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ABSTRACTS

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VERBAL PRESENTATIONS

Learning during surgery

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Although learning during anaesthesia has been demonstrated,[1] there is little consistency in findings across studies. One intriguing suggestion is that surgery appears to facilitate learning.[2] Clinical studies using patients have found learning[3] whereas attempts to replicate these findings in volunteers using lower doses of anaesthetic have been unsuccessful.[4] We tested the prediction that surgery would facilitate learning. Sixty-four patients (35 male, 29 female; mean age 42 yr) were recruited. All patients were ASA physical status 1 undergoing day surgery.

Patients received a standardized anaesthetic consisting of fentanyl 1.5 μg kg^{-1} and then propofol target controlled infusion ranging from 4.53 to 8.54 μg ml^{-1}. Patients breathed 66% nitrous oxide and 33% oxygen spontaneously through a laryngeal mask.

Each patient was assigned randomly to preoperative or intraoperative word presentation. Preoperative word presentation took place after induction and once anaesthetic maintenance was commenced; intraoperative presentation started upon first surgical incision. Word presentation comprised an auditory list of 14 words**,** during which BIS and anaesthetic variables were recorded at 1 min intervals. Implicit and explicit memory were tested on recovery by word stem completion and recognition tests, respectively (Table 1).

No patient had spontaneous recollection of surgical events. Patients in the intraoperative study group responded significantly above baseline on the implicit memory test. In contrast, the preoperative study group did not perform above baseline. Mean BIS did not differ between groups. We conclude that surgery may facilitate learning during anaesthesia.

Keywords: memory; anaesthesia

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Making explicit anaesthetic expertise: methodological consideration and subjects' perceptions

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Knowledge in anaesthesia, as in other practical fields, involves two manifestations: the *explicit*, public knowledge found in textbooks and journals and the *tacit*, personal knowledge gained from experience. Shifts towards competency-based training in anaesthesia risk losing sight of the tacit aspects of anaesthetic knowledge,[1] as they cannot be quantified or standardized.

Table 1 Mean anaesthetic measurements during stimulus presentation and postoperative implicit and explicit memory scores for preoperative and intraoperative study groups; *95% Confidence Interval

	Surgery duration (min)	BIS	Pulse	Mean BP	E'_{CO_2} kPa	RR	TCI μg ml^{-1}	Implicit memory mean (CI)*	Explicit memory mean (CI)*
Pre	31	39.8	66	69	6.8	9	5.2	0.02 (–0.04 to 0.1)	0.01 (–0.03 to 0.06)
Intra	36	43.6	72	75	6.7	15	5.8	0.08 (0.01 to 0.15)	0.00 (–0.02 to 0.03)

The study was designed to explore these two facets of knowledge by studying anaesthetic work in natural (rather than experimental) settings.[2] Two approaches were used. First, anaesthetists were observed at work in theatre, by an 'insider' (former anaesthetic nurse) and 'outsiders' (sociologists). The field notes were then transcribed and the text analysed for recurring themes, phrases, and patterns of behaviour. Where possible, debriefing interviews were conducted after the observation. Second, we conducted semi-structured interviews with anaesthetists, operating department practitioners, and recovery nurses, allowing us to explore the previously identified themes in more detail. We are also using these to seek participants' views about being observed and researched in this way.

None of our participating staff had ever been the subject of research. Some were initially reluctant to be observed, but none refused. To date, 25 anaesthetists (at various grades) have been observed and 16 anaesthetic staff (medical, nursing, and support) have been interviewed. Some of the richest data have been provided by observing trainee anaesthetists at work, but there are particular issues in dealing with these data, which touch on the role of the research, the relationship between the research subjects and the research team and confidentiality. We spent considerable time before the study started ensuring that anaesthetists knew the research team and understood the aims of the study. Possible concerns about the use of the data were assuaged by anonymizing transcripts and frequent feeding back of findings at open 'data workshops' and through individual debriefing. To date the anaesthetists have related positively to feedback about the emerging themes.

These research methods are valid and have long been used in other fields. The use of insider and outsider researchers has not caused problems, and there have been few discordant interpretations of the data. Nonetheless some methodological issues remain unresolved. What is the impact of observation on what is being observed? How far can the findings from this single group of practitioners be applied to others? How should the analysis deal with discrepancies between interview accounts ('post hoc' rationalizations) and observational data, particularly as tacit knowledge, by definition, cannot easily be articulated.

Acknowledgements: We would like to thank all participating staff. The study 'The problem of expertise in anaesthesia' is funded by the North West Regional R&D Fund (RDO/28/3/05).

Keywords: anaesthesia, competence; research, qualitative

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Clinically relevent concentrations of propfol for *in vitro* studies

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It is often assumed that results obtained in *in vitro* studies will have some clinical relevance if the perfusing concentration is close to the concentration observed in blood *in vivo.* A heart tissue:blood propofol concentration ratio close to unity has been noted *in vivo* in rats[1] but tissue:organ bath ratios have not been measured. This study was designed to measure the uptake of propofol by the isolated rat heart *in vitro* from buffered aqueous solution and to study the effect of serum albumin on this uptake.

Table 2 Mean (SD) propofol concentrations ($\mu g\,ml^{-1}$ or $mg\ g^{-1}$) and partition coefficient (λ) after 75 min equilibration. n=6; *P<0.001 *vs* propofol ; **P<0.001 *vs* 2% BSA

	Propofol	Propofol+2% BSA	Propofol+4% BSA
Reservoir	5.09 (2.21)	5.30 (1.34)	7.64 (2.43)
Aortic cannula	3.66 (2.81)	3.73 (1.27)	6.85 (2.57)
Outflow	3.58 (2.19)	3.57 (1.43)	6.82 (2.16)
Heart tissue	93.66 (26.15)	48.68 (8.05)*	27.41 (6.96)*, **
l Heart/Outflow	37.1 (11.2)	16.9 (10.2)*	4.5 (2.2)*, **

Hearts were obtained from female Wistar rats killed by stunning and exsanguination. The heart was mounted in a Langendorff apparatus and perfused at 37°C with Krebs–Henseleit (KH) solution with propofol 10 $mg\,ml^{-1}$ (group 1), propofol 10 $mg\,ml^{-1}$+bovine serum albumin (BSA) 2% (group 2), propofol 10 $mg\,ml^{-1}$+BSA 4% (group 3) or intralipid. Samples of perfusate were collected from the reservoir, the cannula as it entered the aorta, and at the outflow from the glass chamber. Samples were taken before and 5, 15, 30, 45, 60, and 75 min after switching to a test perfusate. After 75 min, the hearts were removed, weighed and frozen at –20°C until analysis for propofol concentration by high performance liquid chromatography.[2]

Propofol concentrations in heart tissue perfused with the addition of BSA were significantly lower than those perfused with propofol alone (Table 2). After 75 min equilibration the propofol concentration in outflow perfusate was reduced to 40–70% of the nominal concentration. Heart/outflow partition coefficients were greatly influenced by the addition of BSA. These results indicate that, in the absence of added protein in *in vitro* test systems, propofol perfusate concentrations, equivalent to plasma concentrations in man, may achieve tissue propofol concentrations greatly in excess of tissue concentrations resulting from equilibration between blood and tissues *in vivo.*

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Keywords: anaesthetics i.v., propofol; model, *in vitro* validation

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Effect of intubation with and without opioids on the subcortical somatosensory evoked response

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Evoked responses usually decrease with increasing anaesthetic depth, and increase with noxious stimuli. These changes are obtunded by opioids. Previous work using desflurane, sevoflurane, and propofol at steady state concentrations has revealed an increase in P_{15}-N_{20} amplitude with increasing anaesthetic depth.[1 2] Using intubation as a reproducible stimulus, we have investigated its effect on the P_{15}-N_{20}, N_{20}-P_{25} and P_{25}-N_{35} amplitudes of the

somatosensory evoked response (SER). These amplitudes represent activity in the pons/thalamus, thalamus/primary sensory cortex, and sensory cortex, respectively.[3]

Eighteen patients aged 27–71 yr were recruited. After induction with sevoflurane in oxygen, vecuronium 0.1 mg kg^{-1} was given and the subjects were ventilated to normocapnoea via a laryngeal mask airway.† After 20 min of anaesthesia maintained at 3% sevoflurane end-tidal, the subjects were randomized to receive alfentanil 50 μg kg^{-1} or saline as a bolus, and intubated 60 s later. The median nerve was stimulated at the wrist with an electrical pulse delivered at a rate of 2.2 s^{-1}, and at intensity above the motor threshold. The SER was derived from the electroencephalogram (EEG) and recorded using electrodes at Fz and C_3. SER data corresponding to 2.6 min blocks at steady state and immediately after intubation (356 EEG sweeps) were log transformed and analysed offline.

In the saline group, intubation caused a significant decrease in the P_{15}-N_{20} ($P<0.005$) and N_{20}-P_{25} ($P<0.05$) amplitudes. This response to intubation was greatly decreased in the SER data from the alfentanil subjects, although the trend remained (see Table 3). The difference between groups (effect of the alfentanil bolus) was significant for the P_{15}-N_{20} amplitude only ($P<0.05$).

Table 3 SER amplitude changes with intubation (data where $P<0.05$ are indicated, *)

Percentage change	P_{15}-N_{20}	N_{20}-P_{25}	P_{25}-N_{35}
Saline			
Mean	–44*	–33*	–16
95% CI	–25 to –58	–7 to –52	57 to –67
Alfentanil			
Mean	–12	–12	2
95% CI	0 to –23	7 to –28	79 to –42

We have shown that the increase in P_{15}-N_{20} amplitude with increasing sevoflurane concentration previously reported[1] is reversible with stimulation: intubation produces a significant decrease in amplitude. Thus, this response appears to behave in a reversed manner to other evoked responses at the subcortical level. High dose alfentanil decreases the SER amplitude changes caused by intubation at both cortical and subcortical levels.

Keywords: brain, evoked responses; intubation tracheal, responses

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The pressor responses to the three phases of nasotracheal intubation

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Nasotracheal intubation is an effective way to secure the airway in patients undergoing maxillofacial surgery, but it is associated with a more profound pressor response than orotracheal intubation.[1] Nasotracheal intubation involves three phases. (1) The tracheal tube is inserted through the nostril and into the pharynx. (2) Direct laryngoscopy is performed. (3) The tracheal tube is passed through the larynx and into the trachea. The objective of this study was to determine how the three phases of nasotracheal intubation contributed to the haemodynamic response.

Sixty ASA I–II patients, aged 16–65 yr, undergoing elective maxillofacial surgery, were studied. They were given a standard general anaesthetic comprising fentanyl, propofol, atracurium, isoflurane 0.5% (end-tidal) in 66% nitrous oxide and 33% oxygen, and then randomized into three groups. In group 1, a shortened nasotracheal tube was inserted through the nostril and into the pharynx. In group 2, a shortened tube was inserted and direct laryngoscopy was performed. In group 3, full nasotracheal intubation was performed. Heart rate and indirect arterial pressure were measured 30 s after the manoeuvre and then every minute for a further 3 min. Data were analysed using one-way ANOVA and Student's *t*-tests with Bonferroni corrections.

The three groups were similar in age, weight, and sex. There was a significant pressor response in all three groups (Table 4). The increase in heart rate and mean arterial pressure (MAP) in group 3 was significantly greater than in groups 1 and 2. The differences between the increases in heart rate and MAP in groups 1 and 2 did not achieve statistical significance, however, the increase in MAP in group 2 was sustained for a longer period.

