONV, general versus regional anaesthesia, volatile anaesthetics, duration of anaesthesia and postoperative opioids. Some contribution have been associated with young age and physical status, nitrous oxide and muscle relaxant antagonists whereas conflicting evidence have been presented in the literature on the role of site of surgery, menstrual cycle, experience of the anaesthetist and gastric tube for decompression. There is flawed or insuficient data on the role of pain and movements in causing PONV. Body mass index and anxiety and personality are disputed factors, i.e. demonstrated not to be associated with PONV. There are several predictive models for PONV. The well documented simplified risk score recommended by Apfel (2) is based on female gender, non-smoking, history of PONV and use of postoperative opioids and has been shown to predict the risk of PONV.

Efficacy of antiemetics: Droperidol has been very effective in both prevention and treatment of PONV, but it was withdrawn form clinical use in the United States and many other countries. It is still available in 6 European countries. The recommended dose for day surgery patients is 1.0 mg/kg up to 1.25 mg i.v. Ondansetron and other 5HT3 antagonists are effective for both prevention and treatment on PONV. With 4 mg dose of ondasetron the numbers needed to treat for prophylaxis and successful treatment (0–48 h) were 6.5 and 3.9 patients, respectively (3,4). Several studies have confirmed that dexamethasone is effective in prevention of PONV (5) and dexamethasone has gained popularity in many countries after withdrawal of droperidol. Choosing anaesthesia with propofol maintenance, instead of inhalational anaesthesia will decrease the incidence on PONV to a similar extent as with one antiemetic proven to have efficacy (6). Metoclopramide, although used as an antiemetic for almost 40 years in the prevention of PONV, is unlikely to have any clinically relevant antiemetic effect (7). So far we do not know what will be the role of NK1-receptor antagonists or combination of histamine-1- and histamine-3-receptor antagonists in the prevention or treatment of PONV.

Combination of antiemetics: Combination of antiemetics is important if the patient has over 40% risk for PONV. Using factorial design in randomised, controlled trial (RCT) one can answer several clinical questions at the same time and also investigate interaction of combinations in multimodal approach (8). When assessing the single and combined benefits of six interventions for the prevention of postoperative nausea and vomiting, IMPACT-study used a 2×6 factorial design (6,9). Each of the 5199 patients was randomly assigned to six interventions: ondansetron (4 mg i.v.) or no ondansetron; dexamethasone (4 mg i.v.) or no dexamethasone; droperidol (1.25 mg i.v.) or no droperidol; propofol or a volatile anaesthetic (isoflurane, desflurane, sevoflurane); nitrogen or nitrous oxide; and remifentanil or fentanyl. These 6 treatments led to 64 possible (i.e., 26) treatment combinations. Ondansetron, dexamethasone, and droperidol each reduced the risk of postoperative nausea and vomiting by about 26%; propofol reduced it by 19%; and nitrogen (i.e., omis-
Postoperative pain management at home – current methods and future perspectives

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Surgical procedures of ever increasing magnitude and complexity are being performed on an outpatient or day-care basis. The potential cost saving of outpatient surgery may be negated by unanticipated hospital admission for poorly treated pain. Contrary to the common belief that ambulatory surgery is followed by mild hospital admission for poorly treated pain. Contrary to the common belief that ambulatory surgery is followed by mild postoperative painful discharge, contact with the hospital after discharge, unanticipated hospital admission and increased costs. Postoperative pain following day surgery may last several days, this can have implications for return to work and for community health services.

As in adults most studies of analgesia in pediatric day-case surgery have focused on the immediate postoperative course and largely ignored the risk of post-discharge severe pain at home, when it becomes the responsibility of the parent. Studies have shown that more than 50% of children experience clinically significant pain after discharge. Despite the high frequency of under-treated postoperative pain a overwhelming majority of patients experience satisfaction with pain control.

Strategies for postoperative pain management
Optimal postoperative pain control for day-case surgery should be effective and safe, produce minimal side effects, facilitate recovery, and be easily managed by patients at home. Analgesia techniques should permit “normal” activities, additional analgesic supplements should be provided to cover any painful activity. Rescue analgesia medication should be provided if the prescribed analgesic is ineffective. It has been shown that the use of pre-packaged take-home analgesics specific to the type of surgery and breakthrough medication can lead to improved pain control, morbidity and sleep.

Choice of analgesic drugs after discharge – current methods
Oral analgesics are the mainstay of continuing pain control at home, when it becomes the responsibility of the parent. Studies have shown that more than 50% of children experience clinically significant pain after discharge. Despite the high frequency of under-treated postoperative pain a overwhelming majority of patients experience satisfaction with pain control.

Surgical procedures of ever increasing magnitude and complexity are being performed on an outpatient or day-care basis. The potential cost saving of outpatient surgery may be negated by unanticipated hospital admission for poorly treated pain. Contrary to the common belief that ambulatory surgery is followed by mild pain; recent studies have shown that under-treatment of pain is common. About 30–40% of discharged outpatients may suffer moderate to severe pain during the first 24–48 h. The commonly used analgesic medications such as paracetamol, NSAID’s, tramadol, dextropropoxyphene may be inadequate in many patients.

Impact of pain after ambulatory surgery
Severe postoperative pain causes extreme discomfort, sleep deprivation and suffering. Along with postoperative nausea and vomiting (PONV) it is the main cause of delayed discharge, contact with the hospital after discharge, unanticipated hospital admission and increased costs. Postoperative pain following day surgery may last several days, this can have implications for return to work and for community health services.

As in adults most studies of analgesia in pediatric day-case surgery have focused on the immediate postoperative course and largely ignored the risk of post-discharge severe pain at home, when it becomes the responsibility of the parent. Studies have shown that more than 50% of children experience clinically significant pain after discharge. Despite the high frequency of under-treated postoperative pain a overwhelming majority of patients experience satisfaction with pain control.

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Choice of analgesic drugs after discharge – current methods
Oral analgesics are the mainstay of continuing pain control at home and it is important to encourage patients to take analgesics pre-emptively and regularly, starting before local anesthetic effect has worn off. For mild pain, simple analgesics such as paracetamol (acetaminophen) may be sufficient. Patients with mild to moderate pain in day surgery benefit from combinations of NSAID’s and weak opioids (most commonly codeine, dextropropoxyphene, and tramadol) in addition to regional or local anesthesia. The patient response to drugs varies, so rescue analgesia for postoperative pain beyond acceptable levels may be needed. Strong opioids are generally avoided because of their well-known side effects including the risk of respiratory depression. However, sustained release strong opioids such as oxycodone are used routinely in many institutions in the USA.

Future prospects – regional techniques at home
Administration of local anesthetic in the surgical wound is effective and safe but the analgesia lasts only a few hours. We have described a technique using an elastometric balloon pump, which allows the patient to self-administer local anesthetic analgesia at home. The technique involves the placement of a multi-hole, thin (22-gauge) epidural or Perifix brachial plexus catheters subcutaneously into the surgical wound, subacromially, intraarticularly or in the axillary brachial plexus sheath (depending on surgical site). The improvement in and availability of catheter techniques and disposable pumps have facilitated the use of local anesthetic based analgesic techniques as a means of providing prolonged, effective, and safe postoperative analgesia.

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Incisional, intra-articular or perineural techniques?

Perineural, incisional and intra-articular catheter techniques are being used increasingly to manage postoperative pain in hospitalized and day surgery patients. Catheters may be placed within the brachial plexus sheath, perineurally, intra-articularly, into the subacromial space, as well as subcutaneously into the surgical wound. Local anesthetic drugs can be delivered through such catheters as continuous infusions, on demand self-administered bolus doses by PCRA or low dose ground infusions with possibility of on-demand bolus doses. Patients receiving local anesthetic by infusion or PCRA may achieve more vigorous postoperative physical therapy with improved analgesia than patients receiving only oral opioid analgesics (8). Although this author was the first to report the use of perineural (and incisional and intra-articular) catheter analgesia at home our preference is for incisional and intra-articular catheter techniques because of their simplicity and safety, which are the two most important prerequisites for such techniques at home. Another reason for restrictive use of ambulatory perineural catheters is that in Sweden (and in most countries outside USA) extensive joint surgery, which is one of the most important indications for perineural catheter techniques, is not an ambulatory procedure at present. The type of procedure that qualifies as ambulatory surgery varies considerably in many countries depending on differences in health care systems and reimbursement policies.

In the ambulatory setting incisional catheter techniques have been used for the following types of surgery: breast augmentation, maxillofacial surgery, bone harvesting from iliac crest, laparoscopic cholecystectomy, inguinal hernia, and hand surgery. For inpatients incisional catheter techniques have been used for hysterectomy, C. section, hip and knee joint replacement, ACL reconstruction, cardiac surgery and sternal fracture.

Choice of pumps

A large number of small, portable infusion pumps are currently available, each with benefits and drawbacks. In general, the larger, heavier, more expensive electronic pumps are more reliable than the elastomeric devices. After ambulatory surgery it may be desirable to use one of non-electronic pumps for its simplicity and disposability (9).

Role of patient (and parent) information

Postoperative pain is often associated with anxiety. Patients should be informed about the need to treat pain and about the various methods to manage pain. The information should be given verbally and in writing. Day patients with severe pain at home do not always take their medication as prescribed and may even mix in their own analgesics. Clear instructions are therefore mandatory. Analgesia needs to be tailored to the severity of pain associated with the procedure. The patient response to drug varies, so rescue analgesia for pain beyond acceptable levels may be needed. Pre-packaged analgesics should be provided for anticipated mild, moderate or severe pain. A follow-up call the next day reassures the patient and provides feedback about analgesic efficacy. A regular audit of the postoperative pain service varies, so rescue analgesia for pain beyond acceptable levels may be needed. Pre-packaged analgesics should be provided for anticipated mild, moderate or severe pain. A follow-up call the next day reassures the patient and provides feedback about analgesic efficacy. A regular audit of the postoperative pain service.

References


216 What are the important determinants of outcome after anaesthesia for ambulatory surgery?

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A positive outcome is the number one goal in surgery, in terms of improving health and life quality with the specific surgical procedure for the patient in question. Concerning the anaesthesia needed for the surgeon to reach his goal, a positive outcome will mean absence of any problems related to the anaesthetic procedure. With a very few exceptions, (e.g. heroin detoxification, reposition from joint luxation) anaesthesia is not expected to have any therapeutic effects.

A discussion of outcome, in terms of problems related to the anaesthesia procedure, may be structured in terms of timing: shortlasting → longlasting → permanent; and severity: discomfort → reduced function → disability → lethal.

As to mortality after ambulatory anaesthesia, the figures are almost zero in most investigations, independent on choice of anaesthetic methods (1). However, this is not self-evident but a result of proper anaesthetic care in well-developed western world societies. Even with prospective studies of 50 000 patients, it is difficult to show any risk factors of mortality because mortality is so rare. Thus, a recent study on 400 000 Dutch patients (mixed emergency, inpatients, outpatients) is of interest, because they were able to show some important aspects of anaesthetic care which were related to reduced mortality: proper check of equipment, experience of the nurse anaesthetist, anaesthesiologist immediately available, reversal of neuromuscular blocking agents and proper post-operative pain care (2). Further, investigations of a 10 times increase in mortality rate in office-based plastic surgery in Florida underlines the importance of anaesthetic care (3). It came out that most of the cases of death were quite major procedures, often in unhealthy patients in non-accredited facilities without an anaesthesiologist present.
Looking at cases of permanent disability after ambulatory anaesthesia, examples may be cognitive dysfunction, nerve damage from local anaesthesia blocks and chronic pain, possibly caused in some cases by improper anaesthetic and post-operative care.

Cognitive dysfunction is described in almost 1 out of 4 elderly patients 1 week after intermediate or major surgery. However, it seems like very few cases become permanent, after 3 months the figures are down below 10% and after one year there is no significant difference from a non-surgical population (4). However, it has been shown that there is a decreased incidence of cognitive dysfunction in the ambulatory setting per se, as the patients are less exposed to unknown environment compared with inpatient care (5).

As to nerve damage, these are very rare but still serious cases, including cauda equina syndrome after high doses of hyperbaric spinal lidocaine and damage to single nerves by improper needle or injection technique during blocks (6).

Whereas most cases of chronic pain are related to the surgical technique, there are some indices as to more frequent occurrence of chronic pain when the initial post-operative pain is not treated properly (7). Whether the concept of pre-emptive analgesia may have a role in this context is still debated, but a recent review concluded on pre-emptive (i.e. before the trauma starts) use of epidural, local anaesthesia or NSAID as beneficial in terms of less post-operative pain (8).

However, most outcome problems of anaesthesia care are shortlasting aspects of perceived quality. In some cases these are just evident for minutes whereas other may have problems for hours and days. Some of these problems may be clearly related to choice of anaesthetic drugs and techniques.

A prominent opioid hangover from general anaesthesia or use of opioids in postoperative care may create a list of problems: somnolence, nausea, obstipation and sleep disturbances. Further, there are indications as to high doses of per-operative remifentanil may create postoperative hyperalgesia. For these reasons a multimodal non-opioid regimen should be used in operative anaesthesia, examples may be cognitive dysfunction, nerve damage, post-thoracotomy pain after thoracic epidural analgesia: a prospective follow-up study. Acta Anaesthesiol Scand 2003;47:653–8.

Further, there are indications as to high doses of per-operative remifentanil may create postoperative hyperalgesia. For these reasons a multimodal non-opioid regimen should be used in operative anaesthesia, examples may be cognitive dysfunction, nerve damage, post-thoracotomy pain after thoracic epidural analgesia: a prospective follow-up study. Acta Anaesthesiol Scand 2003;47:653–8.

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Nausea and vomiting have increased incidence after inhalational anaesthesia and reversal of neuromuscular blocking agents with neostigmine. There are also other risk factors of nausea and vomiting, which may be elucidated before start of surgery resulting in a more dedicated use of anti-emetic prophylaxis (10).

Shivering is usually a shortlasting problem, associated with improper patient warming, but also with the potent inhalational anaesthetic agents. Propofol seems to be better in this aspect and also has the favour of producing a feeling of subjective well-being or a little euphoria during emergence in many patients.

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217 Guidelines in anaesthesia and intensive care: Do we want or need guidelines?
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Guidelines have been defined as “systematically developed recommendations that assist the practitioner and patient in making decisions about health care”. Implementation of guidelines is probably the most effective way to improvement outcome. This is possible when guidelines are based on the current literature as interpreted by experts in a specific field (1). In this way, the most effective treatment is identified including appropriate consideration of possible side effects and associated requirement for resources. Therefore, guidelines may lead to a reduction in expenses in some departments whereas the opposite may be true for other institutions where less effective (but also less expensive) procedures have been in regular use. Within our specialty, numerous guidelines have been published and studies have concluded that implementation of these has improved outcome (2–5).

The most obvious advantage associated with guidelines is that the individual clinician is supplied with a summary of the literature. It is not possible for any anaesthesiologist to read all relevant publications and in an emergency situation, a literature search is not an option. For many clinical challenges, different studies are reporting contradictory findings which can be explained by a number of factors, for instance differences in clinical setting or differences in inclusion/exclusion criteria. Another problem may be poor research methodology, including inadequate statistical power where an important beneficial effect may not be detected. On the other hand, one single study may convince the clinician to change his practice even before any confirmative studies have been published. Systematic reviews can provide important help in such cases but only one single aspect can be covered at a time. It is, however, very difficult to summarise the literature when numerous treatments and combinations are available. Finally, side effects and uncommon complications are infrequently taken into consideration when the efficacy of a treatment is assessed. Clinical experts must therefore participate very actively in the process when guidelines are developed. Then it will also be possible to consider the need for education associated with the implementation (6).

It is a major task to develop guidelines. Luckily, a number of organisations have begun the work and guidelines are currently available for managing several patient groups and situations.
from the American Society of Anaesthesiologists (7). In the Nordic countries, some guidelines have also been developed at different levels and we should be able to use many of the existing guidelines as the basis for general Nordic ones (8). In this way, we can combine our expertise and make it possible to cover a more wide range of our specialty. Thus, the workload for the national societies is less and we may increase the usefulness due to the similarities in culture, education, and organisation. When guidelines are used, a much more uniform clinical data can be collected and quality assurance is therefore more easily conducted.