Nasopharyngeal intubation alone causes significant hypertension and this may account for the greater pressor response to nasotracheal compared with orotracheal intubation. It is conceivable that this response may be amenable to attenuation by topical anaesthesia of the nasopharyngeal mucosa. Nasopharyngeal intubation with or without direct laryngoscopy does not significantly increase the heart rate. One possible explanation for this is the nasocardiac reflex. The placement of the tracheal tube through the larynx and into the trachea results in a significant further increase in arterial pressure and heart rate.

Keywords: intubation nasotracheal; complications, cardiovascular response

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Table 4 Data expressed as mean (SD). *$P<0.05$ within group. $^{\#\S}P<0.05$ between groups

	Group 1	Group 2	Group 3
Maximum increase in heart rate (min^{-1})	0.6 (6.5)$^{\#}$	2.1 (7.6)§	17.6 (13.6)$^{*,\#,\S}$
Maximum increase in MAP (mm Hg)	27.2 (13.3)$^{*,\#}$	31.9 (11.7)*,§	44.9 (13.2)$^{*,\#,\S}$

†LMA is the property of Intravent Limited.

Prophylaxis of nausea and vomiting after spinal morphine analgesia for Caesarean section: comparison between cyclizine, dexamethasone, and placebo

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Low dose intrathecal (spinal) morphine (0.1–0.2 mg) for Caesarean section delivers excellent analgesia but is associated with significant postoperative nausea and vomiting (PONV).[1] A recent study has shown an antiemetic effect of dexamethasone after epidural morphine for Caesarean section.[2] We have evaluated the antiemetic efficacy of cyclizine and dexamethasone compared with placebo in women receiving spinal morphine analgesia for Caesarean section.

Ninety women undergoing elective Caesarean section under spinal anaesthesia were allocated randomly, in a double-blind study design, to receive either cyclizine 50 mg, dexamethasone 8 mg, or placebo as an infusion in 100 ml 0.9% saline on completion of surgery. Spinal anaesthesia was administered at L3-4 or L4-5 intervertebral space with a Whitacre 26G needle using 0.5% hyperbaric bupivacaine 2.0 ml, fentanyl 10 µg, and spinal morphine 0.2 mg. Outcome measures (documented at 3, 6, 12, and 24 h postoperatively by investigators blind to the group allocation) were incidence of nausea and vomiting, requirement for rescue antiemetic medication, severity of nausea on a four-point categorical scale, number of vomiting episodes, and adverse effects. After inspection for distribution, normally distributed variables were compared using ANOVA with post hoc Dunnet's test. Categorical data were compared using chi-squared analysis of contingency tables on SPSS v9.

Severity scores for nausea and vomiting episodes were significantly less in patients receiving cyclizine compared with both dexamethasone and placebo at 3 h and placebo only at 6 h ($P<0.05$ each comparison), but not at 12 or 24 h.

There were no significant differences in pain, pruritus, sedation, arterial pressure, or respiratory rate. Overall satisfaction with antiemetic therapy at 24 h, expressed on a 100 mm visual analogue scale, was higher in cyclizine than either dexamethasone or placebo groups (78 (28) *vs* 58 (31) and 51 (28), $P=0.03$ and $P=0.008$, respectively) (Table 5).

We conclude that cyclizine, compared with dexamethasone or placebo, reduces the overall incidence of nausea, vomiting and need for supplementary antiemetic therapy and also the severity of nausea and number of vomiting episodes in the early post-operative period, after 0.2 mg spinal morphine analgesia for Caesarean section.

Keywords: analgesics opioid, morphine; complications, nausea and vomiting

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Effect of saline volume used to identify the epidural space during CSE anaesthesia for Caesarean section

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Epidural volume may influence the spread of spinal anaesthesia. After epidural analgesia in labour, intrathecal injection of bupivacaine 10 mg has produced total spinal anaesthesia.[1] Likewise, epidural saline injection increases block height after spinal injection of bupivacaine.[2] We have previously demonstrated that the Oxford position confers more predictable control of cephalad spread of spinal block.[3] However, it has been our impression that when performing CSE anaesthesia in the Oxford position, larger saline volumes used to identify the epidural space produced more rapid spread of block. We, therefore, examined the effects of different saline volumes used as part of a CSE technique on subsequent spinal block.

We studied 90 women (aged 23–41 yr) undergoing elective Caesarean section. They were randomized to receive 2, 5, or 10 ml saline to identify the epidural space during needle through needle CSE anaesthesia using the Oxford position. Intravenous fluid preload of 15 ml kg^{-1} Hartmann's solution was given before identification of the epidural space and intrathecal injection of hyperbaric bupivacaine 12.5 mg with fentanyl 12.5 µg. Arterial pressure (AP) was recorded at 1-min intervals until delivery. Ephedrine 6 mg was given on each occasion AP fell below 80% of baseline. Block height was tested every 3 min using light touch with T5 deemed adequate for surgery. Neonates were assessed by Apgar scores and cord gases. Data were analysed using ANOVA with $P<0.05$ considered significant.

Table 5 Incidence of nausea, vomiting, and rescue antiemetic therapy at any time during the study

	Cyclizine (C) (n=30)	Dexamethasone (D) (n=30)	Placebo (P) (n=30)	P value
Nausea at any time, n (%)	10 (33)	18 (60)	20 (67)	P=0.02, C *vs* P; P=0.04, C *vs* D
Vomiting at any time, n (%)	9 (30)	17 (57)	18 (60)	P=0.03, C *vs* P; P=0.04, C *vs* D
Rescue antiemetic at any time, n (%)	4 (13)	17 (57)	19 (63)	P=0.0001, C *vs* P; P=0.001, C *vs* D

Table 6 Onset of anaesthesia, ephedrine requirement and cord gas analysis. Data are mean (SEM). *P=0.009 compared with 5 ml. *P=0.013 compared with 5 ml

	2 ml (n=29)	5 ml (n=29)	10 ml (n=28)	P value
Time to T5 (min)	16.7 (1.1)	18.8 (2.1)	17.4 (2.0)	0.399
Ephedrine required (mg)	21.4 (2.8)	18.9 (3.2)	29.4 (4.2)*	0.009
Arterial pH	7.264 (0.009)	7.275 (0.008)	7.228 (0.015)**	0.013
Venous pH	7.330 (0.007)	7.325 (0.006)	7.311 (0.008)	0.136

No significant differences were found between groups in maternal characteristics, performance of CSE, need for epidural supplements, treatment of nausea and vomiting, and timing of postoperative analgesia. No block extended above T2 was recorded before skin incision. Data on spread of anaesthesia, ephedrine requirement, and cord gas analysis are shown in Table 6.

Excessive upper block height is unlikely when using the Oxford position regardless of saline volume. Using saline 10 ml to identify the epidural space did not produce more rapid spread of block. However, its use was associated with greater ephedrine requirement and deterioration in arterial, but not venous, cord gas values. Smaller saline volumes are, therefore, preferable when performing CSE anaesthesia in the Oxford position.

Keywords: anaesthetic techniques, epidural; anaesthetic techniques, subarchnoid

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Comparison of thresholds for giving phenylephrine during spinal anaesthesia for Caesarean section

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Maternal hypotension is an important complication of spinal anaesthesia for Caesarean section. Mean umbilical artery pH (UApH) at delivery is higher if maternal hypotension is prevented by giving ephedrine promptly.[1] The aim of this study was to compare two thresholds for giving phenylephrine and to examine the effect on umbilical artery pH at delivery.

Thirty-two healthy women with an uncomplicated singleton pregnancy scheduled for elective Caesarean section were recruited. Baseline maternal systolic arterial pressure (SAP) and heart rate were measured before spinal anaesthesia.[2] Patients were allocated randomly to be given phenylephrine 100 μg intravenously whenever SAP had decreased to either 95% of baseline (group A) or 80% of baseline (group B). The anaesthetists were blinded to patient allocation. Arterial pressure was measured at 1 min intervals after induction of spinal anaesthesia. Atropine 0.6 mg was given if maternal heart rate fell by 25% from its baseline. A sample of arterial blood was taken from a double-clamped section of umbilical cord immediately after delivery of the baby. The UApH was measured within 5 min.

One patient was withdrawn because the uterine incision to delivery (UD) interval was 540 s. A second patient was withdrawn because inadequate spinal anaesthesia required conversion to general anaesthesia (Table 7).

We conclude that UApH at delivery is satisfactory when phenylephrine is used during spinal anaesthesia for elective Caesarean section. We have not shown a benefit to the fetus in giving phenylephrine when maternal SAP has decreased by only 5% from baseline.

Keywords: anaesthetic techniques, subarchnoid; sympathetic nervous system, phenylephrine

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A comparison of 0.0625% ropivacaine or bupivacaine combined with fentanyl 2 μg ml^{-1} administered by patient-controlled epidural analgesia in labour

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The relative potency of ropivacaine compared to bupivacaine when used for epidural analgesia in labour is controversial.[1] A double-blind randomized controlled comparison of the two drugs (concentration 0.0625%) combined with fentanyl 2 μg ml^{-1} was performed during the first stage of labour using patient controlled epidural analgesia (PCEA).

Sixty term primigravid women in early labour were enrolled. Analgesia was established using 15 ml of 0.125% ropivacaine or bupivacaine with fentanyl 5 μg ml^{-1} injected through a lumbar epidural catheter, with a further 5 ml given after 15 min if required. Thereafter, PCEA was used: local anaesthetic 0.0625%; fentanyl 2 μg ml^{-1}; 5 ml bolus; 10 min lockout; and no background infusion. Inadequate analgesia was treated with 10 ml of 0.1% trial drug without fentanyl. Hourly drug consumption, rescue dose requirement, sensory and motor block, VAS of pain during

Table 8 Comparison of bupivacaine and ropivacaine. Results are given as mean (SD) or number (%)

Patients (*n*)	Bupivacaine (*n*=25)	Ropivacaine (*n*=28)	95% CI for difference
Entry cervical dilatation (cm)	2.5 (0.8)	2.6 (1.0)	–0.67 to +0.3
Drug consumption (ml h^{-1})	14.2 (2.9)	15.4 (3.9)	–3.5 to 0.6
Rescue doses	14 (56%)	13 (46%)	17–36%
Median VAS h^{-1} (mm h^{-1}) (IQR)	16 [10–24]	16 [7–20]	*P* 0.43 Wilcoxon
Mode of delivery			
Vaginal	10	14	Fischer exact *P*=0.045
Forceps	11	4	
Caesarean	4	10	

Table 7 *Analysis of group B excluding one outlier [UApH 7.09]: 7.32 (7.31–7.33); **P=0.011

	Group A	Group B
Umbilical artery pH, mean (95% CI)	7.32 (7.31–7.33)	7.31 (7.27–7.34)*
UD interval, median (IQR)	70 (52–110)	84 (48–114)
Phenylephrine dose (μg), median (range)	400 (100–1400)	100 (0–300)
Subjects given atropine (mg)**, *n*	13	6
SAP as percentage of baseline, mean (95% CI)	99.0 (95.4–102.6)	94.4 (91.3–97.5)
Subjects with hypotension (*n*), (SAP <70% of baseline)	3	2

contractions and incidence of side effects were recorded. Statistical analysis was with an unpaired *t*-test for differences between means or proportions and Fischer's exact test as appropriate.

Patient characteristics and duration of labour were similar in the two groups. No patient developed motor block. Side effects of nausea and pruritis were infrequent and of minimal severity (Table 8).