It is important to realise that in the department and in specific situations the guidelines may be modified or disregarded according to local organisation, constraints or patients’ preferences. The most safe procedure may be the one you have experience with. Guidelines will not cover all situations and there will definitely be room for innovative ideas and initiatives in individual patients where no experience may be available or in combination with other procedures and concomitant drug administration. Therefore, clinical judgement and the “art of anaesthesia and intensive care” will still exist but in routine management of common scenarios, guidelines have much to offer the busy clinician who will be liberated from literature searches and difficult analyses.

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Why don’t doctors use guidelines? How can we change their attitude?

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The amount of clinical literature is increasing and it is difficult for doctors to evaluate the relevant documentation critically. Also new drugs, methods and tools are introduced that require change of work practice. Evidence based medicine is an approach by which a systematic identification of research results is trying to answer relevant problems taken in consideration the wishes and needs of the individual patients (1). Evidence based medicine has been highly accepted and seen as a necessity in order to improve the quality of patient care, but although evidence based guidelines has been developed, they are not used as frequently as one could wish in clinical practice. There are several examples of this – the use of drugs for the treatment of gastric ulcer and the use of streptokinase to patients with myocardial infarction. Here the evidence was available a long time before practice actually changed. There are several examples also from our own specialty. Kristensen and Møller showed that the knowledge regarding the ASA algorithm for management of the difficult airway was insufficient among Danish anaesthesiologists (2). Only about 40% partially knew the algorithm and less than 30% reported that they fully knew the algorithm (self reported confidence) (2). Further Rosenstock et al demonstrated that 97% of the residents could recall the algorithm (3). The question is why these guidelines are not used by the doctors and how we can change their attitude. The answer to these questions might be answered by looking at the different barriers to the implementation of evidence based guidelines.

The barriers

The individual doctor might not be familiar with evidence based medicine and hence be less willingly to accept the concept. A study of the knowledge of and confidence with evidence based medicine showed that knowledge was limited with a tendency for doctors to overestimate own knowledge (4). Further doctors still use traditional sources of information such as books and discussion with colleagues, when questions regarding how to treat a patient comes up. The study also indicated that the use of new information and critical reading of scientific literature is more limited in the same group of doctors (4). This is a pattern that is unchanged despite of new, more updated alternatives (5,6). Hence there is a risk of using an intuitive clinical judgement instead of a more systematic approach and explicit coupling of objective findings with documented diagnostic or therapeutic findings in the medical literature.

Older, more clinically competent doctors might not accept the evidence and prefer previously, well known methods. Some doctors point out the need for a more holistic view or patient centred approach. According to Greenhalgh there is a problem in transferring the result from a clinical trial directly to clinical problems (8) as the results from evidence based medicine is characterised by relating to the mean of the population and not the individual. A concept called “Misplaced concreteness”

Another barrier to overcome is the disagreement between individual staff members, disagreement within the society of both the acceptance, the implications of new evidence based guidelines and how to implement these. First the new technology is promoted by frontiers, then the method is accepted by opinion leaders and thereafter by the majority of doctors (9).

New guidelines might have implications for the organisation as well. New equipment might be needed which initially will increase cost, shift from older to new and more expensive drugs, training and education of staff, change of existing procedures which might involve collaboration with other specialities etcetera.

Professionals, who seek to enhance quality and patient safety, often define culture as a barrier to change (7). The cultural focus on individual autonomy might conflict with the desired norms of a more standardised approach to the treatment of patients.

How to overcome the barriers

It is necessary that doctors can extract relevant data from the massive amount of information presented to them. Another prerequisite is confidence in getting information and research methodology principles related to evidence based medicine. Education of doctors is needed in order to overcome these barriers. Within the organisation leaders have a responsibility to go first as role models and as responsible the organisational changes needed and the follow up – has the evidence based guidelines been implemented. This can be done by actually measuring if the guidelines are known and used in the department.
A cultural analysis of health care suggests professional values that can be redirected to support change and create new ways of working and then gradually shift the culture (7). Changes must address behaviour, systems and the cultural assumptions that underlie and reinforce existing behaviours and structures in order to be successful (7). We must accept that cultural changes take time, but not that implementation takes time.

References

219

Anaphylaxis, to be or not to be

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Anaphylaxis during the induction of general anesthesia has been increasingly reported during the last decades. Neurromuscular blocking agents (NMBAs) represent the most frequent cause of IgE mediated anaphylaxis, with suxamethonium (SUX) as the prominent culprit. The often severe reactions have raised considerable concern. Since in most cases IgE-mediated mechanisms are involved the patient must be IgE-sensitized at the unfortunate NMBAs exposure.

However, up to half the patients that react have not been exposed to such drugs prior to the anesthesia, and therefore other drugs or environmental substances sharing allergic epitopes with the NMBAs must have initiated the sensitization. The chemical structures of the NMBAs creating the allergenic epitopes proposed to be responsible for the allergic anaphylactic reaction are quaternary ammonium ions (QAI), of which each drug in the SUX family should have at least two. Therefore, the drugs have the potency to cross-link adjacent IgE antibody molecules on the mast cells and basophils and to trigger an IgE antibody mediated release of inflammatory mediators.

The frequency of reactions varies considerably between countries, however. Reports to medical authorities and published data suggest anaphylactic reactions to NMBAs to be much more common in Norway (approx. 1/5000) than in Sweden (approx. 1/85 000). Partly attributed to reporting bias, differences in diagnostic follow-up, genetics or anesthetic practices, such discrepancies could also be explained by differently sensitized populations. A study was performed to document the prevalence of IgE-sensitization to morphine (MOR), SUX and pholcodeine (PHO) in comparable populations selected in Bergen, Norway and Stockholm, Sweden and attempts were made to identify factors in the environment that might explain the geographical differences (1).

A total of 300 superfluous volumes of “allergies” sera were consecutively sampled from the allergy diagnostic laboratories at the Haukeland and Karolinska University Hospitals, in Bergen and Stockholm, respectively. Further, sera from 500 blood donors were collected and, in Bergen, sera from 65 patients having previously reacted anaphylactically during anesthesia were included. The serum samples were tested for IgE antibodies to MOR, SUX and PHO, using Pharmacia Diagnostics’ ImmunoCAP™ Specific IgE assay.

In Norway 0.4% of blood donors, 3.7% of allergies and 38.5% of anaphylactics were IgE-sensitized to SUX, as were 5.0, 10.0 and 66.7% respectively to MOR. In sera from the blood donors and allergies from Stockholm, no IgE antibodies to SUX or MOR were detected. IgE antibodies to PHO were present in 5.8% of blood donors from Norway but in none from Sweden. Approx. 65% of the anaphylactics were sensitized to PHO. The majority of those sensitized (69%) were women. About 70% of the sera with IgE antibodies to MOR/PHO in the allergies group did not react with SUX, and the IgE-antibodies could be inhibited by MOR but not by SUX.

Since it is most unlikely that the sensitized Norwegian individuals, especially the allergic persons and the blood donors, had been exposed to NMBAs during a previous surgical event other possible sensitzers were looked for. Many regular house hold chemicals are known to carry branched amines, e.g. QAIs similar to the structures present in NMBAs. A total of 84 different household and other environmental chemicals (skin care ointments, hair care products, cough syrups, lozenges, tooth pastes, cleansers and motor oils) from Norwegian and Swedish homes were therefore tested for IgE antibodies to MOR, SUX and PHO.

Although several of the environmental chemicals inhibited the IgE binding to SUX and/or MOR, no definite difference in exposure could be found between Norway and Sweden, except for the use of cough mixtures containing PHO. Some of these can be obtained OTC in Norway but only after prescription in Sweden, or are not available in Sweden. The possibility that the higher consumption of opiate drugs, especially those containing PHO, in Norway could explain the much higher prevalence of IgE antibodies to morphine and also anaphylactic reactions to NMBAs needs further studies.

The possible role of PHO was investigated in a pilot study (2). Two persons IgE-sensitized to MOR, PHO and SUX, and two non-sensitized controls, were given a standard dose of a PHO-containing cough syrup for a week. No effect of PHO was seen in the controls. However, after 7 days the two sensitized experienced some urticaria and it was found that their serum IgE had increased dramatically: the IgE levels were 60 and 105 times, respectively, higher than right before the exposure week. This remarkable effect of PHO on IgE production and its possible clinical importance should be further studied.

Patients who have IgE antibodies to QAIs should be considered individuals at risk when subjected to general anesthesia with NMBAs. It should therefore seriously be considered to measure the amount of IgE antibodies prior to the use of such substances for general anesthesia.
Drug provocation in anaesthesia allergy

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Allergic reactions during anaesthesia are very rare and thus in some countries the investigation of these reactions has been centralised in specialised allergo-anaesthesia centres (1–4). In these centres the investigation program usually consists of 1) Specific IgE analysis (only available for latex, some antibiotics and very few anaesthetic drugs) and 2) Skin testing (skin prick testing and intradermal testing). The results of skin testing have recently become subject to some debate, as the specificity and sensitivity are generally poorly defined. In 30–40% of the patients investigated at such allergo-anaesthesia centres it is not possible to identify an offending allergen (1–3). In some patients this could be because the reaction investigated was not allergic at all – or maybe due to an allergy to a metabolite. In other cases the reaction could have been a non IgE-mediated hypersensitivity reaction as defined in the EAACI revised nomenclature for allergy (5). These reactions are not detected by conventional allergy investigation, and the only way to find the causative substance is drug provocation (6). Until now drug provocation has not been done systematically in investigation of anaesthesia allergy. In the field of food allergy and inhalant allergy provocation is carried out more routinely. Concerning drug allergy drug provocation has been reported with antibiotics, NSAIDs and local anaesthetics (7–8).

At the Danish Anaesthesia Allergy Centre (DAAC) we have recently included drug provocation in the protocol used when investigating patients with allergic reactions during anaesthesia. In that way we hope to detect also the allergic reactions to metabolites and the non-IgE-mediated hypersensitivity reactions and thus be able to warn the patient specifically against re-exposure. Drug provocation may also contribute to a better understanding of the mechanisms behind the reactions and to a clarification of the specificity and sensitivity of skin and in-vitro testing.

At the DAAC our investigation protocol now includes the following steps:

1. A full history is taken with evaluation of the severity of the reaction and a clinical examination.
2. Any medication which might suppress an allergic reaction such as antihistamines, antidepressants, corticosteroids etc. is paused in due time before testing.
3. The patient is investigated with specific IgE analysis (for the relevant drugs, if available) and skin prick testing and intradermal testing for all substances, the patient was exposed to prior to the reaction.
4. The drug provocation is performed ‘placebo-controlled’ with initial administration of equal volumes of isotonic saline before provocation. The route of drug administration for provocation is preferably the same as used when the reaction occurred (except the spinal and epidural route).
5. The drug is given stepwise, in many cases starting with 1/100 of the final provocation dose followed by 1/10 and ending with the final provocation dose. The time interval between doses is 30 minutes for drugs given i.v. and 60 minutes for drugs administered by other routes. Blood pressure, pulse and peak-flow are measured before administration of each dose and after 15, 30 (and 60) minutes. The patient is closely monitored for any sign of allergic reaction.

For practical reasons we are not able to carry out drug provocation with neuromuscular blocking agents (NMBAs). For other drugs with a powerful pharmacological effect (e.g. hypnotics, opioids, vasoactive drugs) we have chosen the final provocation dose to be approximately 1/10 of the therapeutic dose. For all other drugs (e.g. antibiotics, local anaesthetics, NSAIDs, colloids etc.) we titrate up to full therapeutic dose.

Drug provocation is not performed in pregnant women and at present not in children. In patients at increased risk of not tolerating an allergic reaction due to co-morbidity the indication for drug provocation is considered carefully.

The observation of the patient and the safety involved in drug provocation must be at the highest level, as it is a high-risk procedure. At the Allergy Clinic we are prepared for and used to treating anaphylactic reactions and have full resuscitation backup when performing drug provocation. Patients are fully informed of the risks involved.

Compared to skin testing, where many drugs may be tested simultaneously, drug provocation is extremely time and man power consuming as only one drug can be tested at a time and sufficient staff has to be constantly at hand for treatment of possible anaphylactic reactions. Because of the time intervals between each provocation dose it is only possible to test one or two drugs per day.

The benefit we expect to get from this new aspect of anaesthesia allergy investigation, is first of all that we will be able to find a causative substance in some of the patients with reactions during anaesthesia and operation, where conventional allergy testing is negative despite clinical signs of anaphylaxis and in some cases elevated mast cell tryptase. Such reactions could either be explained by a non IgE-mediated mechanism or by an IgE-mediated mechanism where the allergen is not identified by skin or in vitro testing. We also hope to be able to clarify some of the cases where results of skin testing are inconclusive, in order to reduce the risk of 1) False negative tests, which may put the patients at risk of a repeated reaction, and 2) False positive tests which may label the patient with an allergy he/she does not have.

References
ICP and CPP management after severe head injury

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Traumatic Brain Injury (TBI) is the leading cause of death among young adults in the western world, and it is estimated that the incidence of closed head injury in the United States is 200 per 100,000. Worldwide, injuries account for 15% of the burden of death and disability and in 2020 injuries are expected to be the third leading cause of death and disability worldwide.

Several drugs aimed at reduction of the primary injury, that have shown promising results in laboratory studies, have been tested in phase three trials, but have failed to be beneficial [1]. Many reasons for these disappointing results have been pointed out, imbalances after randomization with respect to basic prognostic variables or timing of drug infusion to name a few [2]. The increased survival rate for TBI victims during the last 20 years has mainly been attributed to improved intensive care treatment, in particular monitoring and treatment of high intracranial pressure (ICP) and low cerebral perfusion pressure (CPP) [3]. The importance of monitoring intracranial pressure has been established, although lately the benefit has been discussed. In a comparison of two Dutch trauma centers, one utilizing ICP monitoring and one only supporting intensive care it was not possible to detect any difference in neurological outcome of TBI patients [4]. However the trend in neurointensive care today is pointing towards a more profound monitoring. Both insight in physiology seen at the bedside continuing monitoring of changes in physiology and basic prognostic variables or timing of drug infusion to name a few [2].

When the three treatment paradigms are studied in detail, it is interesting that the differences in actual treatment of the majority of patients are minor. The overall goal is to keep ICP low and CPP adequate, it is mainly when ICP increases the differences in treatment paradigms are noticeable. Outcome data from centers with different treatment algorithms, presented in the recent years, have been more or less identical. The importance of close monitoring of the brain by specialists in neurointensive care must not be underestimated [3], we must realize that head injury is a dynamic disease, autoregulation can reappear at any given moment after trauma, a disrupted BBB will become intact and edema will tend to weave. Monitoring must guide the clinician in making the correct decisions and the clinician must be ready to change treatment according to the monitoring, both insight in the brain on the macro- ie. Monitoring ICP, as well as microcirculatory ie. Monitoring Pith level is important.

The next level of treatment algorithms should be based on continuing monitoring of changes in physiology seen at the bedside rather than theoretical physiological models based on laboratory data.

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imbalance between the hydrostatic and the oncotic pressures can have tant consequences for the degree of increase in ICP following trauma (e.g. sodium and chloride ions), which may occur after a head injury. European Brain Injury Consortium. Acta Neurochir (Wien) 1997;139(4):286–294.


The Lund treatment of severe brain trauma
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Introduction
Head injury is one of the most common reasons for death and morbidity for middle age and younger individuals in the western world. The US guidelines for treatment of severe head trauma from 1996 are based on a metaanalytic approach (1), while the European guidelines presented one year later are based on consensus and expert opinions (2). A protocol introduced by Rosner in 1995, favours a high CPP (minimal 70 mm Hg) to squeeze blood through the swollen brain and to reduce intracranial blood volume by autoregulatory vasoconstriction (3). Also the US and the European guidelines initially recommended a minimal CPP of 70 mmHg, but somewhat lower levels are now accepted. An alternative approach was introduced at the University Hospital of Lund in 1992–1994 (4,5). The Lund Concept is a theoretical approach, based on physiological and pathophysiological mechanisms for brain volume regulation and cerebral perfusion and comprises two main goals 1) to prevent or reduce a raised ICP and 2) to improve oxygenation around contusions (5,6). Clinical studies using the Lund Concept show the most favourable outcome (7,8,9).