We were unable to reject the null hypothesis that there was no difference in rate of solution used per hour at a significance level of 0.05. Whilst PCEA with 0.0625% ropivacaine or bupivacaine combined with fentanyl provided effective analgesia, half the patients required at least one rescue dose.

Keywords: anaesthetic techniques, epidural; anaesthetics local, ropivacaine; anaesthetics local, bupivacaine

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The comparative obstetric mobile epidural trial (C.O.M.E.T.). A radomized controlled trial: pain relief

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Epidural analgesia is associated with increased rates of obstetric intervention.[1] Trials demonstrating adverse effects have examined traditional epidural techniques, which commonly result in dense motor block. Low dose 'mobile' techniques using solutions of opioid with low concentration local anaesthetic to preserve motor function are associated with increased maternal satisfaction[2] and reduce instrumental vaginal delivery rate.[3] We present a comparison of pain scores after traditional epidural analgesia for labour and two low dose techniques.

A total of 1054 primiparous women, requesting epidural analgesia, were randomized to receive intermittent boluses of 0.25% bupivacaine (traditional), combined spinal epidural (CSE) followed by intermittent boluses or low dose infusion (LDI), each using 0.1% bupivacaine with fentanyl 2 $\mu g\,ml^{-1}$. Visual analogue pain scores (VAS) were recorded before epidural insertion, at 5 min intervals for the first 30 min and hourly thereafter until delivery.

Compared with traditional epidural analgesia, CSE has a more rapid onset and its greater efficacy is maintained 1 h later (Table 9). However, at 3 h median VAS was significantly higher and no advantage was apparent at delivery. Throughout labour and at delivery there were no differences in VAS between traditional and LDI groups.

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Keywords: anaesthetic techniques, epidural; anaesthesia, obstetric

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Predictors of dissatisfaction with epidural analgesia during labour

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Maternal satisfaction with epidural analgesia during labour is an outcome commonly used for audit and research in obstetric anaesthetic practice. Despite being subjective and prone to influence by non-anaesthetic factors, maternal satisfaction remains the most practical way of assessing the efficacy of epidural analgesia from the woman's point of view. Many large obstetric units use fixed procedure epidural regimens for all their patients. If it were possible to predict which patients were more likely to be dissatisfied with a given regimen, an alternative technique could be targeted appropriately. We, therefore, set out to find predictors of both maternal and midwife dissatisfaction with the fixed procedure epidural and combined spinal epidural (CSE) regimens used in our unit.

The Wansbeck Epidural Audit System (Xentec, UK) was used to collect comprehensive patient characteristics, procedural, obstetric, and follow-up data from 5089 consecutive labour epidurals. All patients received epidural or CSE techniques using 0.1% bupivacaine with fentanyl 2 $\mu g\,ml^{-1}$. Microsoft Access 1997 was used to collate these data, defining epidurals with excellent scores from both patient and midwife as 'successful', and all others as 'poor'. These were compared using a Mann–Whitney *U* test and chi-squared test as appropriate. The predictive value of these factors was tested by backward stepwise logistic regression.

Satisfaction data were available from 4855 epidurals, of which 3633 (74.8%) were defined as successful and 1222 (25.2%) poor. Of the many variables considered, multiparity ($P<0.0001$), increasing body weight ($P<0.02$), the use of epidural rather than CSE ($P<0.0006$), and vaginal rather than operative delivery ($P<0.0001$) were associated with poor epidural satisfaction. The sensitivity of these predictors was not high.

The implication from these data is that we might improve our unit's results by targeting multiparous, obese women with a CSE technique. This approach is currently being tested. The bizarre

Table 9 VAS scores $^{**}P<0.001$, $^{*}P<0.01$ (Mann–Whitney *U* test)

Epidural technique	Median VAS at time after epidural					
	Pre-block	5 min	20 min	1 h	3 h	Delivery
Traditional (*n*=353)	75	64	12	14	15	25
CSE (*n*=351)	78	20**	0**	4**	21*	40
LDI (*n*=350)	75	57	18	10	12	23
n (Total)	1005	939	945	881	589	481

finding of reduced satisfaction after vaginal deliveries may relate to the relatively poor performance of low dose epidurals during the second stage of labour. These findings are only relevant to the epidural techniques and patient mix found in our unit, so we cannot comment on the wider applicability of our clinical conclusions.

Keywords: analgesic techniques, epidural; analgesia, obstetric

Investigation into the use of a new oesophageal pulse oximeter in cardiothoracic surgery patients

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Conventional pulse oximetry may fail when peripheral circulation is compromised.[1] [2] We have investigated the use of a new oesophageal reflectance pulse oximeter[3] in a group of patients with poor peripheral perfusion based on the hypothesis that blood flow to this central site may be preferentially preserved.

After induction of anaesthesia in 50 elective cardiothoracic surgery patients a purpose-built oesophageal reflectance pulse oximetry probe was positioned in the oesophagus. Signals were recorded at various depths of the oesophagus, as the probe was withdrawn, until the site of best signal was determined. Monitoring in theatre was intermittent and during these periods the saturation readings were compared with the arterial saturation of blood gases and co-oximetry results.

Signals were recordable in all 50 patients and oxygen saturation readings were in good agreement with arterial blood gas and co-oximetry results. The results were compared using Bland Altman analysis (Fig. 1). Five of the patients showed a period of peripheral pulse oximetry failure while oesophageal signals remained. These failures occurred on the intensive care unit, when patients were peripherally cool.

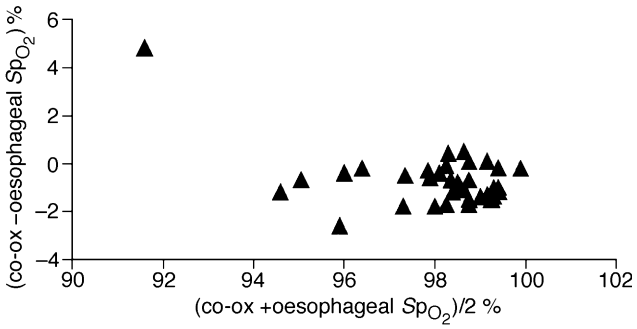

Fig 1 Difference against mean for oxygen saturation data from oesophagus and co-oximetry.

Peripheral pulse oximetry signals are often difficult to obtain in patients with poor peripheral perfusion. Oesophageal pulse oximetry may be a useful alternative way of monitoring arterial oxygen saturation in such patients.

Keywords: gastrointestinal tract, oesophagus; measurement techniques, pulse oximetry

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Continuous arteriovenous oximetry as a measure of perfusion during hypothermic cardiopulmonary bypass

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Whilst considerable research is directed at the causes of neurological injury during bypass,[1] the significance of sudden bypass flow reductions on oxygenation may have been overlooked. It is assumed that cooling protects from ischaemia when bypass flow is reduced to aid surgery. The duration of safe flow reduction has not been determined.[2] Previous studies have attempted to analyse oxygenation from blood sampling.[1] This is not rapid enough to study sudden changes. Continuous arteriovenous oximetry provides a ready method of studying oxygenation during acute flow alterations.

Elective coronary surgery patients received standardized etomidate, alfentanil, rocuronium, and isoflurane anaesthesia. Routine bypass flows of 2.4 litres m^{-2} min^{-1} were used with fresh gas flows adjusted to maintain a Pa_{O_2} of 25–30 kPa and Pa_{CO_2} of 4.5–5.5 kPa. Isoflurane (1%) was administered in the fresh gas. Arterial and venous saturations from oximeters (Ghish Biomedical) on respective bypass circuit limbs were collected by a Labview chart recorder. Simultaneous recordings of pump flow rate were down loaded. Oxygen consumption and delivery were calculated every 3 s. During flow down, oxygen deficit was calculated by subtracting the oxygen actually consumed from the amount that would have been consumed in the same time interval at full flow rate. After flow restoration, the 'recovery' amount of oxygen consumed above basal was calculated similarly (Fig. 2).

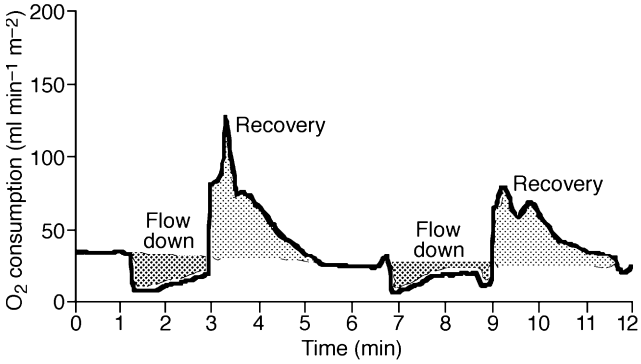

Fig 2 Baseline, flow down, and recovery oxygen consumption. Recovery oxygen consumed is 2.3 times greater than the flow down deficit.

Six patients, (five male and one female) (results; mean (SD) age 60.2 (13.2), surface area 1.81 (0.14) m^2, underwent a bypass of 103 (18) min at a temperature of 31.3 (0.94)°C. Eight flow down events longer than 1 min were analysed. Calculated flow down oxygen deficit, correlated significantly with oxygen consumed during recovery r=0.719 (P=0.022).

Information from arteriovenous oximetry may be used to calculate safe flow down intervals, and optimize bypass flow rates taking account of individual patient's metabolic demands.

Keywords: measurement techniques, oximetry, arteriovenous; surgery, cardiovascular, cardiopulmonary bypass

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The effect of methylprednisolone on uninary N-acetyl-β-D-glucosaminidase/creatinine ratios in porcine vascular surgery

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Urinary *N*-acetyl-β-D-glucosaminidase/creatinine ratio (NAG/creatinine) has been shown to be a sensitive indicator of subclinical proximal tubular damage, and at higher levels correlates with raised plasma urea and creatinine.[1] The perioperative inflammatory response may contribute to renal injury.[2] Methylprednisolone reduces elements of the inflammatory response perioperatively.[3] We hypothesize that in a porcine hind limb ischaemia-reperfusion model prior administration of methylprednisolone may reduce perioperative renal injury.

Twelve 10–12-week-old male pigs were anaesthetized (40 mg kg^{-1} induction then 13 mg kg^{-1} h^{-1} maintenance) and immediately underwent laparotomy, normodynamic fluid resuscitation for 2 h followed by bilateral hind-limb ischaemia for 2 h followed by 2.5 h of reperfusion. Pigs were randomied to two groups. Group C received placebo and group MP received methylprednisolone 30 mg kg^{-1} at induction of anaesthesia. Urine samples were obtained as follows: 30 min after anaesthesia induction (baseline sample **a**), 2, 3, 4, 5, and 6.5 h post-induction (samples **b**, **c**, **d**, **e**, and **f**). Urinary NAG/creatinine was measured at each sample time. Analysis between groups was with the Mann–Whitney *U* test and within groups with Wilcoxon matched pairs.

At samples **d** and **e** (end of ischaemia and 1 h into reperfusion) NAG/creatinine was significantly lower in the MP group (Fig. 3).

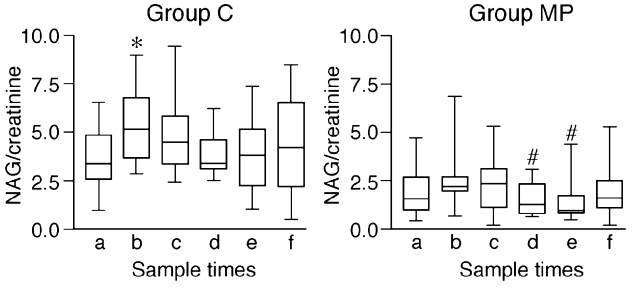

Fig 3 NAG/creatinine ratios in Group C (n=6) and group MP (n=6). Box and whisker plots show median, 25th and 75th percentiles and range. *P<0.05 within group compared with baseline. #P<0.05 between groups.