Prevention of brain oedema
Brain volume is normally controlled by the intact BBB, which means that only water passes the capillary membrane passively, and only water is transferred to the brain tissue following a disturbance of the balance of transcapillary hydrostatic and oncotic pressures favouring filtration. This means dilution of the high crystalloid osmotic interstitial pressure of 5500 mmHg, immediately counteracting further filtration (10). If, on the other hand, the capillary membrane is passively permeable for small solutes (e.g. sodium and chloride ions), which may occur after a head trauma or during cerebral infections, the filtrate will also contain small solutes and the filtration will continue until counteracted by the increase in ICP (6).

The fact that the brain is enclosed in a rigid shell has important consequences for the degree of increase in ICP following imbalance between the hydrostatic and the oncotic pressures (5,6,11). Due to a difference between ICP and the extradural venous pressure, a passive venous collapse is developed just subdurally (Fig. 1). The magnitude of the collapse is dependent on the difference between ICP and the extradural venous pressure. If there is an increase in ICP, there will be an increase in the passive venous collapse, and the venous pressure retrogradely to the collapse will increase in parallel with ICP. This effect of the venous collapse also explains why CPP is calculated as mean arterial pressure minus ICP and not minus venous pressure (5,6). The ICP increase will be partly transferred via the venules back to the capillaries inducing further filtration, and so on. It can be calculated that, at steady state, ICP may increase/decrease up to 8 times the initial imbalance between the hydrostatic and oncotic transcapillary pressures if 80% of the ICP increase/decrease is transferred retrogradely to the capillaries (6).

According to these physiological principles for brain volume regulation of the injured brain, brain oedema can be prevented by reducing hydrostatic capillary pressure and/or increasing oncotic pressure. The former can be obtained by normalising the normally raised arterial pressure by antihypertensive treatments (beta-blockade, alpha2-agonist, angiotensin II agonist) and the latter by infusion of colloids, preferably high concentration albumin (5,6).

Another consequence of the passively variable venous subdural collapse is that the brain is protected from venous pressure variations. This means, for example, that head elevation will not induce drainage of blood from the venous side, and the venous pressure increase by PEEP will not be transferred to the brain, the latter implying that PEEP should be used to prevent pulmonary atelectases. The ICP-reduction following head elevation is caused by the decrease in arterial pressure to the brain (6).

Improved oxygenation around contusions
Hypoxia must be an important factor behind cell damage, especially since all clinical studies evaluating pharmacological neuroprotection from the release of toxic neurochemical factors such as excitatory amino acids and lipid peroxidation (free radicals) have failed to lead to improved outcome. A first measure must be to keep arterial oxygen tension normal. Oxygenation around hemorrhagic and ischaemic contusions can be compromised by blood cell aggregation and wall adhesion, by endothelial cell swelling, and by local vasocnstriction by cytokines and free blood. The release of permeability-increasing toxic substances triggered by hypoxia and cell damage may cause a general increase capillary permeability.

Blood flow to an organ or part of an organ is directly related to the perfusion pressure and vascular resistance. While the perfusion pressure may vary by as most 20–25% in clinical practice, the relative variation in vascular resistance can be much larger. Vascular resistance control is therefore of much greater importance than CPP, and especially in areas with increased resistance, as small variations in vessel radius may result in large relative variations in vascular resistance according to the fourth power relation of the law of Poiseuille. Thus, while CPP may be more of importance for brain edema development as described above, vascular resistance may be of much larger importance for control of perfusion and oxygenation.

By activation of the baro-receptor reflex, hypovolemia reduces cerebral blood flow via release of catecholamines, an effect especially pronounced in a state of increased ICP (12). While the risk for hypoxia in less seriously injured areas is slight, even a minor reduction in blood flow in the pericontusional areas may aggrate hypoxia significantly. Maintenance of normovolemia, therefore is a most important measure to optimize microcirculation and minimize hypoxia. In the Lund Concept this is obtained by infusion of albumin and erythrocytes to normal albumin/pl and normal haemoglobin concentrations. Crystalloids are not used...
The Lund Concept aims at maintaining a normal arterial pressure by keeping the patient normovolemic and, in principle, there is no need for vasoconstrictors or other vasopressors. Vasoconstrictors also may compromise circulation of the pericontusional areas of the brain and may trigger ARDS, renal failure and intestinal ischaemia and their clinical use therefore can be strongly questioned. If given with caution in lowest possible doses, however, the large-vein vasoconstrictor dihydroergotamine may be used in single bolus doses to break a precipitating high ICP (6). Nemoventilation is recommended in the Lund concept as hyperventilation may aggravate hypoxia (5,6).

Stress induces sympathetic discharge and increased catecholamine concentration, which may compromise microcirculation around the contusions, and therefore should be avoided. In the Lund Concept, stress is reduced by keeping the patients sedated, (e.g. midazolam, low-dose barbiturate, propofol, analgetics and clonidine), and by avoiding external cooling. Temperature can be reduced by paracetamol or, if temperature is very high, by a bolus dose of Solumedrol. The nutrition should be mainly enteral, with avoidance of overnutrition (15–20 kcal/kg/day), a measure also reducing fever (5,6).

In summary

The Lund concept reduces ICP and improves perfusion by normalising all essential parameters, such as blood pressure, blood volume, albumin/pl, Hb/pl, electrolytes, stress, ventilation and nutrition, and by avoiding vasoconstrictors. Osmotherapy (e.g. mannitol) is not used. Surgical evacuation of haematomas and available contusions is a component of the Lund Concept, like other guidelines. The Lund Concept means optimal treatment to all head injured patients independent of age, degree of autoregulation, severity of the injury and ICP.

References


223

Inotropes and vasopressors for hemodynamic support during septic shock

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Despite widespread use of sympathomimetic and dopaminergic drugs in septic shock, their effects on microcirculatory blood flow in the gastrointestinal tract are still not well known. Reliable outcome data are not available and the level of evidence for recommendations is low. At the present time the recommended first-line vasopressors and inotropes in septic shock are norepinephrine and dobutamine in contrast to epinephrine and dopamine described by other authors. Despite controversial reports, dopamine is also recommended.

The pathogenesis of microcirculatory dysfunction in septic shock is known to be multifactorial and includes, in addition to circulatory failure, also endothelial damage, impaired vascular reactivity, microthrombosis and more. The access to the microcirculation cannot be predicted from systemic or hemodynamic data alone. However, treatment-induced effects on the microcirculation cannot be predicted from systemic or even regional hemodynamics alone.

Goal directed therapy of a mismatch between oxygen delivery and consumption during early septic shock has been shown to improve outcome. This finding suggests, that correction of circulatory failure might be effective for the resuscitation of the microcirculation. However, increasing systemic oxygen delivery above normal levels failed to improve outcome. A concept that is supported by a recently published animal study. In a porcine model of septic shock, dopamine, doxepamine and dobutamine significantly increased cardiac index. At the same time, superior mesenteric artery flow increased only with dopamine and doxepamine, whereas it did not change with dobutamine. Microcirculatory blood flow in the gastrointestinal tract remained unchanged with all three drugs.

Similarly, published data suggest that although a sufficient perfusion pressure is important to preserve organ function, higher blood pressure is not always better. The hypothesis...
that a “moderate” correction of arterial hypotension improves organ perfusion is further supported by a study of endotoxic shock in a porcine model. Increasing mean arterial blood pressure by 10 mmHg resulted in improved systemic, portal and jejunal mucosal blood flow. Systemic oxygen extraction increased and metabolic acidosis was stabilized. A further increase of arterial blood pressure was not beneficial in another normo-vascular and tissue oxygenation.

References

224 Vasopressin in septic shock

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Vasopressin is a small neurohypophyseal polypeptide, also known as antidiuretic hormone, which main physiologic role is to regulate water and solute excretion by the kidney (1). Under normal physiologic conditions vasopressin has very little effects on blood pressure, but in shock vasopressin levels increase by 10–200 times the normal physiologic levels and causes vasoconstriction of both arteries and veins (1). In addition, it has haemodynamic and thermoregulatory effects, and it stimulates ACTH release. Vasopressin has also been used as a drug – earlier to treat bleeding oesophageal varices – but more recently to raise blood pressure in septic shock (2–4) and augment coronary blood flow during cardiac pulmonary resuscitation (5).

Physiologic effects of vasopressin

There are several vasopressin-receptor subtypes known in humans and it is important to understand that location, distribution and density of vasopressin receptors account for many of the effects of vasopressin in septic shock patients. The most important being the V1-receptors, the vascular receptors, which are located on vascular smooth muscle and mediate vasoconstriction. V1-receptor activation mediates vasoconstriction through receptor-coupled activation of phospholipase C and release of Ca++ from intracellular stores (phosphoinositide cascade) (1,6,7). Distribution of V1 receptors is quite heterogeneous in the systemic vasculature (8). For example it has been shown in experimental septic shock that vasopressin decreases superior mesenteric artery blood flow and portal blood flow while hepatic artery blood flow is increased (9). The V2-receptors, which cause antidiuretic effects of vasopressin are located in the kidney and have main function of osmoregulation and maintenance of normovolema during normal physiologic conditions (1,6,7). The V2 receptors interact with adenyl cyclase to increase intracellular cAMP which causes water retention. V3 pituitary receptors increase ACTH production and the OTR (oxytocin) receptors have been found in the uterus (cause uterus contraction at term) and in the endothelium in some vascular beds such as the pulmonary artery (vasodilatory response via stimulation of the NO pathway) (1,6,10).
Under normal physiologic conditions vasopressin has little effects on blood pressure. The sympathetic nervous system, the renin angiotensin system and natriuretic peptide account mostly for the normal blood pressure and blood volume control (1,6,7,10). Thus, when central venous pressure falls norepinephrine and renin are released. Only with strong stimulus from the baroreceptors vasopressin is released in high doses, which stimulates vascular smooth muscle. In addition, vasopressin, at low plasma concentrations, mediates vasodilation in coronary, cerebral, and pulmonary arterial circulations (1).

Renal effects of vasopressin are stimulated through osmotic receptors and the effect is on permeability of water in the renal collecting duct. Plasma concentrations of vasopressin during normal conditions are approximately 1–6 pmol/L (renal effects) while in shock vasopressin concentrations of up to 200 pmol/L (vascular effects) have been recorded. Vasopressin is released through by biphase response in septic shock. In early shock high levels of vasopressin are transiently released presumably to defend organ perfusion. In late septic shock plasma levels of vasopressin fall again to very low levels compared to other causes of hypotension (2,6,11).

What is the theoretical rational of using vasopressin in septic shock? Failure of vascular smooth muscle to constrict is a prominent feature of septic shock (10). Despite that plasma catecholamine concentrations are high and renin angiotensin system is activated as well (10). Vasopressin concentrations on the other hand are usually low in established septic shock (2,12). Infusion of 0.01–0.04 U/min of vasopressin in septic shock patients increases vasopressin levels to physiologic shock levels (2,11,12). These plasma levels usually increase systemic blood pressure and reduce need for other vasopressors (2,11,12). Vasopressin restores vascular tone in catecholamine-resistant shock states by several mechanisms (10) including activation of V1 receptors, modulation of K$_{ATP}$ channels, modulation of nitric oxide, and potentiation of adrenergic and other vasoconstrictor agents (2,10–12).

What is the clinical rational of using vasopressin in septic shock? There are several clinical studies done on patients in septic shock and in most of those studies vasopressin has increased arterial blood pressure and decreased the need of catecholamines, but decreased cardiac output (3,4,7,13). Most of these studies have been relatively small and focused on physiologic end points. However there are no clinical outcome studies available yet. In addition, there are known complications to the use of vasopressin such as skin ischemia, cardiac ischemia, liver ischemia, intestinal ischemia and possibly multiple organ failure (1,7,13–15). Therefore, one should use vasopressin with great caution in septic shock.

Conclusion
Vasopressin increases blood pressure in septic shock and reduces need for other vasopressors. However, it significantly decreases cardiac output, oxygen delivery and gastrointestinal blood flow, which is of particular concern considering the frequent occurrence of multiple organ failure after septic shock. Thus, large placebo controlled clinical trials are needed to establish safety and usefulness of vasopressin administration in septic shock. Until such studies are available vasopressin should be used with great caution in septic shock and only as a second agent when high doses of norepinephrine are insufficient to reach acceptable perfusion pressure. Vasopressin should only be administered in a low physiologic shock dose of approximately 1–3 U/h (0.01–0.03 U/min) in adult patients while norepinephrine should be titrated to the desired blood pressure (7,12).

References

225
Manipulations with nitric oxide

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Severe sepsis is one of the most frequent causes of morbidity and mortality in critically ill patients (1). In sepsis, pathogens stimulate humoral and cellular components of innate host defense by releasing toxins, like lipopolysaccharide (LPS) of Gram-negative bacteria that binds to specific LPS-binding plasma protein and generates a molecule complex that reacts with toll-like receptors in the membranes of monocytes and macrophages. The complex stimulates transcriptional nuclear factors to express genes for synthesis of pro-inflammatory cytokines and chemokines, as well as eicosanoids, endothelins, reactive oxygen species, and nitric oxide (NO) (reviewed in 2).
Enzymatic oxidation of L-arginine by calcium- and calmodulin-dependent constitutive nitric oxide synthase (NOS), results in the generation of NO and citrulline. Constitutive NOS, which is mainly located in endothelial and neuronal cells, plays pivotal roles in blood pressure regulation and pre- and post-ganglionic signaling. In the effector cells, NO activates soluble guanylyl cyclase that converts guanosine triphosphate to cyclic guanosine monophosphate (cGMP). The NO/cGMP system mediates relaxation of vascular- and non-vascular smooth muscle by reducing free intracellular calcium and hyperpolarizing the cells through activation of potassium channels (3).

In septic shock, LPS and pro-inflammatory cytokines stimulate expression of calcium-independent inducible NOS (iNOS) to excessive generation of NO. A diversity of cells express iNOS, such as neutrophiles, macrophages, endothelial and epithelial cells, fibroblasts, smooth muscle cells, myocytes, and a variety of other cells. Excessively produced NO by iNOS causes cardio-vascular depression, diffuse endothelial injury, disorders of coagulation, impaired metabolism, and cytotoxic effects. Vasodilatation in response to nitric oxide is thought to be one of the main reasons for vascular hyporeactivity to norepinephrine in septic shock. Ultimately, these changes may escalate severe sepsis to multiple organ failure (2).

After entering the vascular lumen, NO is metabolized to nitrite and nitrate by oxy-hemoglobin, which is transformed to methemoglobin. Nitric oxide also interacts with superoxide radical (O2•−) forming peroxynitrite (ONOO−) with subsequent generation of nitric oxide dioxide and dinitrogen trioxide. The latter produces N-nitrosamines and S-nitrosothiols that modify activity of various receptors and ion channels. S-nitrosothiols may inactivate cellular redox systems and modulate transcription factors and signal transduction. Main cytotoxic effects of oxidation with ONOO− include membrane lipid peroxidation, injury to DNA and inhibition of mitochondrial function, cell apoptosis and inactivation of antioxidant defense. Protein-associated nitrotyrosine has been used as suitable marker of injury from derivatives of NO (4,5).