This porcine model may therefore be a useful tool to elucidate mechanisms of perioperative renal injury at vascular surgery and possible protective mechanisms of methylprednisolone.

Acknowledgements: This research is supported by the British Heart Foundation.

Keywords: surgery, vascular; complications, renal damage

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Subclinical perioperative myocardial injury in patients undergoing major vascular surgery

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The risks of cardiac morbidity and mortality associated with major vascular surgery are well known. We describe a prospective cohort study of perioperative myocardial injury in patients who either had cardiac disease or had risk factors for cardiac disease and who underwent elective major vascular surgery in five participating hospitals.

Clinical, ECG, and laboratory data were collected from subjects before surgery. Subjects were followed up until hospital discharge or death. Blood samples for cardiac troponin I (cTnI), and a 12-lead ECG were obtained preoperatively and on each of the first four postoperative days. Blood samples were centrifuged, frozen, and stored locally before being transferred to the University of Bristol for analysis, using the ACCESS^{TM} immunoassay system. The cTnI cut-off for the diagnosis of myocardial infarction using this assay is 0.15 μg $litre^{-1}$.[1] All ECGs were reviewed by a Reader in Cardiology (AB) and new changes recorded.

Sixty-three patients were studied, mean age 70.4 (SD 9.4; range 00–00) yr. Fifty-two (88%) were male. Fifteen patients (25%) displayed cTnI elevations consistent with a myocardial infarction (>0.15 μg $litre^{-1}$). Post hoc analysis suggested that these patients could be divided into two distinct groups. Eight patients had transient and relatively modest cTnI elevations. In this group the median peak cTnI level was 0.20 μg ml^{-1} (range 0.16–0.56). One of these patients developed atrial fibrillation in the postoperative period. This was accompanied by ST-segment depression on the ECG and clinical evidence of heart failure. One other patient developed heart failure without associated ECG changes. The remaining six patients had no clinical evidence of a perioperative cardiac complication. Seven patients suffered more protracted bouts of cTnI release associated with higher peak cTnI levels, median 2.41 μg $litre^{-1}$ (range 0.68–14.42). All seven of these patients suffered an ischaemic cardiac event diagnosed clinically or from the ECG.

These data show that significant cTnI release occurs in the absence of clinical evidence of acute myocardial injury in some patients undergoing major vascular surgery. The findings are consistent with work showing transient cTnI release in patients undergoing cardiac surgery.[2]

Acknowledgements: This study was supported by the Vascular Anaesthesia Society of Great Britain and Ireland and the Division of Cardiac, Anaesthetic and Radiological Sciences of the University of Bristol. Mr M. Ginty performed the cardiac

troponin I analyses. We are grateful to Drs J. Wilson, A. Osbourn, J. McDonagh and R. Innes for assistance with patient recruitment and data collection, and to Dr A. T. Lovell for assistance with the data analysis.

Keywords: surgery, vascular; complications, myocardial injury

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Risk factor stratification for adverse outcome in vascular surgical patients

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We have examined the association between clinical risk factors, perioperative silent myocardial ischaemia (SMI) and elevated serum cardiac protein concentrations (troponins I and T, TnI and TnT, and CK-MB) as markers of cardiac outcomes in patients undergoing vascular surgery.

Patients (aged 42–97 yr, *n*=208, 160 male) undergoing vascular surgery were recruited. The presence of 12 clinical risk factors was determined by history and clinical examination. Perioperative Holter monitoring was conducted in 191 patients and blood sampling for cardiac proteins in 105 patients. Patients were followed-up for 1 yr. Three models were generated by logistic regression (SPSS, v9.0) for both early (⩽1 month) and overall outcomes (up to 1 yr) using: clinical risk factors (Model 1); SMI and clinical risk factors (Model 2); SMI and clinical risk factors plus increase in serum cardiac protein levels (Model 3).

There were 40 adverse outcomes—31 in the first month and nine more in the 12 months after surgery. In Model 1, logistic regression analysis identified histories of angina, congestive cardiac failure (CCF), or smoking as predictors of early outcome and histories of angina or CCF as predictors of overall outcome. For Model 2, the predictors of early adverse outcome were: angina, smoking, SMI, and CCF; only angina and SMI remained predictors of overall adverse outcome. In Model 3, CK-MB, SMI, and angina were all predictors of early and overall outcome (see Table 10).

We conclude a history of angina to be the most important clinical risk factor for predicting adverse outcome in our population, but SMI, a history of CCF and smoking are also useful markers. Our results are similar to those of Pasternack and colleagues and Fleisher and co-workers[1 2] for vascular populations; but we did not find troponins to be useful indicators of outcome. This may reflect the small numbers of patients with elevated troponins and adverse outcomes in this group.

Acknowledgments: This study was supported by the Wellcome Trust from 1992–1997 and by LMA International from 1999 to date.

Keywords: surgery, vascular; risk

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Thrombelastograph® and laboratory markers of thrombophilia

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Using Thrombelastograph (TEG®) coagulation analyser, we have demonstrated that men, women and pregnant women represent a trend of increasing coagulation.[1] Hypercoagulability during pregnancy has been attributed to increased concentrations of fibrinogen, factors V, VII, VIII, X, XI, and decreased concentrations of proteins C and S[2]. TEG® has been described as a device capable of identifying thrombotic tendencies,[3] but has never been shown to correlate with conventional laboratory markers of thrombophilia. Pregnant women offer a natural reservoir of physiological thrombophilia. The aim of this study was to correlate TEG® and conventional laboratory markers of thrombo-

Table 10 *P* values of risk factors for adverse cardiac outcome. (NS, not significant)

Risk factor	Model 1 Early	Overall	Model 2 Early	Overall	Model 3 Early	Overall
Angina	0.002	0.003	0.004	0.007	0.035	0.091
CCF	0.006	0.056	0.018	NS	NS	NS
Smoking	0.009	NS	0.006	NS	NS	NS
SMI	–	–	0.016	0.006	0.074	0.013
CK-MB	–	–	–	–	0.001	0.005

Table 11 Correlation values. *Significant at $P<0.05$, **significant at $P<0.01$

TEG®	PT APCR	APTT Prot C	Fib Prot S	V AT III	VII	VIII	X
r	NS	NS	–0.21**	NS	–0.22**	–0.26**	–
0.29**	0.26**	NS	0.21*	NS			
k	NS	NS	–0.42**	NS	–0.35**	–0.37**	–
0.37**	0.36**	NS	0.37**	NS			
α	–0.17*	NS	0.51**	NS	0.36**	0.36**	
	0.32**	–0.33**	NS	–0.38**	–0.17**		
MA	–0.21*	NS	0.70**	NS	0.42**	0.44**	
	0.44*	–0.45*	0.19#	–0.45*	NS		

philia using subjects demonstrating the range of naturally occurring thrombotic tendency.

We recruited 150 ASA I volunteers; 50 pregnant women at term, 50 men and 50 non-pregnant women. Anyone with a history of thromboembolism, or taking anti-platelet drugs was excluded. A 22G cannula was inserted into a forearm vein. After discarding the first 2 ml to avoid contamination by tissue thromboplastin, 10 ml of blood was taken for TEG® analysis and for a modified thrombophilia screen, including PT, aPTT, fibrinogen, factors V, VII, VIII, X, activated protein C resistance (APCR), proteins C and S, and antithrombin III (AT III). TEG® was performed on fresh whole blood using disposable cups and pins in a standardized manner. Statistical analysis was performed using Pearson's correlation *r*.

Results of significant correlation (*r*) are shown in Table 11.

TEG® analysis correlates strongly with fibrinogen, factors VII, VIII, and X, APCR and protein S. Weak correlations were found with prothrombin time, protein C and AT III. TEG® analysis may have potential for use as a simple, inexpensive, rapid, point of care screening tool for thrombophilia in high risk patients, and this needs further investigation. Results of TEG® analysis may be used to determine which patients require further investigation or treatment.

Acknowledgements: Source of Funding: Obstetric Anaesthetists Association and Yorkshire Regional Health Authority

Keywords: equipment, Thrombelastograph®; blood, thrombocytopenia

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When is it safe to site an epidural in patients on high dose enoxaparin?

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High thoracic epidural analgesia in patients undergoing coronary artery bypass has been associated with reduction in the stress response,[1 2] better analgesia,[3] earlier extubation,[4] and fewer serious arrhythmias.[4] These benefits are particularly attractive in patients with unstable angina undergoing surgery. However, patients with unstable angina are now treated with enoxaparin 1 mg kg^{-1}. It has been recommended that patients on low molecular weight heparin (LMWH) should not have an epidural until 10–12 h after receiving up to 40 mg enoxaparin.[5] We have used Thrombelastograph® coagulation analysis and factor Xa inhibition to investigate how long it takes for coagulation to return to control levels after high dose enoxaparin.

Forty patients were studied. Twenty patients were control undergoing elective coronary artery bypass surgery and 20 were receiving enoxaparin 1 mg kg^{-1} daily. The control patients had a 5 ml blood sample taken before induction of anaesthesia and the enoxaparin group had 5 ml blood samples taken at 6, 8, 10, 12, and 24 h after subcutaneous enoxaparin 1 mg kg^{-1}. Each sample underwent Thrombelastograph® coagulation analysis immediately and was analysed for factor Xa inhibition subsequently.

There were no significant differences between the groups in height, weight, age, sex, or smoking history. ANOVA and Student's *t*-test demonstrated a significant increase at the 5% level in factor Xa inhibition and prolongation of the *r* value but not maximum amplitude on Thrombelastograph® analysis at 6, 8, 10, and 12 h. At 24 h the *r* value and factor Xa inhibition had returned to control levels (Table 12). There was a statistically significant correlation between *r* time prolongation and factor Xa inhibition with an r^2 value of 0.67.

Table 12 Values are expressed as means with standard deviation (SD). *Signifies a significant result at the 5% level

	MA (mm)	Xa Inhibition (iu ml^{-1})	*r* value (mm)
Control	61.4 (6.4)	0.05 (0.05)	20 (0.27)
6 h	55.7 (8.2)	0.67 (0.07)*	40 (7.5)*
8 h	57 (7.1)	0.6 (0.1)*	34 (7.5)*
10 h	58.2 (6.1)	0.42 (0.08)*	31 (6.25)*
12 h	60.0 (7.5)	0.28 (0.075)*	27 (5)*
24 h	60.7 (7.3)	0.04 (0.03)	20.5 (0.33)

We conclude that it is necessary to wait 24 h after high dose enoxaparin before siting an epidural. Our results also suggest that the *r* value may be a useful surrogate for factor Xa inhibition in patients on enoxaparin.

Keywords: anaesthetic techniques, epidural; blood, coagulation, enoxaparin

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Effect of transcervical papaverine and bupivacaine on postoperative analgesia after laparoscopic application of filshie clips

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In comparison with diagnostic laparoscopy, Filshie clips applied during laparoscopic sterilization can cause additional abdominal pain induced by ischaemia or spasm. Papaverine is a smooth neuromuscular blocking agent that may improve this pain if administered directly to the fallopian tubes. Previous trials evaluating administration of transcervical bupivacaine[1] and lignocaine[2] to Filshie clips have shown positive results. The aim of the study was to evaluate if transcervical papaverine would reduce this pain and to compare this effect with those of bupivacaine and placebo.

Sixty-six ASA I–II females, undergoing laparoscopic sterilization, were recruited and allocated randomly to either papaverine 30 mg or 0.375% bupivacaine 30 ml or 30 ml of saline. Patients were given a standard anaesthetic comprising propofol 2–4 mg kg^{-1}, fentanyl 1 mg kg^{-1} and a neuromuscular blocking agent. Patients' lungs were ventilated to normocapnia with nitrous oxide and isoflurane in oxygen via a standard laryngeal mask airway.† Suppositories of diclofenac 100 mg and i.v. ondansetron 4 mg were given. Before application of a Filshie clip to the medial third of each Fallopian tube, the appropriate solution was injected through a Spackman's cannula placed into the cervix of the uterus. Residual neuromuscular block was antagonized with neostigmine 2.5 mg and glycopyrrolate 500 mg at the end of surgery.

Postoperatively, rescue analgesia comprised two tablets of cocodamol 30/500 and i.m. morphine 10 mg. Patients were assessed as soon as they were awake (time 0), at 30 min and then at 1, 2, 3, and 4 h by an observer blinded to the treatment. Exclusion criteria were allergies to bupivacaine and papaverine, chronic pain syndrome, pelvic inflammatory disease and adhesions, regular analgesic ingestion and operative difficulties.

Of 66 patients recruited, three did not complete the study. There were no significant differences between the three groups in age and median body mass index. Analgesic consumption did not differ significantly between the groups in terms of: number of patients having analgesia within the first postoperative hour; number of patients having cocodamol only, morphine only or the combination of cocodamol and morphine. There were no significant differences between median visual analogue pain scores, sedation scores, incidence of postoperative nausea and vomiting, and requirement for rescue antiemetics. In conclusion, transcervical papaverine did not provide additional analgesia for laparoscopic sterilization.

Keywords: surgery, laparoscopic sterilization; analgesia, postoperative

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Efficacy of transcutaneous spinal electroanalgesia on thermal sensation and pain thresholds in healthy volunteers

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Recently modified TENS machines, which are capable of delivering extremely brief (4 ms) electrical pulses are now available.[1] The pulses are thought to penetrate deep enough to exert modulating effects within the spinal cord. This technique is called Transcutaneous Spinal Electroanalgesia (TSE). It has been shown to improve general mood and pain tolerance in healthy normal subjects.[2] Quantitative Sensory Testing (QST) allows physiological measurement of sensory neurological function, including tolerance to hot and cold stimuli.

Twenty healthy individuals were recruited in this randomized double-blind crossover trial. After a normal neurological examination, QST was performed on the thenar eminence of the dominant hand before and after TSE treatment. A psychological questionnaire of positive and negative mood states (Positive and Negative Affect Schedule) was also performed before and after treatment. Each volunteer repeated the session twice on two separate days receiving either active or control TSE treatment. Power analysis revealed that based on Towell, Williams and Boyd's work, 16 individuals would be needed to detect a 20% change of threshold in temperature (°C). Statistical analysis was carried out using a paired *t*-test for quantitative data.

There were no significant differences between active and control treatments in any of the measured variables (Table 13).

We have found that a single treatment of TSE does not significantly affect thermal sensation, pain sensation, or mood in healthy volunteers.

Keywords: pain, heat sensation; pain, threshold

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The effect of obturator nerve block on chronic hip pain

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Osteoarthritis of the hip is a common condition, which leads to pain and disability. It has been demonstrated that regional block of the hip can lead to increased range of movement in patients who have limited mobility.[1] Patients who have osteoarthritis of the hip attend the pain clinic while waiting for arthroplasty, presenting with pain, limited movement and poor quality of life. The aim of our study was to assess in the outpatients setting the effect of obturator nerve block on hip function and depressive symptoms in ambulant patients with osteoarthritis of the hip.

Ten adult patients who attended the outpatients' clinic with osteoarthritis of the hip were studied. A full history and examination was performed. A physiotherapist assessed pain, functional ability, and activities from which a Harris hip score was calculated. A full range of movement was measured. The co-existing psychological symptoms were assessed by applying the Zung scoring system. A pain intensity score was obtained (range 0–10). A separate investigator performed an obturator nerve block. This was performed by an anterior approach with full aseptic technique and the use of a peripheral nerve stimulator to localize the nerve. A constant current of less than 1 mA was used. Five to seven millilitres of 0.5% bupivacaine was used. The patient was rested in the supine position. After 30 min the range of movement was measured by the same physiotherapist.

The patients were reassessed after 6 weeks and 3 months. At this stage a full history and examination was performed. A movement score, Harris hip score, Zung score, and pain intensity score were measured. Wilcoxon signed rank test was used to analyse the data.

We demonstrated an immediate improvement in movement score after the procedure, which persisted for 6 weeks. Median movement scores were 82 initially which then increased to 96 immediately after block (P=0.005) and then 98 after 6 weeks (P=0.03). After 12 weeks movement returned to the baseline state. Obturator nerve block significantly decreased pain intensity score

Table 13 Comparison of active and control TSE treatments

Variable	Change °C active TSE (mean (SD))	Change °C control TSE (mean (SD))	Significance *P* value and (95% CIs)
Cold sensation	0.05 (0.7103)	0.1212 (0.81)	0.779 (–0.4,0.5)
Warm sensation	–0.01 (1.22)	0.2750 (0.7651)	0.403 (–0.41, 0.93)
Cold pain	–1.22 (3.1)	–0.6 (3.7)	0.502 (–1.03,2.4)
Heat pain	–0.1180 (1.7)	0.61 (3.06)	0.829 (–1.5,1.8)
Positive affect	0.9 (2.3)	0.1 (2.26)	0.371 (–2.6,1)
Negativea affect	0.25 (1.2)	0.15 (1.2)	0.776 (–0.8,0.6)

after 6 weeks (P=0.03) but after 12 weeks pain intensity scores returned to baseline levels. Median Zung scoring decreased from 25 to 19 after 6 weeks (P=0.09) then 18 after 12 weeks (P=0.18). We did not demonstrate a significant change in Harris hip score over the period of the study.

We conclude that obturator nerve block causes an immediate improvement in range of movement in patients who have osteoarthritis of the hip. The increase in movement persists for 6 weeks. This increase in movement is associated with a decrease in pain intensity score over the same period of time. We report that this may be a clinically valuable outpatient technique to improve symptoms in patients awaiting surgery.

Keywords: pain, chronic; anaesthetic techniques, regional, obturator nerve block

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Spread of injectate with superficial cervical plexus block in the cadaver

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Carotid endarterectomies are commonly performed using either a superficial cervical plexus block or a combined (superficial and deep) block.[1] The deep block is designed to deposit local anaesthetic close to nerve roots and might be expected to provide better anaesthesia and muscle relaxation. However, both blocks are equally effective.[1] The anatomy of the superficial cervical space might explain this finding. Winnie and colleagues described the spread of injectate during deep block,[2] but the spread during superficial block has not been examined.

We used six cadavers. Injections were made using a 23G needle and 30 ml syringe. In two cadavers (C1, C2), we performed an injection of 30 ml 0.01% methylene blue dye into the intact neck, just deep to the investing fascia, as if performing a superficial cervical plexus block. In two cadavers (C3, C4), we first dissected away skin to expose the investing fascia. We then injected dye just deep to this fascia. We performed two 'control' injections. In cadaver C5, dye was injected only subcutaneously. In cadaver C6, we performed a standard deep cervical plexus block. In all cadavers we performed careful dissection to ascertain the spread of dye.

In C1 to C4, dye was found in the superficial space just below the investing fascia and also deep to the prevertebral fascia, coating the scalene muscles and the phrenic nerve. In C1 and C3, dye was even found to be tracking down to the axillary sheath, suggesting communication between the superficial cervical space and the brachial plexus. In C5, dye remained subcutaneous and did not spread. In C6, the dye was confined to the deep cervical space, with no retrograde spread to the superficial space.

We have demonstrated the potential for communication between superficial and deep spaces of the neck. Traditionally, the prevertebral fascia is regarded as impenetrable, at least by infections and tumours.[3 4] Our novel result might, however, explain the observation that both deep and superficial blocks have equal efficacy: the local anaesthetic enters the same anatomical spaces. We might speculate that a large volume of injectate might open up channels in the prevertebral fascia, whereas these channels might be closed by inflammatory processes. Microscopic tumour spread along the perineurium from superficial to the deep roots of the cervical nerves has been demonstrated, suggesting that routes may exist between the two spaces of the neck.[5] Artefacts produced by cadaver fixation are unlikely in view of our control results. We conclude that in the normal human neck, the superficial and deep spaces communicate and that this might underlie the observed efficacy of superficial block for carotid artery surgery.

Keywords: anaesthetic techniques, cervical plexus block; anatomy

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Evaluation of early extubation after liver transplantation

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The safety and efficacy of early extubation after liver transplantation are controversial. A recent study suggested that 18% of patients were suitable for this procedure[1] and had similar outcomes (including reintubation rates) to patients ventilated postoperatively. We have recently implemented a fast-track procedure using broad entry criteria, and collected data to assess the safety and wider applicability of the technique.

Over a 1-yr period we performed 120 liver transplants. Of these, we considered 78 elective liver transplant patients as potentially suitable for fast tracking, defined as in-theatre extubation and early discharge to the ward. Patients with fulminant liver failure, those who were inotrope or dialysis dependent, and those with significant cardiac disease were excluded. Patients were anaesthetized using a modified anaesthetic technique using short acting agents, including remifentanil[2] and desflurane.[3] In those whose platelet count exceeded 80×10^9 litre^{-1}, a thoracic epidural catheter was placed for postoperative analgesia. The remainder received PCAS morphine postoperatively. Patients were managed according to a standard procedure.[4] Extubation was attempted in theatre wherever the anaesthetist felt this possible. ITU stay, hospital stay, reintubation rate, and graft function were studied. We also studied preoperative factors indicative of successful extubation.

Of the 78 patients enrolled, 59 (78%) were successfully extubated. Forty patients received epidurals, of whom 34 were extubated. Twenty-five of 38 patients allocated to PCAS were extubated in theatre. None required reintubation. Preoperative creatinine (80 (3) *vs* 89 (6)), age (47, 41–54 *vs* 50, 37–59 yr), ALT, bilirubin, Child-Pugh score (7, 5–9 interquartile range in the extubated patients, *vs* 8, 4.5–10.5) and albumin (33 (0.8) vs 30 (1.4) g litre^{-1}) were similar between extubated and ventilated patients. PT was slightly lower in extubated patients, 15.6 (0.5) s *vs* 19.2 (2.3) s, P<0.02.

Postoperatively, fast-track patients had a shorter time to hospital discharge, 13 (11–18) days *vs* 25 (17–35) days, P<0.0003; and a shorter time in intensive care, 21 (3) h *vs* 5 (3.4) days, P<0.0003. Renal function was better postoperatively in the extubated group, creatinine 98 (10) *vs* 143 (19), P<0.05. After construction of a propensity score for early extubation (P=0.004), a quintiles analysis suggested that patients suitable for fast tracking would have a hospital stay shorter by 17 days than those

not, but that a 15 day reduction in stay could be attributable to the fast tracking process.

A majority of patients undergoing elective liver transplantation can be fast-tracked. Those sicker preoperatively are less likely to be successfully extubated in theatre. A randomized trial is required to establish whether reduced duration of stay is directly attributable to early extubation. Based on these data, such a study would need at least 26 evaluable patients per group for a power of 80% at the P=0.05 level.