Ambiguity exists as to whether excessively generated NO should be modulated or not. Nitric oxide synthase is endogenously inhibited by asymmetric dimethylarginine (ADMA), which is synthesized by endothelial cells and competes with L-arginine about the same amino acid channel transporter (6). Early experiments on hyperdynamic sepsis indicated favorable effects of the iNOS inhibitors Nω-nitro-arginine methyl ester and L-ω-mono-methyl-arginine that reversed the hyperdynamic state and normalized extraction ratio of oxygen without decreasing consumption. Other investigators showed that animals receiving inhibitor either before or shortly after LPS, presented with exacerbation of vasoconstriction and hypotension, which resulted in a higher mortality (reviewed in 7). Discouraging results also have been reported by López et al. who randomized 797 patients with septic shock into a placebo-controlled double-blinded study of Nω-methyl-L-arginine hydrochloride, which was stopped prematurely because Day-28 mortality amounted to 59% in the treatment group vs. 49% in the placebo group. An objection against their work was, in some patients, a worsening of circulatory failure, which might have been partly caused by overcorrection of vascular tone (8).

Our own studies on endotoxemic sheep revealed that inhaled NO gas reduce lung microvascular pressure and fluid filtration, and improve oxygenation. In contrast, the NOS inhibitor aminoguanidine increased lung microvascular pressure, while extravascular lung water content (EVLW) remained unchanged from controls because lung lymph was removed faster in sheep subjected to inhibition of NOS (9). Surprisingly, the combined inhibitor of NOS and guanylyl cyclase, methylyxanthine (“methylene blue” – MB) improved cardiovascular dysfunction and, additionally, inhibited the early phase rise in cyclooxygenase products, which abolished the febrile response. Moreover, MB improved oxygenation and increased the lung lymph drainage during the late phase of endotoxemia (7).

Beneficial effects of continuously infused MB were confirmed in a randomized controlled clinical pilot study showing that MB counteracts myocardial depression reduces nitrate production and improves oxygenation at concurrent reduction of inotropic support in victims of septic shock (10). We hypothesized that further beneficial effects could be obtained by combining inhibition of NOS and cGMP by continuously infusing MB and inhaling NO gas. Experiments on endotoxemic sheep confirmed that the combination had favorable effects on EVLW, hemodynamics and gas exchange compared to controls, or either of the substances administered alone. Methemoglobin also decreased on exposure to the combination compared with inhaled NO alone (2). A clinical pilot study has been started where patients with septic shock complicated by acute lung injury are consecutively randomized to a study of the effect of the combination of inhaled NO and infused MB.

Conclusion. Ambiguity still exists as to whether manipulations with NO could be of benefit to victims of septic shock due to the fact that such manipulations may have different effects on outcome depending on a diversity of circumstances. It is likely, that complete inhibition of NOS does more harm than good, and it is conceivable, albeit not proven, that carefully applied inhibition of NOS can be beneficial in cases of excessively produced NO.

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226 Trauma team training: Where to start and where to go?
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The treatment of multiple trauma is a demanding challenge for any hospital. It is of major importance that the proper resuscitative measures are made in correct order, and that life threatening conditions are identified and treated accordingly. One of the most important parts of a trauma system or chain of survival, is the hospital trauma team. However, the focus is often on the individual trauma team member’s competency, but for the patient it is the sum of the trauma team’s concerted performance that matters. ATLS is regarded as the “gold standard” of trauma treatment, but this course is exclusively for the individual physicians. Therefore, it is not sufficient to just adopt the ATLS-course as the single measure for improving quality in trauma care. One also needs to improve the quality of the trauma team as a team.

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The safe and efficient treatment of severely injured patients relies on the multiprofessional team’s ability to interact optimally. In such situations time pressure and lack of information and experience are common constraints. The teams most often consist of persons that do not regularly work together. This requires not only practical skills and theoretical knowledge, but also leadership, clear communication and smooth co-operation (1). Modern medicine is very complicated, and the human factors tend to be forgotten in technology. Investigations have shown that the initial phase of trauma resuscitations is where most protocol deviations and treatment mishaps occur (2).

The investigations of errors in aviation have clearly shown that it is human factors and sub-optimal team co-operation that lead to disasters. Therefore the concept of crew resource management (CRM) has been developed to improve aviation safety by addressing the problems of leadership, communication, and co-operation (3). Table 1 lists some of the most important components of team functions. Of these components situational awareness is perhaps the most important, because knowing “what is going on right now” and hopefully “why” will influence the team’s ability to handle the current situation (4,5). The team leader’s skills in guiding the team and also the team’s ability for optimal function, is also a direct result of their communication capability. Some principles for good team communication have been described in human factors programs in medicine (6). Good team communication must be embedded in the organisations as a culture where effective teamwork and communication are recognised and supported by management. It must also be inaugurated so that doctors and nurses are instructed about inter-personal dynamics, medical errors and human factors. They must also be trained in the knowledge, skills and attitudes necessary for teamwork. Concepts about communication must further be reinforced and the team leader’s competences be further developed through repetition, because it cannot be delivered through a single lesson. Last but not least the effectiveness of communication training must be data-driven, which means that one must monitor the teams’ function. This is not easy, but can be achieved by carefully planning of a comprehensive program (4–6).

On this background we must design trauma team training programs that are both suited to the actual local situation and demands, and that can fulfill the above mentioned goals. In Scandinavia few hospitals get enough trauma cases to enable the trauma teams to perform optimally, just by doing the regular work. Training is the best way to make up for this gap between expected and actual experience. We have demonstrated that this has so far not been the case in Norway (7). On the other hand we have tried to use simulation as the main part of a national training program for improving trauma care (BEST: Better and systematic trauma care) (8).

Different types of simulator training are used in the training of doctors. Even though simulation as a learning method has been used in different areas e.g. aviation and nuclear power industry, it has only recently been taken into medical education. Modern simulation is a useful tool for improving healthcare quality and safe medical care. It is encouraged to copy this material, in order to arrange local training. The simulation case histories are based on real cases, with appropriate X-ray films and lab. results. After the course all educational material is left at the hospital. The hospital is encouraged to copy this material, in order to arrange local training. The Home page of the BEST-project gives a more detailed description of the project (8).

From our experience with more than 400 team simulator sessions (>2300 participants) all over Norway, it also important that the teams get feedback on their performance, and have the opportunity to have a second run in the simulator. This enables each individual team member to actually demonstrate some improvement, and in this way understand the use of such training.

However, simulation and debriefing is not so easy as it sounds. It requires a set of special skills. These skills, particularly the interpersonal and educational skills as well as course management skills, must be developed through deliberate training and are refined through experience and practise. One must be able to function as a facilitator in the educational environment of a simulation, and not just being an instructor or a specialist. One rule is to never let a team fail completely (e.g. loose the patient). Encouraging the team members to identify areas for improvement by themselves by asking the correct questions, rather than just judging them and giving verdicts, will also improve the educational experience for the participants (9).

As we know more about the importance of effective team function and the other parts of a comprehensive trauma system, one remaining factor still is the commitment to providing trauma treatment (10). This will always be the fundemental for high quality and safe medical care.

### References


<table>
<thead>
<tr>
<th>Table 1. The crucial components of optimal team function (4–6)</th>
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<tbody>
<tr>
<td><strong>Situational awareness</strong></td>
</tr>
<tr>
<td><strong>Problem identification</strong></td>
</tr>
<tr>
<td><strong>Decision-making</strong></td>
</tr>
<tr>
<td><strong>Workload distribution</strong></td>
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<tr>
<td><strong>Time management</strong></td>
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<tr>
<td><strong>Conflict resolution</strong></td>
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The BEST training program has now been tried locally in more than 80% of the Norwegian trauma hospitals. The training is done in each hospital’s trauma room using a standard resuscitation mannequin as a simulated patient. After a brief review of the emergency call to the medical dispatch centre, the team is given some minutes to plan and prepare for admitting the simulated patient. They use their own familiar team set-up and procedures, and all necessary disposable equipment. Each team member plays his own professional role. A short report from the “ambulance crew” can be given to the participants before the simulated patient arrives, to encourage preparations. The preparation and treatment of the simulated victim is video-recorded. During the simulation the facilitator will give the physiological data after each monitoring procedure is properly performed. After approx. 25–30 minutes, or when the team is ready to leave the emergency room, the facilitator stops the simulation. After the simulation the complete team is debriefed in a separate room (without observers), reviewing the video using a structured format. This session normally takes 30 minutes. A second simulation is then done with the same team, but with a new case. Debriefing is done again, and finally the team is encouraged to summarise areas of potential improvement discovered during the simulation. The simulation case histories are based on real cases, with appropriate X-ray films and lab. results. After the course all educational material is left at the hospital. The hospital is encouraged to copy this material, in order to arrange local training. The homepage of the BEST-project gives a more detailed description of the project (8).


www.bestnet.no


227

How to manage fluid therapy during cesarean section

Drebin D

Hypotension, defined as systolic pressure <90–100 mmHg or a ≥30% reduction in pressure, is a common side effect of spinal anesthesia in caesarian section. Preload administration has remained a cornerstone of prevention of hypotension. However, its reliability has been questioned, and a few have also abandoned preload administration. Volume deficit was early recognized to enhance hypotension during sympathetic blockade, and volume replacement lessened this response. Recommendations vary from the administration of large amounts of crystalloids or colloids, to the giving up that procedure and treat hypotension when it occurs using vasopressors instead. In a survey to determine the routines in practice, 87% of the responders stated that they routinely administered preload. The fluid of choice was Hartman’s solution, and about 1 liter was given. The left lateral position was used by 40% of the physicians, and ephedrine was the most common drug to treat hypotension when occurring, used by 95% of the physicians.

It was shown in 1965–1968 that rapid administration of intravenous fluid could partly restore uterine blood flow and hypotension (1–4). However, these sensational results have not been reproduced, although many investigations have been undertaken. The use of preload was later called into question because the preventive effect was inadequate and unpredictable. Administration of 1000 millilitres compared to 200 millilitres resulted in similar hemodynamic responses (5). In addition to its questionable effect, potential hazards from exaggerated fluid therapy, such as fluid accumulation in the lungs during puerperium (6) and increased postoperative mortality (7) brings the question up front.

Jackson R et al officially abandoned preload routine because of lack of efficiency of preload. They report that no difference in hemodynamics could be discerned when preload of 200 milliliters of crystalloid solution was compared to 1000 milliliters (5) A dose of 20 ml/kg of crystalloid solution reduced hypotension to 30%; hypotension occurred in 55% when no preload was given (8). The investigators concluded, “Though volume preload in the elective cesarean section is advocated, the requirement for a mandatory administration of a fixed volume before spinal anesthesia for urgent cases has been abandoned.” Increasing the dose to 30 milliliters produced no improvement, but reduced the colloid oncotic pressure (9). Colloids are slightly better to prevent hypotension, however, the effect is still not reliable enough to call for a mandatory use. The incidence of hypotension remains around 30% when colloid preload are used (10,11).

Colloid (volume support during the onset of anesthesia) was slightly better than preload in preventing hypotension (12), which is suggested to be a result of the volume effect of fluid being very short, most of the crystalloid volume effect is eliminated within 20 minutes (13). One patient group that are more circulatory stable than normal are the women with preeclampsia (14). In this state the blood volume is reduced, but fluid is even more promptly excreted as urine, and to some extent, fluid also escapes the vascular system to form edema (15).

Many ways to increase the efficiency of fluid have been explored. These comprise varying issues such as the span between the preload and the anesthesia, the amount and composition of the preload (crystalloid or colloid) hypertonic solutions, the influence of the spread of the anesthesia, the speed of onset of the block, the patient age, preanesthetic parameters such as elevated blood pressure and so forth. But the conclusion of a meta-analysis from 2001 is still valid (16): preload cannot fully prevent hypotension, but the incidence can be reduced from about 50% to 30%. To a certain degree, the effect seems to be dependent on the dose, and consequently colloids are more effective than crystalloids, but other strategies such as vasopressors or leg wrapping are necessary. Colloid preload might also reduce the incidence of nausea (17) and might shorten the recovery period.

A perfectly effective single routine management seems to be unattainable because the circulatory response is variable. Volume support can in a direct manner handle the relative hypovolemia that occurs from venous distension. However, the decline in systemic vascular resistance cannot be targeted with fluid therapy. To do so it would be necessary to elevate cardiac output to the same magnitude as the drop in resistance. This would probably require a volume expansion of several liters, which certainly would cause other side effects. Moreover, the persistence of the treatment must match the time coarse of the neural block.

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Phenylephrine or ephedrine for maternal hypotension?

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Ephedrine has been the most commonly used vasopressor in obstetric practice because of its sparing effect on uteroplacental perfusion found in animal experiments (1). This effect has been explained by its partial β-agonism that increases cardiac output (1) and by its decreased tendency to constrict uterine arteries during pregnancy due to increased NO-activity (2). Vasopressors possessing more α-adrenergic activity have previously been avoided in obstetrics because experimental data suggest that they may compromise uterine blood flow (1–2). Ephedrine has, however, been recently associated with lower umbilical artery pH values compared with phenylephrine, which is a pure α-agonist, when used for the prevention or treatment of maternal hypotension during elective Caesarean delivery under spinal anaesthesia in uncomplicated, term pregnancies (3–5). In addition, the efficacy of prophylactic ephedrine in preventing maternal hypotension seems to be of limited value (3,6), whereas a combination of ephedrine and phenylephrine or phenylephrine alone may be more effective (3,7). Furthermore, the incidence of maternal nausea and vomiting seems to be higher with ephedrine than with phenylephrine (3–4). On the basis of these clinical findings, phenylephrine has been suggested as the first-line treatment strategy for maternal hypotension (7).

It has been suggested that increased fetal metabolic rate secondary to β-adrenergic stimulation is the mechanism for lower umbilical artery pH values with ephedrine (4). If this is the case, it may be relevant to question whether the lowering of pH by ephedrine is of any harm, as fetal catecholamine stimulation before delivery may have some benefits (8). On the other hand, none of the vasopressor studies has shown any difference in neonatal clinical outcome.

It is also noteworthy that the use of phenylephrine has not been studied in complicated pregnancies. There are some animal data suggesting that during increased placental vascular resistance, the fetal effects of maternal phenylephrine treatment may be different from those in the case of normal placental function (9–10).

Conclusions

On the basis of recent clinical research, ephedrine can no longer be regarded as the self-evident vasopressor of choice in obstetrics, as none of the vasopressor studies has shown any difference in neonatal clinical outcome. During elective Caesarean delivery under spinal anaesthesia in uncomplicated, term pregnancies, phenylephrine may have some maternal and fetal benefits compared with ephedrine. Further research is, however, required on the use of phenylephrine during human fetal compromise.

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The pregnant patient with heart disease
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The haemodynamic changes of pregnancy have been well investigated, however, mostly in healthy women. In the woman with cardiac disease it is supposed, although less well studied, that these circulatory modifications go in the same direction and by and large to the same extent. During pregnancy, compared to the pre-pregnant state, cardiac output is increased up to 50%. This is achieved by an increase of stroke volume and, but to a lesser extent, by increased heart rate. During labour and delivery a further circulatory demand is superimposed.

Maternal heart disease may reduce the circulatory reserve making it difficult to adjust to these circulatory demands and, even if the woman does, her potential to cope with complications of pregnancy may be restricted. Cardiac assessment of the pregnant woman might be difficult because a number of symptoms and signs of a normal pregnancy imitates those of symptomatic heart disease. Fluid retention, tachypnoea, heart murmurs and syncope may all occur in normal pregnancies. In the woman with heart disease it is likely that the obstetrician underestimates and the cardiologist overestimates the significance of such symptoms.

The prevalence of heart disease in the reproductive female population ranges from 0.5 to 4%. Worldwide, rheumatic heart disease, particularly mitral stenosis, is the dominating lesion. However, in Europe and North America the decline in rheumatic heart disease and the success story of paediatric cardiology and heart surgery have changed this pattern. Congenital heart disease, very often surgically corrected, has become the most important category. New categories, like univentricular circulations, patients with prosthetic valves and many more have been formed. Our experience of pregnancy in these patients is limited, sometimes very scant.