Keywords: anaesthesia; liver, transplantation

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Interleukin 13 and inflammatory markers in human sepsis

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Interleukin-13 (IL-13) is an anti-inflammatory cytokine whose effects include inhibition of the production of inflammatory cytokines, including TNF-α, IL-1β, IL-6, IL-8 by LPS-stimulated monocytes, prolongs survival of human monocytes and increases surface expression of MHC class II molecules and CD23. It strongly inhibits tissue factor expression induced by LPS and protects endothelial and monocyte surfaces. It has been shown in mice to protect against sepsis and is necessary for survival after CLP in mice.[1] To date, there are few reports of IL-13 in septic humans. Therefore, we have assayed this cytokine, together with other markers of inflammation in human sepsis, to characterize its pattern of expression.

Thirty-one patients with sepsis or septic shock were recruited. Blood samples were taken from each patient on admission, days 1, 3, 5, and 7. Routine blood results were noted as well as descriptive data. A clotted sample was centrifuged at 2000 r.p.m. for 20 min and the serum frozen to allow later analysis. A high-sensitivity ELISA was used to quantify TNF-α. IL-13 and IL-2 were assayed by standard ELISA, and HLA-DR on CD-14 positive monocytes measured by flow cytometry after labelling with immunofluorescent monoclonal antibodies.

Patients had a median age 56 (45–69, interquartile range). APACHE II score was 17.5 (15–23). There were 24 men and seven women. Twenty-three of the 31 patients developed septic shock. Patterns of expression of HLA-DR were characteristic of previous reports of similar patient populations, showing greater depression and slower recovery in the shocked than the non-shocked patients (Fig. 4). IL-13 was detected in the plasma of 24 of the 31 patients at baseline.

TNF was elevated in all patients but more so in those with septic shock.

We have characterized patterns of IL-13 expression in human sepsis and septic shock. IL-13 may also pressage the recovery in HLA-DR expression on CD14 positive monocytes.

Keywords: infection, sepsis; immune response, interleukin-13

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Biochemical predictors of outcome from intensive care

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An improved understanding of predictors in the intensive care unit (ICU) setting would provide prognostic information useful for making treatment decisions. The acute physiology and chronic health evaluation II (APACHE II) system is a widely used score to provide indications of probable outcome from intensive care. However, this system is largely based on physiological variables that may reflect propensity for change in response to the illness within the individual rather than disease severity itself. We, therefore, conducted a cohort observational study to assess the relationship between biochemical variables and mortality of ICU patients regardless of diagnosis.

Two hundred patients were recruited and a single blood sample taken within the first 24 h of ICU admission. Concentrations of plasma interleukin-6 (IL-6), lipid peroxide, and protein-bound thiol groups, plus total antioxidant capacity, were determined. Albumin, urate, lactate, prothrombin time, and fibrinogen were also recorded from the results of routine pathology laboratory measurements. Non-parametric data were expressed as median (range) and analysed by Mann–Whitney U test and normally

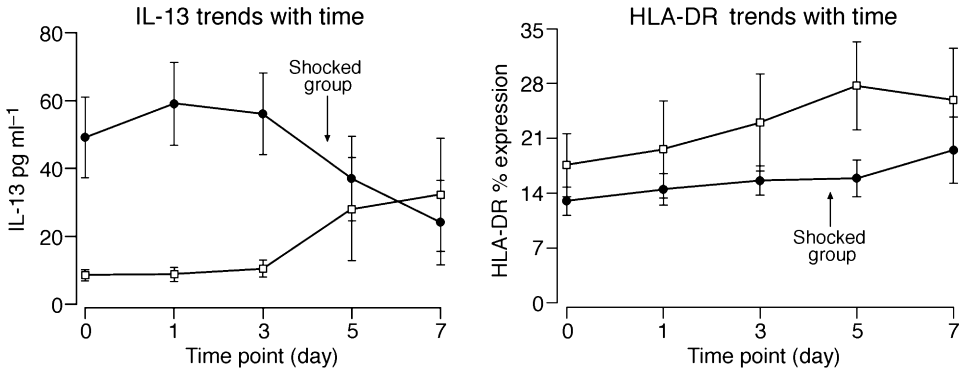

Fig 4 Patterns of expression of IL-13 and HLA-DR in shocked and non-shocked patients (mean (SEM)).

distributed data were expressed as mean (SD) and analysed by Student's *t*-test.

Of the 200 patients recruited 114 were men and 86 were women, with a median age of 60 (18–92) yr. Median ICU stay was 3 (1–55) days; 45 patients died and 155 survived. Serum urate, lactate, and IL-6 were significantly higher in non-survivors than survivors 0.44 (0.12–0.93) *vs* 0.32 (0.10–1.04) mmol litre^{-1}; 2.9 (0.6–28.0) *vs* 1.8 (0.6–19.0) mmol litre^{-1}; 1547 (18–7682) *vs* 116 (10–4431) pg ml^{-1}, respectively (P<0.001 in each case). Antioxidant capacity was significantly lower in non-survivors (1.11 (0.16) mmol litre^{-1}) than survivors (1.26 (0.17) mmol litre^{-1}, P<0.001). Serum albumin and lipid peroxide concentrations were also significantly lower in the non-survivors 28.0 (8.2) *vs* 30.5 (6.6) g dl^{-1} and 2.20 (0.01–8.60) *vs* 3.13 (0.01–8.75) μmol litre^{-1}, respectively (P<0.05). Prothrombin time, fibrinogen concentrations and protein thiol group concentrations did not differ significantly between survivors and non-survivors. Logistic regression analysis revealed that IL-6, total antioxidant capacity and serum urate are independent predictors for ICU mortality (Table 14).

Table 14 IL-6, antioxidant and urate concentrations

Variable	*P* value	Odds ratio (95% confidence interval)
Interleukin-6 (pg ml^{-1})	<0.001	1.0009 (1.0005–1.0013)
Total antioxidant capacity (mmol litre^{-1})	<0.001	0.0020 (0.0001–0.0350)
Urate (mmol litre^{-1})	<0.05	18.853 (1.73–204.9)

The predicted ICU mortality can be estimated using the following equation:

Logit (P) = (IL-6×0.0009)+(antioxidant capacity×–6.2253)+(urate×2.9367)+4.1294

Acknowledgements: We gratefully acknowledge the help and cooperation of the ICU nursing and medical staff.

Keywords: intensive care

The effect of propofol and ketamine on phosphodiesterase activity

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The neurotransmitter activity of nitric oxide is involved in excitatory amino acid-mediated neurotoxicity, consciousness, learning, and memory. Effects on the nitric oxide–cGMP pathway have been implicated in anaesthesia. Most of the effects of nitric oxide are mediated by activation of guanylate cyclase leading to production of cGMP[1]. Sedative drugs decrease intracellular cGMP in the brain. This could be either a result of a decrease in production via effects on guanylate cyclase activity or increases in degradation of cGMP through increased phosphodiesterase activity. Several isoforms of phosphodiesterases metabolize the cyclic nucleotides cAMP and cGMP into the inactive compounds 5'AMP and 5'GMP, respectively. The aim of this study was to investigate the effects of anaesthetic agents on phosphodiesterase activity.

We adapted a spectrophotometric assay for measuring phosphodiesterase activity *in vitro*. The technique uses the change in absorbance at 340 nm in a series of coupled enzyme reactions using cAMP as substrate, in the presence of NADH. Analyses were conducted in triplicate at four concentrations of propofol and ketamine, at enzyme substrate concentrations ranging from 0.5 to 10 K_m. Lineweaver–Burke plots were then constructed in order to determine the effects of propofol (10, 1, 0.1, and 0.01 μM) and ketamine (100, 10, 1, and 0.1 μM) on K_m and V_{max} of a mixture of phosphodiesterases purified from bovine heart. Results were expressed as percentage change compared with K_m and V_{max} in the absence of the anaesthetic agent. Single linear regression analysis was used and P<0.05 was considered statistically significant.

Neither propofol nor ketamine changed V_{max}. Propofol reduced K_m by 58.9 and 79.6% at 10 and 1 μM, respectively (P<0.01) whereas lower concentrations had no effect. Ketamine had no effect on K_m at any concentration. Neither of the anaesthestics had any affect on the activity of any of the other coupled enzymes used to determine phosphodiesterase activity.

A reduction in K_m in the absence of a change in V_{max} is indicative of an enzyme agonist, whereas an increase in K_m is suggestive of a competitive antagonist. We have shown that at concentrations relevant to those obtained in the circulation clinically, propofol acts as an agonist in this *in vitro* setting. Further investigations are required to determine which particular isoforms of the phosphodiesterases are affected by these anaesthetic agents.

Acknowledgements: We are grateful to the Royal College of Anaesthetists and the Association of Anaesthetists for financial support.

Keywords: enzymes, phosphodiesterases; anaesthetics i.v., propofol; anaesthetics i.v., ketamine

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Propofol and halothane vs sevoflurane in paediatric day case surgery: induction characteristics and recovery time

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As day case surgery aims to minimize disruption of the patient's routine, anaesthetic agents that enable a safe and rapid return to the community should be used.[1] The aim of this study was to compare the induction characteristics and recovery time of a propofol induction and maintenance with halothane/N_2O/O_2, or sevoflurane/N_2O/O_2 induction and maintenance in paediatric patients.

Three hundred and twenty two unpremedicated children, aged 3–13 yr undergoing day case general or ENT surgery were randomized to receive either a propofol (with lidocaine) induction with halothane/N_2O maintenance, or a sevoflurane/N_2O induction and maintenance technique. Time from starting anaesthesia until entering the operating theatre (induction time), anaesthetic maintenance time, and times when ready to leave the recovery room and go home were noted. The incidence of adverse events during induction was recorded. Statistical analysis using SPSS^{TM}10 was carried out with unpaired Student's *t* or chi-squared tests as appropriate (Table 15).

The children who had propofol had a shorter induction time than those having an inhalation induction with sevoflurane. In contrast, the children who had anaesthesia maintained with sevoflurane had a shorter recovery time than those in the

Table 15 Comparison of propofol/halothane and sevoflurane groups. Mean (SD) where appropriate

Group (*n*, number per group)	Propofol/halothane (*n*=156)	Sevoflurane/sSevoflurane (*n*=166)	*P*
Age (yr)	7.2 (2.6)	7.17 (2.7)	n.s.
Female:Male	1:2.1	1:2.3	n.s.
Induction time (min)	3.1 (1.9)	5.0 (2.3)	0.001
Maintenance time (min)	9.5 (7.0)	10.1 (6.7)	n.s.
Recovery time (min)	26.4 (8.8)	23.2 (8.8)	0.002
Time to home discharge (min)	136.9 (127.2)	136.6 (96.4)	n.s.
Excitatory movement (*n*)	10	30	0.002

propofol/halothane group. There was no difference between groups in the time spent on the postoperative ward before discharge home. The incidence of excitatory movement during induction was significantly greater in the sevoflurane group. Twenty-two patients in the propofol group reported pain on injection. No differences were found between groups in the incidence of laryngospasm, breath-holding, or coughing during induction.

Although i.v. induction with propofol has been associated with a shorter induction time than sevoflurane in adults,[2] the longer recovery time may negate this advantage. No differences were found between groups in time to discharge home. The incidence of pain on injection with propofol may make i.v. induction less pleasant for paediatric patients, whilst the restlessness already reported in adults during sevoflurane induction[3] may discourage anaesthetists from using this technique in children.