High-risk conditions during pregnancy have been identified. They carry a maternal mortality risk up to 50%, morbidity is substantial and foetal outcome is jeopardised.
These high-risk conditions are:
- Severe pulmonary hypertension, irrespective if associated with a septal defect (Eisenmenger syndrome) or not.
- Severe left heart obstruction (aortic and mitral stenosis).
- Severe cyanotic heart disease.
- Marfan syndrome with aortic dilatation.
- Any cardiac disorder with poor functional class (NYHA III or IV).
- Severe coronary heart disease.
- Mechanical heart valve prostheses necessitating anticoagulant therapy.

The cardiologist has to inform the woman with heart disease about the prospects of a pregnancy and also on the risk of recurrence in the offspring. In certain conditions pregnancy should be discouraged and termination recommended if pregnancy has occurred.

Mendelian inheritance exists but is uncommon in congenital heart disease. However, compared to the normal population (risk = 0.8%) the woman with congenital heart disease faces a 4–15 fold increased risk of having a child with congenital heart disease.

The pregnant patient with heart disease should be managed by a medical team consisting of anaesthesiologists, cardiologists and obstetricians. The management of labour and delivery should be discussed and decided well in advance. By means of a “check-list document for labour and delivery” a structural management plan is provided.
PLENARY LECTURES

Hypertension in 2005: who should be cancelled?

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National surveys reveal incomplete detection, inadequate treatment and poor control of hypertension1. Yet, treatment of hypertension is effective in preventing long-term adverse outcome2. The same applies to isolated systolic hypertension (ISH)4.

Pathophysiology and complications of arterial hypertension

Hypertension causes end-organ damage resulting in increased morbidity and mortality. Patients with arterial hypertension may have an increase in cardiac output (younger age group), systemic vascular resistance (older subjects), or both. Vascular tone may be elevated because of enhanced α-adrenergic activity or increased release of angiotensin or endothelin. Several growth factors, including angiotensin and endothelin, increase the vascular muscle mass (vascular remodelling). The increased load on the left ventricle causes left ventricular hypertrophy: The autonomic nervous system, including baroreceptor sensitivity, the renin-angiotensin system, and the distribution of body fluids are altered in essential hypertension.

Complications of arterial hypertension

1. Left ventricular hypertrophy (LVH) impairs diastolic function and is an independent risk factor for cardiovascular disease, especially sudden death.
2. Heart failure generally starts as diastolic dysfunction and progresses to systolic failure and cardiac congestion.
3. Coronary artery disease is accelerated by chronic hypertension. Pressure-related increase in oxygen demand and decrease in coronary blood flow (caused by atheroma) contribute to ischaemic events. The widening of the pulse pressure is a strong predictor of coronary heart disease8.
4. Renal disease may take years to become evident.
5. Strokes may result from intracranial haemorrhage, thrombosis, or thrombo-embolism.

Long-term treatment of arterial hypertension

Life-style modification is essential and consists in moderate sodium restriction, weight reduction, decreased alcohol intake, and increased exercise. Anti-hypertensive drugs must decrease cardiac output or peripheral vascular resistance; they include: thiazide diuretics, β-blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor antagonists (ARA), calcium antagonists, α- and β-blockers, direct vasodilators, and centrally acting drugs (α2-adrenoceptors and imidazoline2-receptor agonists).

For patients with blood pressures within 140–159/90–99 mmHg, treatment is indicated if there is target organ damage or a ten year risk of coronary heart disease greater than 15%. Patients with blood pressures 160–199/100–109 mmHg should be treated unless it settles spontaneously to 140–159/90–99 mmHg and there is no target organ involvement. For patients with blood pressure higher than 180/110 mmHg treatment is always indicated8. The same applies to isolated systolic hypertension (ISH)4. Hypertensive disease in surgical patients

Arterial hypertension is a risk factor for cardiovascular complications of anaesthesia and surgery because of organ damage: coronary artery disease, cerebrovascular disease, left ventricular hypertrophy, and impaired renal function. Hypertension increases the risk of postoperative death and, as shown in a meta-analysis of observational studies, perioperative morbidity5.

Hypertensive patients are at risk of exaggerated hypotension at induction of anaesthesia, excessive pressor responses to laryngoscopy, endotracheal intubation and extubation, as well as hypertensive crises during the perioperative period. Hypertensive episodes are often associated with arrhythmias and/or myocardial ischaemia.

Intra-operative haemodynamic abnormalities are associated with peri- and postoperative cardiovascular events (cardiac death, myocardial infarction or stroke). As patients with uncontrolled hypertension often develop major haemodynamic abnormalities, preoperative treatment of hypertension is justified.

Management of preoperative hypertension: ideal versus empirical approaches

Treatment of hypertension, especially with β-blockers, renders the circulation more stable. Thus treatment of hypertension should be maintained throughout the perioperative period and all untreated hypertensive patients should be treated before elective surgery. However, this policy could cause a considerable number of deferrals of elective operations. This may not be associated with a significant reduction of the risk of complications, at least in patients with relatively mild hypertension. Thus, an empirical, approach based on the severity of the hypertension has developed. Patients with severe hypertension (stage 3: >180 mmHg and/or >110 mmHg) should be treated before elective surgery, a view endorsed by the 2002 ACC/AHA guideline6. For patients with moderate hypertension (stage 2: 160–179 mmHg/100–109 mmHg) treatment is recommended if there is target organ involvement. For those with mild hypertension (stage 1: 140–159 mmHg/90–99 mmHg) treatment is optional.

The major obstacle to agreed guidelines is that no study has, as yet, conclusively shown that treatment of hypertension significantly improves outcome. Most studies have not distinguished between history of hypertension, treated, and untreated hypertension. No study has subdivided patients into subgroups as a function of the severity of their hypertension. This may explain why hypertension is not always identified as a significant risk factor. In addition the level of admission blood pressure may not be critical for adverse outcome. Yet a linear relationship has been found between silent myocardial ischaemia and increasing admission blood pressure6.

Preoperative evaluation

There is a need to answer four questions:

1. Is hypertension primary or secondary? Pheochromocytoma, hyperaldosteronism, renal parenchymal hypertension, renovascular hypertension, or aortic coarctation must be excluded.
2. Is hypertension severe? This requires multiple blood pressure readings to distinguish “white coat” hypertension from sustained hypertension.
3. Are target organs involved? Target organ damage may require further investigations and/or treatment.

4. Are there anaesthetic implications of the anti-hypertensive medication?

**Diuretics.** Hypokalaemia raises the question of preoperative potassium replacement. Rapid normalisation of plasma potassium may worsen the transmembrane K+ gradient, thereby increasing the risk of arrhythmias13. However, electrophysiological indicators of hypokalaemia make slow replacement over 24–48 hours necessary.

**Beta-blockers** are well tolerated. They confer haemodynamic stability, reduce perioperative myocardial ischaemia12 and generally improve outcome13–14.

**Calcium channel blockers** do not exaggerate the hypotensive response to anaesthesia15.

**ACE inhibitors** may cause hypotension; some authors recommend omitting them on the morning of surgery. This practice, however, may increase the need for active management of hypertensive episodes15.

**Angiotensin receptor antagonists** are generally stopped the day before surgery because of the risk of severe hypotension during anaesthesia16,17.

**Alpha2-adrenoceptor agonists** provide haemodynamic stability by reducing sympathetically mediated increase in peripheral vascular resistance. Clonidine causes anoxia and sedation. It decreases the need for inhalation anaesthetics, and improves the quality of regional anaesthesia. A recent study has shown clonidine to reduce the risk of adverse outcome15. Dexmedetomidine is more selective for α2-receptors than clonidine. It attenuates both haemodynamic and stress responses to surgery.

**Perioperative risks and their management**

Laryngeal spraying with local anaesthetics is generally ineffective in preventing the hypertensive response to laryngoscopy, intubation and extubation. Beta-blockers (including esmolol) confer protection. Intravenous bolus doses of phentolamine, glyceryltrinitrate, sodium nitroprusside, labetalol, and prostaglandin E1 are also effective. As hypertension is associated with tachycardia and myocardial ischaemia its prevention is necessary.

Severe perioperative hypertension is a major threat, especially increases of blood pressure in excess of about 20 to 30 per cent of the preoperative value. Consequences of pressure surges include bleeding from vascular suture lines, cerebrovascular haemorrhage, and myocardial ischaemia/infarction.

Perioperative hypertensive crises are generally caused by a sympathetically mediated increase in peripheral vascular resistance. The choice of antihypertensive agent depends upon the clinical scenario, i.e. whether there is tachycardia, myocardial ischaemia, cardiac failure, or renal functional impairment (Table 1).

**Conclusion**

Thirty years after the first detailed studies of the responses to anaesthesia of hypertensive patients, specific evidence-based guidelines for their preoperative management are still lacking. Better monitoring, better anaesthetic agents, and better recovery have made anaesthesia safer. Nevertheless, the availability of very effective drugs to control of hypertensive crises should not be taken as indication that proper preoperative preparation is no longer necessary. Devastating elevations in blood pressure can develop over 5–10 heart beats: no drug, even injected intravenously immediately can act quickly enough. Therefore surgery in patients with severe hypertension should be deferred in order to obtain good control. The same is true of patients with moderate hypertension and significant target organ involvement. This approach coupled with the availability of potent hypertensive agents makes it possible to reduce the risk of cardiovascular complications in surgical hypertensive patients.

Perioperative beta-blockade is increasingly advocated for patients with coronary artery disease presenting for anaesthesia and surgery. It may also offer better perioperative protection than other antihypertensive agents and should be considered, with adequate monitoring of the circulation.

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to examine the impact of genetic variability on disease charac-
genomics as “the use of genetic information from clinical studies
This three billion dollar undertaking was completed in an
The project provides a unique resource with tremendous
Ziegler and colleagues recently defined perioperative
decortication of a rapidly progressive parapneumonic effusion
its practitioners encounter all manner of patients, administer a
a sornucopia of pharmacologic agents, and care for the sickest of the
A sage opines that the sicker you are, the more genomics
matters. However, genomics will also shed useful light on the
preoperative, presymptomatic identification of genetic-based
risk factors for otherwise healthy patients. For example, preop-
erative genomic testing will facilitate pharmacogenomic identi-
fication of important variations in drug absorption, distribution,
transport (ADMET) as well as altered
dynamic variables and was the cause of death. This
24–72 h) and help the clinician focus appropriate
of the impact of genomics on perioperative care is all the more
impact of genomics may be a false sense of security and that investigators may overlook
potential benefits of applying tools such as genomic testing to
identify patients presymptomatically for perioperative risk or to
risk stratify those with life threatening illness, such as sepsis,
who present acutely to the ICU. Meiler and colleagues in a recent
commentary in the Anaesthesia Patient Safety Foundation Newslet-
er raised the issue of perioperative modulation of anesthetic
response and inflammation on long-term outcome. Genomic
screening and risk stratification regarding inflammatory
response might allow directed pre-emptive therapy resulting in
long-term improved outcome similar to perioperative beta-
blockade in high-risk patients.

Genomic testing
Future applications and the clinical impact of genomic testing
may be recognized in a previously healthy middle age female
who presents with community acquired pneumonia, septic
shock and purpura fulminans. Application of evolving genomic
technology will facilitate timely identification and sensitivity of
the infecting organism (within 2–4 h of admission as opposed to
the current 24–72 h) and help the clinician focus appropriate
antimicrobial therapy avoiding inadequate or inappropriate
treatment particularly in patients with resistant organisms.
Pharmacogenomic testing will allow recognition of variation in drug
action and metabolism for the patient who is likely to receive
10–20 medications during her ICU admission. Admission identification
of variations in inflammatory mediators is likely to lead
to identification of those at risk for a deleterious imbalance in the
pro-inflammatory and anti-inflammatory cascades. This
will hopefully allow tailored therapies that modulate host response
to improve outcome. For example, some patients may benefit
from cytokine inhibition or alteration in intrinsic coagulation.
Several days after ICU admission, this patient undergoes
decortication of a rapidly progressive parapneumonic effusion
that results in on-going pulmonary compromise. Perioperative
genomic testing further facilitates risk stratification for this
patient by identifying abnormalities in hemostasis, cardiac
pathologies, and anesthetic drug responsiveness. The sum of

Table 1 Goals of the Human Genome Project (http://www.ornl.gov/
si/techresources/Human_Genome/project/about.shtml)
- Identify all of the approximately 20,000-25,000 genes in human DNA
- Determine the sequences of the 3 billion chemical base pairs that make up human DNA
- Store this information in databases
- Improve tools for data analysis
- Transfer related technologies to the private sector
- Address the ethical, legal, and social issues that may arise from the project

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231
Perioperative genomics

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In 1990, the U.S. Department of Energy (DOE) and National
Institutes of Health (NIH) with international participation by at
least 18 other countries and multiple investigators, funded The
Human Genome Project. Project goals are outlined in table 1.
This three billion dollar undertaking was completed in an
accelerated fashion and published in 2003.

The modern anesthesiology practice on patient outcome. LaGasse
important given the recent re-examination of the impact of
moderate anesthesiology practice on patient outcomes. Young
and others have called into question data on morbidity and mor-
tality as it relates to our day-to-day practice. Concerns over
the overestimation in reduction of anesthetic mortality (often quoted
as <1:250,000) include worries that practitioners may have a
false sense of security and that investigators may overlook
the potential benefits of applying tools such as genomic testing to
identify patients presymptomatically for perioperative risk or to
risk stratify those with life threatening illness, such as sepsis,
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these applications allows individualization of care of this critically ill patient that.

Summary
Medical practice is undergoing accelerated evolution. The integrated combination of the completed human genome project with extensive database development and powerful statistical predictive tools, innovative imaging techniques, and rapid access to bioinformatics will change the face of perioperative medicine over the next several decades. Genomic tools will enhance presymptomatic diagnosis; make possible identification of pharmacogenetic characteristics that impact individual response to the plethora of perioperative medications such as sedatives (variation in the cytochrome p450 enzyme system), analgesics (opioid mu receptor variability and alteration in opiate metabolism), bronchodilators (altered adrenergic receptor responsiveness and beta agonist metabolism), neuromuscular blocking agents (butyrylcholinesterase activity), and cardiovascular drugs (differences in metabolism of beta-blockers, altered receptor function) to name a few; aid in the prediction of patient risk for anesthesia care and ICU outcomes; and facilitate research activities. These changes will result in increased individualization of patient care and hopefully improve outcomes and patient safety during the rigors of perioperative stress.

Keys to the successful incorporation of genomics in our practice include education, broader understanding of identifying the clinical validity and utility of genomic testing, and use of bioinformatics tools to properly apply these exciting and potentially powerful tools without unreasonable or unfounded expectations.

References

232

**Friends or foes – are general anesthetic drugs linked to long-term toxicity?**

**Peroumansky**

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A common assumption shared by the majority of health care professionals is that general anesthetics induce a temporary state of unconsciousness accompanied by amnesia and a suppression of reflexes in response to even the most noxious stimuli that is fully reversible upon wash-out of the drugs. Implicit in this assumption is also the notion that once the drugs have been cleared, the body typically returns to the same state as it has been before anesthesia.

The purpose of this talk is to draw your attention to recent research that seriously challenges this benign view. Laboratory evidence on multiple levels indicates that numerous organ systems are affected by anesthetics and that some alterations persist after the complete removal of the drug. The question is not whether these changes do occur but whether they have any identifiable impact. Clinical studies have been published that may serve as very preliminary evidence that long lasting effects may have clinically measurable consequences.

The recent discovery that volatile anesthetics can be cardioprotective if used in the appropriate way should make us aware that familiar drugs can have unexpected effects and that the we should be open to the possibility that many organ systems are subject to modulatory effects of general anesthetics beyond those that are obvious and that not all these effects may turn out to be beneficial.