Acknowledgements: Funded by the National Co-ordinating Centre for Health Technology Assessment (UK).

Keywords: anaesthetic techniques, inhalation; anaesthetics volatile, sevoflurane; anaesthetics volatile, halothane

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The effects of glyceryl trinitrate and dobutamine on cerebral haemodynamics

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Glyceryl trinitrate (GTN) and dobutamine are often used in critically ill patients. Their effects on cerebral haemodynamics are not well established. We aimed to measure their effects on middle cerebral artery blood flow velocity (MCAFV), cerebral autoregulation (CA), cerebrovascular reactivity to carbon dioxide ($CRCO_2$), estimated cerebral perfusion pressure (eCPP), and critical closing pressure (CCP), as assessed by transcranial Doppler ultrasonography.

We recruited ten healthy volunteers, aged 24–40 yr. Study set up included continuous measurement of MCAFV, end-tidal carbon dioxide ($P_{E'CO_2}$) monitoring and non-invasive arterial pressure measurement. Baseline values of mean (MAP) and diastolic arterial pressure (DAP), and systolic, mean and diastolic MCAFV's were recorded. CA was assessed by performing a transient hyperaemic response test and calculating the strength of autoregulation (SA).[1] C_{RCO_2} was assessed by measuring MCAFV after induced changes in $P_{E'CO_2}$ and calculated as per cent change in MCAFV per kPa change in $P_{E'CO_2}$.[1] These measurements were then repeated after the MAP was increased to a target of approximately 25% above the baseline value with an infusion of dobutamine, or, on a separate occasion, decreased by target of approximately 25%, with an infusion of GTN. Estimated cerebral perfusion pressure was calculated as: $MCAFV_{mean} \times [(MAP - DAP)/(MCAFV_{mean} - MCAFV_{diastolic})]$.[2] Critical closing pressure was calculated as: MAP – eCPP.[2] Paired *t*-test was used to compare these parameters before and after dobutamine, and before and after GTN infusion (Table 16).

Dobutamine increased MAP by 19%, eCPP by 10 mm Hg and CCP by 7 mm Hg, suggesting an increase in vessel tone. There was no significant change in MCAFV, SA, or $CRCO_2$. GTN decreased MAP by 13%, and CCP by 31 mm Hg, whilst increasing eCPP by 19 mm Hg. MCAFV decreased by 17%. Both SA and $CRCO_2$ were preserved.

Keywords: brain, blood flow; sympathetic nervous system, dobutamine; sympathetic nervous system, glyceryl trinitrate

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Attempting to estimate the rate of perfusion of the cerebral site of action of sevoflurane

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Table 16 Cerebrovascular haemodynamic parameters (mean (SD)). *$P<0.05$

	Pre-dobutamine	Post-dobutamine	Pre-GTN	Post-GTN
MAP (mm Hg)	89 (9)	106 (8)*	83 (5)	72 (4)*
MCAFV(cm^{-1})	52 (11)	56 (13)	52 (12)	43 (10)*
SA	41.07 (0.15)	1.03 (0.19)	1.14 (0.21)	1.31 (0.2)
$CRCO_2$ (%kPa^{-1})	37 (12)	37 (11)	37 (9)	43 (8)
ECPP (mm Hg)	53 (14)	63 (11)*	44 (13)	63 (18)*
CCP (mmHg)	36 (14)	43 (10)*	38 (10)	9 (15)*

Finding out how and where anaesthetics act in the brain remains an important area of research. As neuronal activity is closely coupled to glucose metabolism and cerebral blood flow, attempts have been made to use positron emission tomography (PET) to identify sites of anaesthetic action within the brain.[1]

An alternative approach has been to use the time to unconsciousness (defined here as failure to respond to an auditory stimulus) during a controlled inhalation induction to estimate the rate of perfusion of the cerebral site or sites involved. The data in the literature are not entirely satisfactory for this purpose[2] and we have, therefore, conducted a series of cases in an attempt to improve the accuracy of this estimation.

Fifteen patients of ASA class I–II aged 16–65 yr undergoing minor day case surgery were studied. An electronic metronome set to give a bleep at 1-s intervals was placed on the pillow during induction and patients were asked to press a button in response to each bleep. The method was explained to each patient and the bleep demonstrated at the preoperative visit.

Induction was by 8% sevoflurane in oxygen via a co-axial system with a 5 litre reservoir bag. Breathing was controlled by the exhortations of the anaesthetist to be a series of deep breaths. This was found to be more consistent than the vital capacity method. Tidal volumes and inspired and expired sevoflurane concentrations (from a Datex AS3 monitor) were recorded using a chart recorder. The bleeps and responding button presses were also recorded on the chart so that the time from start to cessation of response could be easily measured.

We assumed that the arterial anaesthetic tensions equalled the end-expired partial pressures and that the rate of increase of anaesthetic tension in the site of interest was proportional to the difference in tension between that site and arterial blood. The constant of proportionality, k, is the quotient of the perfusion and the tissue/blood partition coefficient. For convenience we fitted an arbitrary continuous function to the end-expired data that then allowed accurate numerical calculation of the tension at the site of interest for any value of k. The value of k was varied to obtain a tissue tension of 0.78% (MAC_{awake}) at the time of loss of response. Assuming a tissue/blood partition coefficient of 1.7, we calculated the perfusion from this value of k. Allowance was made for transit time between lung and brain.

The mean time taken to unconsciousness for the 15 patients studied was 43.9 s (95% CI 38–45). The mean calculated perfusion rate was 82 ml 100 g^{-1} min^{-1} (median (95% CI) 76 (61–95)).

Keywords: anaesthetics volatile, sevoflurane; brain

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POSTER PRESENTATIONS

A nested case-controlled study of risk factors for perioperative cardiovascular death

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We have reported a nested case-controlled study of risk factors associated with cardiac death within 30 days of general anaesthesia in patients undergoing elective non-cardiac surgery. The study examined patients undergoing surgery between 1979 and 1990, identifying arterial hypertension, preoperative renal impairment (serum creatinine >200 mmol $litre^{-1}$) and a past history of myocardial infarction as risk factors associated with perioperative cardiac death.[1] However, the past decade has seen advances in the management of cardiovascular disease and perioperative care. We have, therefore, conducted a further case-controlled study using data for the period 1991–1998 to examine the possible impact of these changes.

Oxford Record Linkage Study database of medical records was interrogated to identify patients aged more than 16 yr who died from cardiovascular causes within 30 days of non-cardiac and non-neurological surgery.[1] Patients were matched with controls for the same surgeon and operation, and age ± 10 yr. The notes of the cases and controls were examined, the certified cause of death confirmed, and data recorded on cardiac risk factors, intercurrent medications and perioperative investigations.

Eighty-three cases were identified (23 vascular, 17 orthopaedic, 15 urological, and 28 abdominal surgery patients); 55 cases and 47 controls were male; and the age ranges were 62–91 and 60–89 yr, respectively. Death occurred between days 0 and 29 (median day 8). Univariate analysis identified four risk factors associated with cardiac death: history of angina (OR 2.30, 95% CI 1.06–5.41); previous history of cardiac failure (OR 4.40, 1.63–14.87); treatment with diuretics (OR 2.42, 1.20–5.20), or nitrates (OR 15.0, 2.31–631.43). Multivariate analysis was then performed using logistic regression. Risk factors were included in the model if they achieved significance at the 5% level. Automated modelling procedures were not used. To allow for comparison with other previous studies, adjustment was made for sex and for residual confounding by age. When clinical risk factors were examined, but data on intercurrent medication excluded, cardiac failure (OR 4.27; 1.60–11.38) was the only significant risk factor in the model. When data on drug therapy were included in the modelling process, it was found that treatment with nitrates was a significant factor and treatment with diuretics could be substituted for cardiac failure. These gave a model with an OR of 15.77 (2.02–122.75) for nitrates, and OR of 2.87 (1.30–6.30) for diuretics as risk factors for perioperative cardiac death.

These data should be interpreted with caution. However, they would support an impact of changes in the treatment of intercurrent disease on the occurrence of perioperative complications. In contrast to our earlier study,[1] we have shown no association between past histories of myocardial infarction or arterial hypertension, or renal impairment and cardiac death. Several factors may account for these differences: different and more potent intercurrent drug therapies for cardiac diseases, better perioperative arterial pressure control, and better monitoring in the intra- and immediate postoperative periods.

Keywords: complications, perioperative death; risk factors

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Methylprednisolone administration reduces renal proximal tubular injury during cardiac surgery

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Significant renal tubular dysfunction, measured using urinary *N*-acetyl-β-D-glucosaminidase (NAG), has been documented after cardiac surgery with cardiopulmonary bypass (CPB).[1] Large

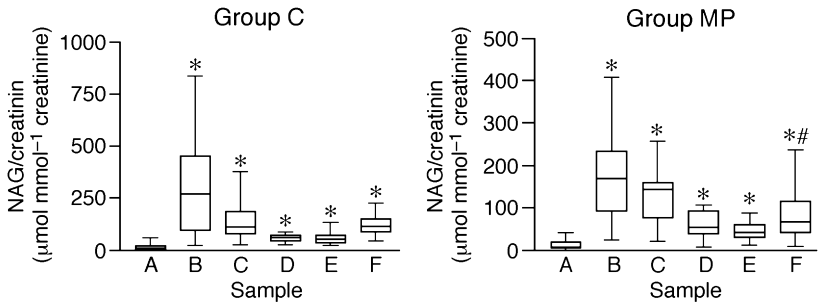

Fig 5 NAG/creatinine ratios in group C (n=17) and group MP (n=16). Box and whisker plots show median, 25th and 75th percentiles and range. *P<0.01 within group compared with baseline. #P<0.05 between groups. Note difference in scale between C and MP groups.

increases in urinary anti-inflammatory cytokines are observed at CPB implying their production in the kidney, in response to glomerular filtration of plasma pro-inflammatory cytokines.[2] Urinary IL-1ra concentrations have been shown to correlate with proximal renal dysfunction as indicated by NAG production.[2] Methylprednisolone reduces the plasma pro-inflammatory response during cardiac surgery and is accompanied by a reduction in urinary anti-inflammatory cytokines.[3 4] This study investigated whether methylprednisolone administration would reduce proximal tubular dysfunction.

Thirty-three ASA grade III–IV patients undergoing elective coronary artery bypass grafting were allocated randomly to receive methylprednisolone 30 mg kg^{-1} before induction (group MP) or placebo (group C). Urine samples were obtained for NAG and creatinine measurement as follows: baseline (sample A), after cross-clamp release (sample B), and 2, 6, 24, and 48 h post-CPB (samples C, D, E, and F, respectively). Results were analysed using non-parametric repeated measures analysis of variance with Dunn post-test or Wilcoxon signed rank and Mann–Whitney test as appropriate.

Urinary NAG/creatinine ratios increased significantly in both groups over the study period (P<0.01) compared with baseline (Fig. 5). The increase demonstrated in Group MP was significantly lower in comparison to group C at 48 h post-CPB (P<0.05).

These findings would suggest that the renal injury in the methylprednisolone group was of a lesser magnitude and shorter duration than that in the control group, indicating that methylprednisolone may provide some degree of protection against renal dysfunction after cardiac surgery. The exact mechanisms involved require further investigation.

Keywords: surgery, cardiovascular; complications, renal damage

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Does end-tidal carbon dioxide affect speed of induction of anaesthesia with propofol?