Laboratory evidence of lasting changes in the central nervous system (CNS)

- Increased β-oligomerization of proteins after exposure to volatile anesthetics (1)
- Increased cytotoxicity of β-oligomers if combined with anesthetics in cultured cells (2)
- Brief exposure to desflurane causes changes in protein expression in the brain that far outlast the presence of the drug (2)
- Anesthetics induce neuronal degeneration in the developing brain, the effect of combined application of drugs acting via different mechanisms has more than additive effects (3)
- Neonatal exposure to anesthetic drugs has measurable effects on learning in adulthood (3)
- Exposure to adult/aged rats to inhalational anesthetics causes lasting impairments of spatial memory performance (4)

Laboratory evidence of lasting changes in the immune system

- Increased rates of apoptosis in peripheral lymphocytes after anesthetic exposure (5)
- Changes in the T-helper cell type ratio (6)
References


233

Anesthesia for laser surgery of the upper aerodigestive tract

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The use of the laser as a surgical instrument provides a minimally invasive approach to tumors and other pathological lesions of the upper aerodigestive tract. This is a collective term designating the oropharynx, hypopharynx, tongue, epiglottis and glottis, larynx and trachea. The laser beam allows one to operate in nearly inaccessible areas with extreme precision. The palette of operations ranges from pinpoint removal of vocal cord papillomas to major tumor resections. Laser surgery of laryngeal cancer can avoid laryngectomy with its socially stigmatizing tracheotomy (for review of the field, see [1]).

The properties that make the laser beam a useful surgical instrument also make it a potential risk for patient and operating room personnel, and the surgical use of lasers is therefore regulated by national agencies. Direct hits with the laser beam can ignite flammable materials, such as the endotracheal tube or surgical drapes, and even reflected beams can cause severe eye injury.

Anesthetic management of patients for laser surgery must accommodate the specific requirements of microlaryngoscopy, provide rapid and predictable recovery from deep anesthesia, secure the airway and provide adequate ventilation, and reduce the inherent risks to the patient [2]. The typical patient with a larynx tumor is a heavy smoker with chronic alcohol abuse [3]. These patients pose special problems for the anesthetist due to increased incidence of postoperative complications and cross-tolerance to opioids and hypnotics [4–6].

Airway management is a primary concern in ENT laser surgery, particularly when the larynx is involved. A cuffed endotracheal tube provides the best protection for the lower airway, but can interfere with surgical progress. The ET tube must be as small as possible to minimize obstruction and as large as possible for sufficient ventilation. In our experience, a 5 mm ID endotracheal tube is the narrowest that still permits one to deliver an adequate minute ventilation for an adult patient. Ventilation through a narrow endotracheal tube requires of the ventilatory mode: respiratory rate is reduced, expiratory time is increased and extrinsic PEEP is removed.

Special laser tubes with metal wrappings or entirely of metal are available that are designed to be flame retardant [7, 8]. All have the disadvantages of a larger outside diameter for the same inside diameter, and of a ten-fold higher price, without completely banishing the risk of laser-ignited fires. In some countries, the choice of these ET tubes is dictated by legal considerations. We use a tube that is more combustible and take particular precautions to avoid ET tube fires: positioning the tube as far as possible from the operating site, covering visible portions of the tube with wet pledgets, and keeping inspiratory oxygen concentration under the level required for sustained combustion.

Jet ventilation is an alternative to endotracheal intubation that might be useful under some circumstances. It use is not widespread, however, since it requires specialized equipment, offers...
little or no airway protection, and is associated with a high incidence of serious complications [9]. Certain operations in the glottis require removal of the ET tube and phases of apnea. This technique must be carefully coordinated between the surgeon and the anesthetist.

Microlaryngoscopy is an intense stimulus that persists without lessening to the end of the operation. Anesthesia must be kept at a deep plane until the laryngoscope is removed, yet still permit rapid awakening and recovery to ensure rapid turnover. Our preferred regimen is total intravenous anesthesia with propofol and remifentanil. Relaxation is only required for insertion of the endotracheal tube and positioning of the operating laryngoscope.

Most laser surgical procedures have a low postoperative pain potential, and adequate analgesia can usually be provide with timely administration of an NSAID and acetaminophen. Residual pain is manageable with small doses of an opioid.

References

234
Mechanisms of general anesthesia – current state and perspective
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More than 150 years after their introduction into clinical use, we still lack a comprehensive theory of general anesthetic action. In other words, we expose millions of people to drugs that cause fundamental changes in the organ that is central to our human identity without understanding what these drugs do in the human brain. We have identified a host of actions on the cellular and molecular level. Nevertheless, we do not understand which of these actions are necessary to achieve the desired behavioral aims (lack of awareness/unconsciousness/amnesia, immobility), which actions are unnecessary but harmless ‘side-effects’, and which actions, if any, may have long-lasting or delayed undesirable consequences.

It is impossible to concisely and inclusively summarize a whole field of research into the mechanism of action of general anesthetics in a single lecture. Therefore, the focus will be on milestones in the history of research, important current hypotheses and those directions in research that, in my opinion, are most likely to make substantial advances. The lecture is conceptually divided into three parts.

Part I: how did we get to where we are now?
The discovery by H. Meyer and E. Overton of the relationship between lipid solubility of anesthetics and their potency, has remained unchallenged until today. However, it has led the research community into the quest for the holy grail of a ‘unitary, lipid-based theory of anesthetic action’. After many decades of research and numerous elegant hypotheses based on the premise that lipid membranes were the site of action of general anesthetics, contradictions and inconsistencies became apparent. A lipid membrane-based hypothesis of anesthetic actions leading to the clinical anesthetic state has very few followers left. The preferred hypothesis today is ‘multiple protein-based’, and assumes that anesthetics bind to hydrophobic pockets on membrane proteins. N. Franks and the late W. Lieb published the pivotal experiments leading to this fundamental change in target search (from lipid membranes to membrane proteins) 21 years ago (1). As for the brain sites where general anesthesia is produced, the concept of MAC as a universal measure of anesthetic depth, introduced by Dr. Edmond Eger in the 1960s (2) provided an invaluable tool for research and clinical practice but may have led to the impression that all CNS aspects of the anesthetic state can be seen as a unitary phenomenon mediated by uniform mechanisms.

Part II: where are we now?
Currently, the anesthetic state is understood as being composed of multiple substrates each of which is achieved via distinct mechanisms at different sites in the brain (3). It is likely that a unitary state of general anesthesia (comprising all of the substrates) can be achieved by any anesthetic drug administered at an appropriately high concentration leading to an indiscriminate depression of the whole central nervous system, simultaneously affecting multiple pathways and, to some degree or other, every neuron in the brain and the spinal cord. This, however, requires high drug concentrations with all the potential sequelae. Therefore it is important to realize that the behavioral state of general anesthesia can be thought of as consisting of multiple components, each of which can be preferentially induced in a concentration and agent-specific manner employing individual cellular/molecular pathways in various brain areas. This potential selectivity is possible because general anesthetics interact with specific proteins at discrete sites. As an example of the highly selective potential of anesthetic drug interaction with proteins I will discuss the anesthetic binding site on the GABA$_A$ receptor and I will also present the current target-based classification of general anesthetics.

Part III: how do we get ahead?
• The pharmacologic approach: a. The introduction of the so-called non-anesthetics/non-immobilizers into the experimental paradigm looked very promising a decade ago (5). Non-anesthetics can be looked upon as ‘placebos’ that were supposed to separate relevant anesthetic effects from irrelevant ones. Non-anesthetics yielded some insights (e.g. the exclusion of nicotinic acetylcholine receptors from the list of mediators of immobility) but as their mechanisms of actions are also poorly, they must be used in very thoughtfully
Progress in the management of sepsis – the surviving sepsis campaign. How the management of sepsis has improved and will improve further

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Introduction

Sepsis is an acute condition that kills rapidly, and requires a combination of therapeutic approaches, since no single therapy is available. The management of sepsis in hospitals is significantly better today than it was 30 years ago. However, sepsis-associated mortality rates still remain unacceptably high, and we believe that we must work together to embrace new strategies in order to improve patient outcomes still further. The recent improvement in outcomes has been characterized by the successive introduction of multiple interventions and therapies and is an ongoing process. We believe that the current wave of clinical trial data relating to a number of new interventions should be viewed in the context of this trend towards ever-improving management of the condition.

Sepsis-associated mortality

Sepsis is an aggressive and multifactorial syndrome that has been ranked as the tenth-leading cause of death in the US. Data from the 1995 US Census showed that the condition accounted for approximately 236,000 deaths annually. Moreover, the actual number of deaths associated with the condition may be even higher than current estimates suggest. Patients usually die of sepsis during the course of an underlying disease, and deaths are often attributed to these conditions rather than to sepsis. Placebo-controlled trials, which provide the best benchmarks for assessing changes in mortality as new interventions are developed, suggest an overall mortality rate associated with sepsis of 28–50% at 28 days. This gives a picture only of mortality in patients admitted to ICU with sepsis. Such benchmarks are important when one considers that mortality rates of up to 80–90% have been observed in some institutions. This persistent, high mortality rate ranks sepsis alongside some of the biggest acute killers in hospital, namely AMI, stroke.

A recent meta-analysis revealed only a modest decrease in septic shock-induced mortality over the last 30 years, despite the successful implementation of therapeutic strategies; the authors suggested that this might be explained by a worsening risk profile amongst affected patients. Other data indicate that sepsis-induced mortality rates have remained the same or increased. Data also predict that the overall incidence of sepsis is increasing by approximately 1.5% per year. It thus appears that, without ongoing improvements in the way sepsis is managed, death rates from sepsis will increase.

Achieving mortality reductions in sepsis

Several important studies have been completed in recent years that have identified successful evidence-based therapeutic and disease management strategies for critically ill patients including those with sepsis. This research has expanded our understanding of the biochemistry of sepsis, improved definitions of sepsis, and enabled more rapid identification of sepsis patients and more successful treatment of underlying infections. Most importantly, for the first time, therapies have been developed that have shown consistent, positive effects on mortality. Currently available strategies for the management of sepsis patients include: timely patient identification and diagnosis; rapid identification of causative organisms; appropriate, timely antimicrobial therapy; improved ventilatory techniques (low-pressure ventilation); appropriate (goal-directed) hemodynamic support; targeted pharmacological therapies (drotrecogin alfa [activated]); immunological therapy; glycemic control (intensive insulin therapy); supportive nutrition; effective supportive therapies (prophylaxis against stress ulcers, administration of anticoagulants, dialysis); and patient management by highly qualified clinicians and nursing staff. These strategies have helped to reduce the incidence of infections, support failing organs and prevent complications. They demonstrate that reductions in mortality are achievable, and that an incremental, combination therapy-based approach is the key to diminishing sepsis-associated mortality.
Monitoring mortality rates

Most of the available data concerning the impact of new therapies, and developments in supportive care, have been derived from carefully conducted and controlled clinical trials. These results cannot always be applied evenly to everyday hospital populations, since mortality rates may vary widely, both between countries and between institutions. The increasing application of evidence-based medicine is crucial if effective strategies are to be implemented rapidly.

Many registries are ongoing around the globe to determine the efficacy of patient management strategies in reducing sepsis-associated mortality. These include: ANZICS (Australia/New Zealand); Cub’rea (France); GiViTi (Italy); ICNARC (UK); NICE (The Netherlands); Project Impact (USA); and SICS (Scotland). In addition, the following registries are currently being established: ERIC (Europe); CCRNet (Canada); SepNet (Germany); The PROGRESS Study (international); and SCCTG (Sweden).

Guidelines

The current literature on sepsis management has been analysed, using established evidence based medicine techniques, and this has resulted in the Surviving Sepsis Campaign (SSC) Guidelines. These guidelines are published in the March and April 2004 issues of the journals Critical Care Medicine and Intensive Care Medicine. These guidelines represent a historic event as they are endorsed by the following 11 societies: American Association of Critical-Care Nurses; American College of Chest Physicians; American College of Emergency Physicians; American Thoracic Society; Australian and New Zealand Intensive Care Society; European Society of Clinical Microbiology and Infectious Diseases; European Society of Intensive Care Medicine; European Respiratory Society; International Sepsis Forum; Surgical Infection Society; Society of Critical Care Medicine. These societies have come together to endorse evidence-graded guidelines designed to improve the outcome in severe sepsis.

The SSC was formed in 2002 as an initiative of ESICM, ISF, and SCCM, supported in part by unrestricted industry educational grants. Its mission is to document a significant reduction in mortality from sepsis within 5 years. The implementation of the SSC guidelines will represent a major step toward reaching that goal. Beginning early this year, the first step in implementing the document of these guidelines will be the initiation of a guidelines based “sepsis bundle” in the Institute of Healthcare Improvement collaborative. Similar bundles will be introduced in other hospital groups and in trials designed to demonstrate the efficacy of the guidelines in reducing sepsis mortality. Cost benefit analyses of the guideline introduction are also planned. The next progress report from the SSC will take place in Sicily in September.

References


236 Effects of restricted intravenous fluid therapy in colorectal surgery: outcome, physiological and hormonal changes


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Aim: The aim of this trial was to investigate the effect of a restricted intravenous fluid regimen versus a standard regimen on outcome and physiological changes in elective colorectal surgery.

Background: Two thousand five hundred and sixty colorectal resections are performed in Denmark each year due to colorectal cancer alone. Additional resections are performed for benign diseases. Complications following colorectal resection are unfortunately common and are reported in up to 69% of patients. Standard intravenous fluid therapy during operation causes a postoperative bodyweight increase of 3–7 kilogram. The possible influence of intravenous fluid volume on the development of complications is unknown, but associations between intraoperative fluid volume and complications as well as postoperative weight increase and mortality has been shown.

Methods: We performed a clinical randomised observer blinded multi centre trial. A total of 172 patients planned for colorectal
Plenary lectures

Resection were randomised to either a restricted or a standard intra- and postoperative intravenous fluid regimen. The restricted regimen was designed to maintain the patients body-weight unchanged throughout the time in hospital. The standard regimen followed current practice. The patients were followed-up for 30 days.

Results: Administered intravenous fluid volume, diuresis and weight changes are shown in figure 1.

Outcome: The restricted intravenous fluid regimen significantly reduced postoperative complications both by intention-to-treat (33% vs. 51%, \( P = 0.013 \)) and per-protocol (30% vs. 56%, \( P = 0.003 \)) analyses. Number of both cardio-pulmonary—(7% vs. 24%, \( P = 0.007 \)) and tissue-healing complications (16% vs. 31%, \( P = 0.04 \)) was significantly reduced. A dose–response relation between postoperative complication frequency and weight increase the day of operation was found (\( P < 0.001 \)). Four included patients died, all of cardiopulmonary complications 24%, \( P = 0.04 \) was significantly reduced. A dose–response relation between postoperative complication frequency and weight increase the day of operation was found (\( P < 0.001 \)). Four included patients died, all of cardiopulmonary complications and belonging to the standard group (\( P = 0.12; \) absolute risk reduction 5.6% (95% CI: 0.3–10.9%)).

Physiology: We found no significant differences in intra- or postoperative BP, HR, or administration of pressor substances between the groups. The trial had 95% power to determine a difference of 6 mmHg in systolic BP, 4 mmHg in diastolic BP and 7.6 heartbeats per min. Patients in the standard group showed potential deleterious physiological changes in the form of lower arterial pH, lower concentration of bicarbonate, negative base excess, decreased oxygen tension, and oxygen saturation in the immediate postoperative period compared to the patients in the restricted group. Furthermore, the standard fluid regimen caused haemodilution with lower concentrations of serum albumin and total-protein. Higher concentrations of serum-creatinine but not urea were found in the restricted group the day of operation, but no differences between the groups were found the following days. When analysed by AUC including the entire period of measurement s-creatinine and s-urea was similar between groups. One case of renal failure was observed in the standard group following sepsis. No differences in s-cortisol were found, but patients in the restricted group had higher s-aldosteron on postoperative day 1, 3, and 5.

Conclusion: In patients undergoing elective colorectal resection, restricted intravenous fluid therapy significantly reduced the postoperative complication rate and the risk of death. Hyperchloraemic acidity and haemodilution was avoided, while the aldosterone response was increased, but restricted fluid therapy did not influence BP, HR or the use of pressor substances. 7–9.

References

237

Update on chest trauma

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Physiologic derangements from chest injuries are multidimensional. The combination of pulmonary failure, hemorrhage, and cardiac failure, threatens tissue oxygenation by different mechanisms. Improvement in mortality from chest trauma during recent years has resulted from modern diagnostic techniques as well as surgical management strategies such as application of damage control principles.

Pneumothorax/hemothorax

Concerns about exacerbating spine injuries or producing adverse hemodynamic changes preclude obtaining a chest roentgenogram in the sitting position, in order to diagnose pneumothorax and to quantitate the hemothorax. Thus computed tomography of the chest may have to be added to routinely obtain supine chest x-rays. When a normal lung is imaged by a 3.5–7.5 MHz ultrasound probe, its motion and so-called "comet-tail" artifacts (multiple echodense spots) may be visual-
ized during respiratory excursions. In the presence of pneumothorax, neither of these signs may be observed in the ultrasound image.

Hemothorax may cause hemorrhagic shock, mediastinal shift, and airway management difficulties. The volume and rate of blood drained via a chest tube determines the necessity for thoracotomy (2). Other indications for emergency thoracotomy include significant hypotension and/or tachycardia, persistence of “white lung” on the chest x-ray in the presence of a properly placed chest tube, difficulty of ventilation, pericardial tamponade, massive air leak from the chest tube, and cardiac or great vessel injury.

**Flail chest**

Fracture of several ribs at two or more sites, or disarticulation of ribs from their cartilaginous attachment to the sternum in addition to a fracture produces a flail chest, which may result in arterial hypoxemia and/or hypercarbia. However the primary cause of morbidity and mortality after blunt chest trauma is severe pulmonary contusion rather than paradoxical movement of the chest wall (3). The pathology of lung contusion involves atelectasis, interstitial and intraalveolar hemorrhage, and alveolar disruption. Although these changes begin within a few minutes after injury, they may take up to 3–4 hours to complete. Thus chest roentgenograms and arterial blood gases should be expected to deteriorate gradually within the first few hours of injury (3).

Although arterial hypoxemia may precede radiographic abnormalities, it may not reflect the size of the contusion because of restriction of blood flow to the injured lung by hypoxic pulmonary vasoconstriction. A PaO₂/FIO₂ ratio <300 after the initial resuscitation phase is considered a risk factor for development of acute respiratory failure. Quantifying the contusion volume may have prognostic value; patients with contusion volumes greater than 20% of total lung volume are more likely to develop ARDS and pneumonia (4,5).

Early treatment aiming to decrease elastic recoil and the work of breathing is of utmost importance. This can best be accomplished by applying continuous positive airway pressure (CPAP) of 10–15 cm H₂O by face mask in spontaneously breathing patients without respiratory failure. Prophylactic use of tracheal intubation and mechanical ventilation is associated with an unacceptably high incidence of tracheobronchitis and pneumonia leading to sepsis, multiorgan failure, and death. At present, except in instances when tracheal intubation and mechanical ventilation are necessary (PaO₂ < 60 mmHg in room air, or <80 mmHg with supplemental O₂, and conditions other than thoracic injury), the vast majority of patients do well with CPAP. When impending respiratory failure indicates tracheal intubation, airway pressure release ventilation (APRV) may be a reasonable choice (6,7). Other ventilation maneuvers include differential lung ventilation via a double lumen endobronchial tube and high-frequency jet ventilation (HFJV) for bilateral severe contusions with life threatening hypoxemia (8).

Continuous epidural analgesia is the best pain management technique available for blunt chest trauma. Parenteral opioids, are less effective, multiple intercostal blocks are labor intensive and short lasting, and continuous thoracic paravertebral block, although described, awaits further clinical evaluation (9).

**Traumatic hemopericardium**

Traumatic hemopericardium can develop after both blunt and penetrating chest injuries and unlike chronic pericardial effusions, even small accumulations of blood result in cardiac tamponade. Inflow occlusion at the atrioventricular valves leads to decreased right ventricular filling. Evacuation of a small amount of blood from the pericardium by pericardiocentesis usually restores the blood pressure temporarily. Transthoracic or, in intubated patients without suspected esophageal injury, TEE can aid in diagnosing and evacuating the pericardial blood. Diastolic collapse, defined as approximation of the LV walls during dias-tole, is a sign of tamponade and is associated with a reduction in systemic blood pressure of 15–20% or more.

The characteristic clinical signs of chronic pericardial effusion are virtually useless in acute traumatic tamponade. Pulsus paradoxus refers to a greater than 10 mmHg decline in the systolic arterial pressure during inspiration in a spontaneously breathing patient, and is simply an exaggeration of the normal 3–6 mmHg respirophasic variation. It lacks specificity, as it can also occur in patients with uncomplicated hypovolemia. Furthermore, its absence does not exclude tamponade. A concurrent septal defect, severe left ventricular failure, or aortic regurgitation may preclude a paradoxical pulse. Radiographic and electrocardiographic findings are not specific, although ST segment elevation and diminished QRS voltage may be observed if significant pericardial blood accumulates. Electrical alternans—the phasic alternation of R wave amplitude—may be more specific but can also occur in patients with tension pneumothorax. Total electrical alternans (phasic alternation of P and R wave amplitudes), although rare, is considered a pathognomonic sign. Echocardiography is the most reliable tool as it can demonstrate the volume of pericardial blood and the presence of ventricular diastolic collapse. Diastolic collapse may be absent in patients with a hypertrophic ventricle or in those with high intraventricular pressures.

Pericardiocentesis with echocardiographic guidance or surgical drainage and intravascular volume restoration should preferably precede administration of any anesthetic. Unlike pleural blood, pericardial blood clots easily. Thus it may be possible to drain only a fraction of the pericardial fluid, but even this amount will produce significant hemodynamic improvement. If general anesthesia is to be induced before pericardial damage, it should be done after preparation and draping of the chest.

Drugs that decrease myocardial contractility or produce peripheral vasodilation may precipitate hemodynamic depression. Ketamine is the classical anesthetic induction agent, but even with this drug the blood pressure may deteriorate. Positive pressure ventilation should be carefully maintained with low airway pressures and without positive end-expiratory pressure (PEEP).

**Blunt Cardiac Trauma**

By definition blunt cardiac trauma encompasses a wide variety of pathologic conditions, including varying degrees of myocardial damage; coronary artery injury; cardiac free wall, interstitial or interventricular septal or valvular ruptures; and with impalement by a fractured sternum or rib, a penetrating injury from blunt trauma (10, 11). The term blunt cardiac injury (BCI), formerly called myocardial contusion, refers to myocardial damage involving myofibrillar disintegration, edema, bleeding, or necrosis that, depending on its severity, clinically presents as minor EKG or cardiac enzyme abnormalities, complex arrhythmias, or cardiac failure. Some of these abnormalities may be caused by myocardial injury from direct mechanical or indirectly as a result of coronary occlusion or exacerbation of preexisting coronary artery disease by the stress of trauma.

There is no gold standard to diagnose blunt cardiac trauma. However, EKG, blood concentration of troponin I, and echocardiography are important. Although delayed (>24 hours) appearance of serious EKG abnormalities may occur very rarely, it has been demonstrated that a normal EKG on admission virtually eliminates the risk of complications of blunt cardiac trauma and the need for further
evaluation, as long as the patient is hemodynamically stable, has no history of cardiac disease, is less than 55 years old, and does not have multiple injuries or significant chest wall trauma. In the presence of any of these compromising conditions, cardiac monitoring for at least 24 hours is indicated. Although serum creatine kinase (CK) and creatine kinase MB (CK-MB) determinations, have lost their value as diagnostic tests, troponin I is specific for cardiac muscle. However, negative CK-MB or Troponin I levels do not rule out clinically relevant BCI, because in many cardiac trauma patients, muscle disintegration is not significant enough to release detectable enzyme values. Yet even a small area of myocardial damage can cause arrhythmias if it is in a critical location.

Echocardiography provides information about myocardial function, cardiac structural abnormalities, cardiac preload, systolic cardiac function, and air embolism, helping in diagnosis and hemodynamic management of BCI (12). TEE is more valuable than transthoracic echocardiography (TTE) which has limited usefulness in mechanically ventilated patients, in those with pleural effusion or pneumothorax, and when placement of the patient in left lateral decubitus position is difficult. Depending on its type and extent, BCI can increase surgical risk. An increased incidence of intraoperative arrhythmias and hypotension has been reported in patients with preoperatively diagnosed myocardial contusion (13). In most patients, arrhythmias last no more than a few days (10,13). Ventricular wall motion abnormalities may persist for up to a year, but any increased risk of perioperative complications appears to last for no more than one month (10). An intracardiac thrombus complicating a myocardial contusion may be present for more than a year after injury, further emphasizing the need for preoperative echocardiography even well after the accident. Hypotension may be caused by hypovolemia, pump failure, or both. Pump failure is usually caused by right ventricular dysfunction exacerbated by increased pulmonary vascular resistance due to pulmonary contusion, aspiration of gastric contents, or acute respiratory distress syndrome. An initial right ventricular free wall dilatation may be followed by leftward ventricular septal shift, which alters the geometry and shortening of the left ventricle. Thus left ventricular filling pressures increase and the cardiac output decreases. This should by no means be a signal to decrease fluid loading. On the contrary, volume replacement should continue with concomitant use of inotropes and pulmonary vasodilators. Positive pressure ventilation may also be adjusted to minimize intrathoracic pressure and thus right ventricular afterload. High frequency jet ventilation with its relatively low mean airway pressure may be beneficial in these circumstances (10).

Traumatic thoracic aortic injury

Clinically, aortic injury should be suspected in chest trauma patients with unexplained hypotension, external signs of direct chest injury, pulse deficits between right and left arms or between upper and lower extremities, retrosternal or intercostal pain, hoarseness, systolic precordial flow murmurs, or lower extremity neurologic deficits. Only 20–30% of instances of mediastinal widening on chest films are associated with thoracic aortic injury. Other chest roentgenographic findings suggestive of aortic injury are blunted aortic contours, wide paraspinal interface, opacified pulmonary window, broad paratracheal stripe, displaced left main stem bronchus, rightward deviation of the esophagus and trachea, and left hemothorax. Contrast-enhanced spiral CT and multiplane TEE are highly accurate and have substantially decreased the need for aortography (12). These two techniques are equally capable of diagnosing subadventitial aortic injuries which require surgical intervention. Lesions of the intima and media, which can be treated conservatively but which may later result in pseudoaneurysm, and concomitant blunt cardiac injuries are much more likely to be detected by TEE than by CT (12).

Various perioperative clinical and anesthetic pitfalls during management of thoracic aortic injuries can be categorized as diagnostic pitfalls, airway management pitfalls, central line placement pitfalls, pitfalls related to the use of anesthetic drugs, and pitfalls related to spinal cord ischemia. Measures to circumvent these problems will be discussed. (15,16,17)

References

Postoperative delirium in the elderly

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Introduction
The population is aging. For example, in the United States, those over 65 years old comprise 12% of the population, yet account for one third of the health care expenditures and surgical procedures. Although medical, surgical and anesthetic advancements make perioperative care of the elderly relatively safe, the incidence of complications increases with age. Postoperative delirium (POD) is common in the elderly. The incidence may exceed 50% in certain surgical populations. This is significant because POD is associated with a variety of adverse postoperative outcomes, including increased length of hospital stay, mortality, major morbidity declining functional status, and, possibly, long-term cognitive decline.

Diagnosis
Delirium is a disturbance of fluctuating consciousness that develops over the course of hours to days. There is altered cognition or perception not due to dementia. In addition, there must be evidence that the condition is the result of a general medical condition. POD generally occurs on postoperative days 1–3. Thus, anesthesiologists often do not deal directly with it. However, proper perioperative care may play a role in modifying risk factors and prevention.

Clinical diagnosis of delirium can be challenging. The Confusion Assessment Method (CAM) is a useful instrument for the diagnosis of POD (see Figure). Nursing staff can easily administer the CAM. It requires little training and has sensitivity and specificity exceeding 90%. The CAM has also been modified for use in ventilated patients.

Pathophysiology and etiology
Putative mechanisms for POD include altered central nervous system oxidative metabolism, increased cortisol or other inflammatory mediators and embolic phenomena. The latter may be especially important in cardiac and orthopedic surgical patients. However, POD is likely multifactorial and the result of acute insults in vulnerable patients. Central nervous system changes associated with age make the elderly especially prone POD. These include decreases in brain mass and neuron density, less neurotransmitter production, and fewer receptors. Finally, the presence of age-related diseases, such as dementia, stroke, depression and alcoholism may play a role.

Risk factors for delirium in medical patients include age, preexisting cognitive impairment, depression, substance abuse, severe systemic illness, dehydration, and visual and auditory impairment. However, there are fewer data on POD. This is significant because there are at least two reasons why POD may be different than medical delirium. First, at admission, characteristics of medical and surgical patients differ. For example, nearly all patients hospitalized for medical reasons are acutely ill or suffer from exacerbations of chronic disease. In contrast, many operations are elective and patients have been managed to ensure optimal physical status prior to entering the hospital. Second, surgery and anesthesia represent a significant stress not present in medical patients. For example, the anesthetics and analgesics, and postsurgical pain may contribute significantly to POD.

Preoperative factors: Preoperative factors associated with POD include increased age and preexisting brain pathology, including mild cognitive impairment and dementia, depression, alcoholism, dementia, and stroke. Other predictors include decreased functional status, major electrolyte and metabolic derangements, withdrawal syndromes, and polypharmacy. Type of procedure is also an important predictor of delirium. Operations with a high likelihood of POD include (in descending order of frequency) hip fracture and aortic aneurysm repair, cardiac, other orthopedic, intrathoracic, intraperitoneal, and ophthalmological.

Intraoperative factors: Conventional wisdom is that POD is more often associated with general anesthesia (GA) than with regional anesthesia (RA). In theory, RA involves a lesser pharmacological insult to the brain. However, rates of POD are the same with either technique. Several classes of drugs commonly used in the operating room are associated with delirium. Benzodiazepines markedly increase the risk of POD. That these agents are often used for sedation during regional anesthesia may partially explain the similar rates of POD with RA and GA. Anticholinergic agents that cross the blood-brain barrier, such as atropine and scopolamine lead to POD by decreasing cholinergic neuron activity. Opioids are associated with delirium in medical patients, but, as a class, they are not associated with POD. However, perioperative use of opioids is ubiquitous and no study has adequately powered to address this issue. Meperidine is an exception – it is associated with POD, likely because its atropine-like structure leads to decreased brain cholinergic activity. Massive blood loss, the need for transfusion and marked electrolyte or glucose abnormalities are also associated with POD. However, it is unclear whether they induce POD or are merely indicators of sicker patients or more severe surgical insult. Finally, hypoxia and hypocarbia may precipitate POD by decreasing oxygen delivery to the brain.

Postoperative factors: Postoperative pain increases the risk POD. Interestingly, maximum pain and pain with movement are not predictive of delirium. Only rest pain is associated with POD. Little else is known about the postoperative risk factors for POD. However, in medical patients, in-hospital predictors of delirium include the use of physical restraints, malnutrition, the addition of three or more medications, the use of a urinary catheter and iatrogenic events such as volume overload, urinary tract infections, pressure ulcers, etc. Finally, discharging patients to home as early as possible reduces the risk of delirium.

Prevention and management
The first step in preventing POD is to identify those at risk. The preoperative visit should include a drug history and screening for depression, substance abuse and cognitive decline.
Intraoperatively, the specific anesthetic technique is probably less important than the care with which it is applied. Adequate oxygenation and perfusion should be maintained. When appropriate, patients should be normocarbic. Glucose and electrolyte...
abnormalities should be corrected. Benzodiazepines, centrally acting anticholinergics and meperidine are best avoided. In order to compensate for alterations in body composition and drug clearance that occur with aging, dosages should be altered and short-acting agents are preferred.

Postoperatively, pain should be treated aggressively while avoiding drugs associated with delirium. Patients should be reoriented frequently. Ambulation and mobilization should be encouraged. Patient should use their glasses and hearing aids. The environment should be conducive to normal sleep-wake cycles. Finally, adequate hydration should be provided. Patients should be discharged home as soon as possible.

POD may be the presenting symptom of a number of complications, including sepsis, urinary tract infections, myocardial infarction, stroke, pneumonia, etc. Thus, the first step in treating POD is to identify and treat organic causes. Measures should be taken to reorient the patient. If agitation is endangering the patient, haloperidol or atypical antipsychotics may be used. If the delirium is due to a withdrawal syndrome, beta-blockers, clonidine and benzodiazepines maybe indicated. (This is the only instance in which benzodiazepines are used for POD.) For alcohol withdrawal, thiamine should be administered also. Finally, psychosocial and occupational and physical therapy referrals will aid in functional rehabilitation.

References


HONORARY LECTURES

239 What has changed in my ICU during the past 25 years?
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Although 25 years is a very short time in the history of mankind it is a long time in the history of modern medicine and particularly so in the history of intensive care medicine. Even in the modern society there have been great changes since 1980. In 1980 there were no real computers, only word processors, and there were no cell phones and no Internet.

In hospital medicine we did not have CT scan or MRI and in anaesthesia and intensive care we did not yet have capnograph or pulse oxymeter, although these two devises had already been invented. My ICU opened 30 years ago in an ordinary surgical ward that had been renovated and changed to become an 11-bed ICU. The unit, although far from being spacious, had for the time modern cardiovascular monitors for invasive monitoring including Swan Ganz Catheters, as well as then modern Siemens Servo ventilators.

The unit was staffed with 12 positions for nurses and 6 positions for other staff.

It was a general ICU and although the majority of patients were surgical patients we also had medical patients and pediatric patients.

Today we are still in the same locality and even though it has recently been renovated it has not become bigger and now we only have room for 8 really sick ICU patients and 2 beds for intermediate care patients. It is still a general ICU but our patients are much sicker and older now. Those surgical patients we treated 25 years ago are now treated in the recovery room.

We have been through 6 generations of Servo ventilators and also 5 generations of cardiovascular monitors with all the updates, improvements and added parameters to monitor, which have been developed during the years.

The nursing staff has almost tripled compared to 25 years ago and there are mainly nurses now.

Nursing in Iceland is a university education and in addition there is a postgraduate degree in ICU nursing and anesthesia nursing. Thus the level of education of our nurses has very much improved, which of course has benefited the care of the patients.

Our goal is and always has been one nurse per ICU patient around the clock.

The treatment methods have changed with time and development in medicine including development of new drugs and equipment. Also there are more evidence based treatment methods now than 25 years ago.

Furthermore we have increased our endeavour to fulfill the psychosocial and spiritual needs as well as the medical needs of our patients and their relatives.

Finally, the macromedicine of last century is evolving into micromedicine of this century and the future. This must continue and it will carry us into an era beyond the human genome.

240 Organizing academic medicine
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In biology the obvious problem is if the hen or the egg came first? Concerning dynamic academic activities an organization cannot be planned ahead. It has to be tailored in order to fit the activity. It is not fruitful to build and structure the other way around.

Academic medicine equally concerns health care, education and research. Modern health care systems and financial restraints often finds food for thought and driving forces in organization technologies of which various modes are tested but only rarely evaluated. Frequent re-organizations have been carried out during the latest 10 to 15 years and a main goal has been cost cutting. This is all sound and good for lots of societal reasons but it has created situations in which the best interest of academic medicine, i.e. for the three equally important pillars, indeed has been challenged.

Academic medicine must be governed according to rules and guidelines other than those that apply for medical practice focused on health care productivity alone. In most Scandinavian countries education and research are led by the Ministry of Education whereas health care serves under the Ministry of Social Affairs. This creates basic problems and bureaucracy since various agreements and regulations will have to appear. In addition, if health care is decentralized into independent county councils while universities report directly to the Ministry, administration increases and mutual proposals have to fare long ways before decisions. In essence, this means that all parts of academic medicine preferably ought to be governed by the same Ministry. Furthermore, re-imbursement problems could be solved since academic medicine should be re-imbursed differently than health care services with no responsibilities for education and research.

The factors addressed above plus weakened financial resources for clinical research have resulted in a lesser impact relative to basic research and a falling position for clinical academic medicine in for instance Sweden compared with countries that strategically put more money into clinical research. Such circumstances are, however, the given facts we have to work with at any one time. Within these phrames several things can be achieved for the good of both medical care, education and research. In the following, short comments will be given on 6 different success indicators. They are:

- the population base
- identification of unique possibilities
- development of bio- and medical informatics
- bringing basic and clinical research closer
- develop multidisciplinary research activities
- establish core facilities and academic environments

The population base
What is known about the region you work in? Most likely the relative number of aging individuals will increase. What does this mean for you practice, your education and research. Since your academic hospital must educate and create new knowledge

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Honorary lectures

via research you must know the volume and mix of patients needed to fulfill the tasks of education and research. This means lots of patients with common diseases, acute medical problems and traumatology. In addition, you must also take responsibility, as a referral center on a national or Nordic basis, for highly specialized care and for the treatment and care of rare disorders.

Unique possibilities
These could be related to geography, local industries, or highly developed levels of knowledge and skills. Do benchmarking, self-assessments and ask for external revisions. Concentrate and Focus. Measure and analyze to identify your top activities. Are they high but slim and dependent on single individuals? Or are they both high and broadbased? Is the edge in a particular field on education? Research? Or a clinical profile? Ideally it should be edge activities in all three.

Bio- and medical informatics
The more than 50 years of outstanding development in molecular biology and molecular medicine have put medical research at a starting line where phenotyping (medical informatics) and genotyping/proteomics (bioinformatics) have just begun. The needs of informatics must be satisfied in future leading academic institutions. Which parts are suitable to develop on your own and how do you plan for partnerships? How are biobanks being linked together?

Merging basic and clinical research
In accordance with what has been said about informatics above neither basic medical nor clinical research can stand tall on their own anymore. Hence, future will allow only Medical Research linking researchers and educators with clinicians. The worldwide trend is clear. New biomedical centers are being built up in proximity to university hospitals or within the hospital campus itself.

Multi-disciplinary research
Not only is there a trend away from basic and clinical research into Medical research but there is also a most vital growing trend to crossfertilize with research ideas between physicists, chemists and medical researchers. In addition to this, humanistic and nursing sciences are relatively unexplored fields that most likely will have a great impact on medical sciences in the future.

Academic environments
Learning organizations like university hospitals must find a balance between health care productivity and academic productivity. Efficiency must go with fantasy and creativity. A major factor is time to do academic work. It is the most important. Another determining factor is a well-equipped institution with advanced core facilities to attract the best and a design with several places where to meet, discuss and interact.

Conclusion
Academic medicine must find a balance between health care and academic productivities. Leaders must be recruited that are capable of both clinical and academic leaderships. More and better positions must be created for research and academic work.
LATE ABSTRACTS

241
Extravascular lung water and lung aeration after oleic acid in sheep
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Aims: We compared extravascular lung water (EVLW) content, determined by transpulmonary single thermodilution (EVLWSTD) and thermal-dye dilution (EVLWTD) techniques, with lung aeration, as assessed by lung computed tomography (CT), before and after oleic acid (OA) induced acute lung injury (ALI) in sheep.

Methods: Nine yearling sheep were enrolled in a prospective study. Animals served as their own controls, and underwent CT before and after OA-induced ALI. OA was infused intravenously over 30 min (0.08 ml/kg). The overall duration of the study was 2 hrs. EVLWSTD and EVLWTD were determined by PiCCO-plus and COLD-Z021, respectively (Pulsion Medical Systems, Germany). We used linear regression analysis to evaluate the relationships between EVLWSTD, EVLWTD and volumes of well-, poorly and non-aerated lung tissue, respectively, as determined by Pulmo CT program (Siemens, Germany). P < 0.05 was regarded statistically significant.

Results: EVLWSTD and EVLWTD demonstrated a close agreement (r = 0.93, P < 0.05). After OA these variables increased by 85% and 155%, respectively (P < 0.05). In parallel, well-aerated lung volume declined by 48% whereas poorly-aerated and non-aerated volumes increased 3- and 5-fold, respectively (P < 0.05). Both EVLWSTD and EVLWTD correlated significantly with absolute volumes of well- (r = -0.64 and r = -0.60), poorly- (r = 0.54 and r = 0.58), and non-aerated (r = 0.56 and r = 0.62) lung volumes.

Conclusions: In OA-induced ALI, the rise in EVLW is associated with reduced well-aerated- and increased poorly- and non-aerated lung volumes. Thus, during ALI, accumulation of EVLW might contribute to lung congestion and atelectasis.

242
Artificial Blood, Current Perspectives
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To begin with, the terms “artificial blood” and “blood substitute” are both misnomers because current products intend to enhance the oxygen carrying capacity of blood or the platelets. This presentation will deal with products that increase the oxygen carrying capacity, because they offer a potentially greater market situation. An alternative term for these materials is oxygen therapeutics.

The desired properties of oxygen therapeutics are: oxygen carrying capacity, sufficient plasma retention time, uniform donor type, no vasoconstriction, no renal toxicity, no immunomodulation, and long shelf time. Moreover, it is important that the ingredients are rich in supply, and that the production cost is competitive.

Two main driving forces have led to the initiation of blood substitute programs: the military, which requires large volumes of blood at the site of causalities, and the medical community, which need products that are free for infectious agents. The public perception of the need for viral free materials escalated in 1982 with the first report of AIDS. However, the risk of an infection from blood transfusion is currently very low. The risk of transfusion-transmitted infection have been estimated to: for human Immune-deficiency virus, 1 in 493,000; for human T-cell lymphotropic virus, 1 in 64,000; for hepatitis C virus, 1 in 103,000; for hepatitis B virus 1 in 63,000 (1). One sterility check showed bacterial contamination in 0.6% of the packed red blood cell units (2). The risk of transferring miscellaneous infectious agents is very low, but the consequences are difficult to evaluate. A potential risk of transfused blood is blood type incompatibility, as a result of clerical error. Another major concern is the impending shortage of bank-blood. In the USA the number of transferred units increases at a rate far greater than donor collection.

There are two major classes of oxygen therapeutics, the hemoglobin based products and the perfluorocarbons emulsions. Perfluorocarbons are synthetic halogenated hydrocarbons originally designed to handle reactive uranium compounds. Perfluorocarbons have a limited oxygen carrying capacity because the need of a detergent markedly reduces their efficiency. Side effects include: hepatosplenomegali, flu-like symptoms, and a slight thrombocytopenia. Because of unfavorable outcomes, no perfluorocarbon is currently in clinical trial.

Many of the candidate solutions have been based on hemoglobin. Hemoglobin has an increased potential to load and unload significant amounts of oxygen within a small range of oxygen partial pressure due to the sigmoidal oxygen binding curve. However, several hemoglobin-based programs have been suspended because of adverse events in the treatment groups. The first large failure appeared in 1999, when an internal crosslinked αα-Hb showed increased mortality rates in a clinical trial on trauma victims. The protocol of this study has been criticized because the outcome could have been predicted by the pre clinical studies. These showed a marked vasoconstriction and by that, a reduced oxygen delivery (3).

The first testing of a crude hemoglobin solution to treat anemia was reported in 1916 (4), and in 1949 a desperate attempt to treat a severe post partum hemorrhage with cell a free hemoglobin solution was undertaken (5). The blood pressure returned promptly, but the patient died a few days later of renal failure. Cell free hemoglobin exerts a toxic effect when it is infused in the plasma. Side effects include systemic and pulmonary hypertension (due to vasoconstriction), bradycardia, renal failure, pancreatitis, abdominal pain, gastrointestinal dysfunction and jaundice. Residual red cell stroma contributes significantly to the side effects.

However, new purification methods are capable of eliminating cellular debris, which alleviates many of the toxic side effects. Molecular modification is still needed to prevent hemoglobin from degradation. Vasoconstriction remains as a hallmark pattern of the hemoglobin solutions. Therefore, the modifications are specifically designed in attempt to avoid vasoconstriction. However, the results vary and with few exceptions, mild to moderate vasoconstriction remains. The problem with vasoconstriction is that although the oxygen carrying capacity is increased with the hemoglobin content, the drop in cardiac output causes a reduction in oxygen delivery.
Late Abstracts

For these products, no immunomodulation is expected, because the cellular and plasma components of blood are removed during manufacturing, and they can be used uniformly independent of the recipient blood type. Hemoglobin can be harvested from outdated human bank-blood and animals, and hemoglobin can also be produced using recombinant technique.

Hemoglobin is a tetramer that normally is protected from breakdown within the red cell. When hemoglobin is transfused the molecule is rapidly degraded into αβ dimers and monomers (6). These can be readily diuresed or further degraded. There are several methods to stabilize hemoglobin: formation of lipid vesicles, αα-crosslinking, polymerization or surface decoration with larger molecules such as polyethylene glycol or dextran.

Lipid vesicles are complicated and expensive to produce and have a short half-life. Crosslinking is a covalent bridging of the dimers. Polymerization of hemoglobin is achieved by linking the αβ dimers by chemical or physical means, such as gluteraldehyde. Surface-modified hemoglobins are conjugates of hemoglobin and large molecules such as polyethylene glycol or dextran. The cell free hemoglobins are only a fraction of the size of a red cell and can penetrate more efficiently along the capillaries, pass obstructions such as blood clots, clogged arteries and fat emboli to oxygenate cells (7).

It was originally believed that the levels of hemoglobin concentration, oxygen affinity, and oncotic pressure should be like that of blood, while the viscosity should be closer to that of water. However, this view has been challenged (7, 8). A new theory of targeted O2 release is proposed by Intaglietta M, Winslow RM et al. (9). In essence, it is the availability of oxygen of the entire microcirculation that needs to be copied, and not the p50 alone.

The rate limiting step for the transport of oxygen from the red cell to the tissue is when oxygen leaves the red cell to enter the plasma.

During normal conditions, the exit of oxygen from a red cell consumes a significant fraction of the pO2-gradient. The remaining gradient drives oxygen to its final destination at a normal rate. In the presence of plasma hemoglobin, however, the release of oxygen to the plasma is facilitated because a “receiver” adjacent to the red cell can catch the oxygen. Hence a smaller fraction of the pO2-gradient is consumed. Now the unusually high pO2-gradient is consumed. Now the unusually high release of oxygen to the plasma is facilitated because a “receiver” adjacent to the red cell can catch the oxygen. Hence a smaller fraction of the pO2-gradient is consumed. The remaining gradient drives oxygen to its final destination at a normal rate.

The result is that oxygen becomes highly available at the endothelium, which results in precapillary vasodistraction. A high oxygen affinity and a maintained viscosity counteract these events: the high affinity slows the rate of oxygen release from the plasma closer to normal levels, while the viscosity contributes to vasodilation by a shear stress induced nitric oxide oxide release. The result is that closure of capillaries is avoided.

Plasma hemoglobin interferes with some laboratory tests. This calls for a close communication with the regional laboratory before any material can be used. The half-life of most materials is still far from the half-life of red cells (120 days), and ranges between 0.5-2 days. It is nevertheless suggested to be sufficient during surgery and emergency resuscitation (7). The iron load must be considered if repeated dosing is required.

Recombinant human erythropoietin has been suggested to be used to reduce transfusion. However, a cost estimate to avoid one transfusion related fatal event was calculated at $72 million, and avoidance of one adverse event at $4.7 million (10).

Roughly 50% of the red cells are used for treatment of anemia of varying etiologies, and the remainder in surgery and trauma. When anticipating were blood substitutes will be used, we tend to look on were bank-blood is used, while the principal end point in clinical trials is the reduction in the requirement of bank-blood. But, seeing that new materials have other properties than blood, they might well be used to treat other conditions than anemia, for example to oxygenate ischemic tissue, or to increase oxygenation of solid to tumors to improve radiosensitivity (11).

For almost a decade, investigators have optimistically anticipated that blood substitutes will be available within a few years. It is not too surprising that many programs have been suspended since discontinuation are commonplace in the pharmaceutical development arena: the rate of a subsequent failure of a phase 1 candidate drug is roughly 50%. Success depends on a delicate balance between effects, side effects, the market, and specific beneficial new properties, and manufacturing costs.

References