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Kinetic models suggest that the rate limiting factor of anaesthetic induction for i.v. anaesthetic agents is the delivery of the agent to the brain.[1] Increased cerebral blood flow enhances the cerebral uptake of anaesthetic agents.[2] Increasing arterial carbon dioxide partial pressure (Pa_{CO_2}) increases cerebral blood flow.[3] The increased cerebral blood flow associated with hypercapnia should, thus, increase anaesthetic delivery to the brain and could reduce induction time. Hypercapnia can be induced in the anaesthetic room by rebreathing from a Bain circuit.[4] We studied how rebreathing affected induction time with propofol.

We allocated randomly 47 healthy patients undergoing minor gynaecological procedures to breathe from a Bain circuit supplied with either a low (2 litre min^{-1}) or high (12 litre min^{-1}) flow of oxygen. Oxygen breathing started 1 min before the infusion and continued throughout induction. To give the agent at a comparable rate in different subjects, we estimated the induction dose of propofol from age and weight, diluted 1.6 times this dose into 40 ml, and gave it i.v. at a rate of 5 ml min^{-1}. In this way, the mean time to induction would be 300 s. Induction time was measured from start of infusion to the time an outstretched arm came down from 45° to horizontal. Time to induction was compared with Student's t-test, and P<0.05 was considered significant. Values are given as mean (SD).

The patient groups were comparable (low flow (n=24): age 29 yr (range 16–51), weight 64 kg (8), height 165 cm (7); high flow (n=23): age 27 yr (15–45), weight 63 kg (9), height 164 cm (5)). FE'_{CO_2} increased by 1.3% (0.4%) and decreased by 0.1% (0.6%) during low and high flow induction (P<0.001). Mean times to induction of anaesthesia were 184 (54) and 202 s (46) for low and high flow, respectively (P=0.216). There is no correlation between DFE'_{CO_2} and time to induction (Fig. 6). The power of the study, to show that a slow i.v. injection of propofol will act 25% more rapidly when rebreathing is encouraged, is 0.94. A possible explanation for our findings could be a parallel increase in cardiac

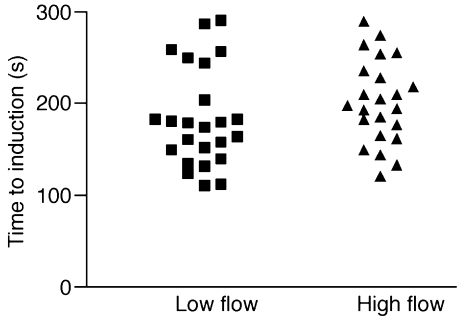

Fig 6 Time to induction with low and high fresh flow.

output and thus a similar rate of delivery of propofol to the brain in the two groups.

Keywords: anaesthetic techniques, induction; ventilation, rebreathing

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Interaction of i.v. anaesthetic induction agents with recombinant human m1–m3 muscarinic receptors expressed in Chinese hamster ovary cells

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Previous reports suggest that the effects of i.v. anaesthetic agents propofol, ketamine, and thiopental on airway tone may result from parasympathetic modulation.[1 2] In the present study, we examined if these agents interact with human m1–m3 muscarinic receptors stably expressed in Chinese hamster ovary cells (CHO-m1, m2, and m3, respectively).

Receptor interaction was determined by displacement of l-[*N*-methyl-^{3}H]scopolamine methyl chloride ([^{3}H]NMS) binding. CHO-m1, m2, and m3 cell membranes (n=5–10) were incubated in buffer containing approximately 0.4 nM [^{3}H]NMS and thiopental, propofol (10^{-6}–10^{-3} M), ketamine (10^{-5}–10^{-2} M) and non-anaesthetic barbiturate, barbituric acid (10^{-6}–10^{-3} M) as described previously.[3] In addition, as an index of receptor function, intracellular Ca^{2+} ($[Ca^{2+}]_i$) was measured fluorometrically in fura2 loaded whole cells stimulated with 1 mM methacholine.[4]

Ketamine dose-dependently displaced [^{3}H]NMS binding to CHO-m1, m2, m3 membranes with pK_i (mean (SEM)) values of 4.34 (0.14), 3.53 (0.10), and 3.61 (0.02), respectively. However, ketamine did not affect either basal or methacholine stimulated increase in $[Ca^{2+}]_i$ in CHO-m1 cells (m2 and m3 were not used as the interaction in binding was weak). Thiopental significantly displaced [^{3}H]NMS binding to m3 (but not m1 or m2) with a pK_i of 4.12 (0.06). In addition, thiopental (10^{-5}–10^{-3} M) dose-dependently inhibited methacholine stimulated increase in $[Ca^{2+}]_i$ in CHO-m3 cells. Propofol and barbituric acid were inactive at m1, m2, and m3.

We conclude that thiopental may act as an m3 antagonist, while ketamine and propofol are likely to be functionally inactive at airway muscarinic receptors.

Keywords: anaesthetic techniques, i.v.; parasympathetic nervous system, recombinant muscarinic receptors

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The effect of moxifloxacin on release of interleukin-8 from human neutrophils

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Interleukin 8 (IL-8) is a neutrophil chemotactic and activating factor produced in response to inflammatory stimuli including lipopolysaccharide (LPS). Although IL-8 has a major role in the host response to infection via recruitment and activation of neutrophils, increased concentrations are associated with poor outcome. We have previously shown that the fluoroquinolone antibiotic ciprofloxacin increases IL-8 mRNA expression and IL-8 protein release in endothelial cells.[1 2] Although moxifloxacin (Avelox, Bay 12–8039, Bayer Plc) has a similar mechanism of action to ciprofloxacin, it is structurally different and its immunomodulatory effects are unknown. We investigated the effect of moxifloxacin on IL-8 release from stimulated human neutrophils.

Neutrophils were isolated from 20 healthy volunteers aged 20–47 yr, using single density gradient centrifugation, and incubated with 2 μg ml^{-1} LPS plus 0–50 μg ml^{-1} moxifloxacin at 37°C in 95% air/5% carbon dioxide for 20 h. IL-8 was measured in cell culture supernatants using enzyme immunoassay. Data are expressed as median (range) and were analysed using Friedman analysis of variance and Wilcoxon signed rank tests.

Although IL-8 release was variable between subjects, release of IL-8 increased in all cases from 19.5 (0.9–225.9) to 37.9 (1.8–387.0) pg ml^{-1} on exposure to LPS (P=0.05). In cells also treated with moxifloxacin, IL-8 release decreased with increasing concentrations of the antibiotic (P=0.02) and levels were significantly lower than in the absence of moxifloxacin at all concentrations (P<0.05, Fig. 7). Exposure to moxifloxacin had no effect on cell viability.

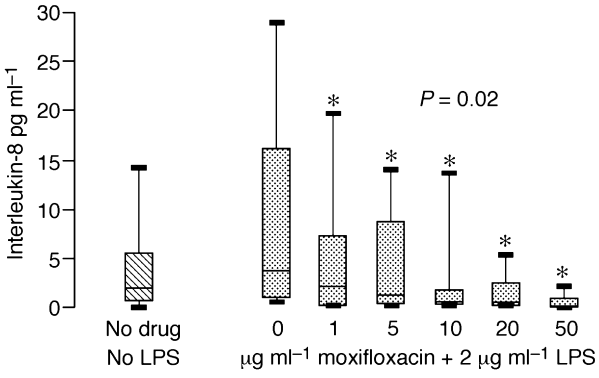

Fig 7 Effect of moxifloxacin on IL-8 release from human neutrophils stimulated with 2 μg ml^{-1} LPS (n=20). Box and whisker plots show median, 25th and 75th percentile and range. P value refers to Friedman analysis of variance. *Wilcoxon signed ranks test compared to cells not exposed to moxifloxacin, P<0.05.

Moxifloxacin decreased LPS-mediated IL-8 release from human neutrophils, in contrast to our previous findings with ciprofloxacin. This implies that the structure of these antibiotics has a profound effect on their immunomodulatory properties and further studies are required.

Acknowledgement: We are grateful to Bayer Plc for financial support.

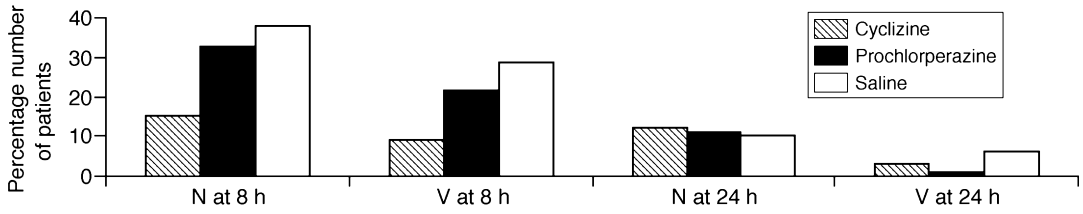

Fig 8 Incidence of PONV.

Keywords: antibiotics, moxifloxacin; immune response, interleukin-8

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Cyclizine reduces the incidence of nausea and vomiting after elective Caesarean section with intrathecal diamorphine

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Regional anaesthesia is now used for the majority of elective Caesarean sections in the UK, and intrathecal opioids are administered to allow both a reduction in the dose of local anaesthetic, whilst also providing postoperative analgesia. Recognised side effects include postoperative nausea and vomiting (PONV). Audit in our unit revealed an incidence of 48%, with a reported incidence of up to 75%.[1] Our study compared the effectiveness of cyclizine, prochlorperazine, and placebo in reducing the incidence of PONV in women undergoing spinal anaesthesia with intrathecal diamorphine for elective Caesarean section.

We recruited 224 ASA I or II patients into the study. The women received our standard spinal anaesthetic technique, and were randomized to receive either 50 mg cyclizine, 12.5 mg prochlorperazine, or 1 ml saline. This was given at the end of the procedure as an i.m. injection into the anaesthetized thigh. The patients were questioned on the ward at 8 and 24 h with regards to nausea, vomiting, and side effects, within these time periods. Data were collected and analysed on SPSS version 9 for Windows©, and a chi-squared test was performed on all PONV data. A P-value of <0.05 was considered statistically significant.

Eight patients were excluded (four in the cyclizine, one in the prochlorperazine, and three in the placebo group). Three were excluded because of severe PONV in recovery requiring i.v. ondansetron, three were lost to follow-up, one withdrew consent before injection, and one was sedated and ventilated after postoperative complications unrelated to the study. Groups were comparable with respect to age and obstetric history. Results are shown in Figure 8. In the first 8 h after the Caesarean section, the incidence of PONV was significantly reduced in the cyclizine group when compared with the prochlorperazine and placebo groups. In the subsequent 16 h, the incidence of PONV was similar in all three groups.

The requirements for supplementary antiemetics, and reported side effects, were similar between the three groups.

Keywords: vomiting, antiemetics, cyclizine; anaesthesia, obstetric; vomiting, nausea

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Local anaesthetic and opioid drug absorption within epidural filters

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Drug binding and bacterial challenge[1] testing is an essential part of evaluating new epidural filter membranes before clinical use. The aim of this study was to assess potential drug absorption by a new epidural filter membrane after infusions of commonly used local anaesthetic and opioid drugs utilizing a previously established *in vitro* model capable of detecting small amounts of drug binding to filters. The sensitivity of the model was facilitated using drug concentrations much lower than that clinically administered.

Three batches of four drug solutions (bupivacaine 25 $\mu g\,ml^{-1}$; ropivacaine 100 $\mu g\,ml^{-1}$; fentanyl 2 $\mu g\,ml^{-1}$; diamorphine 80 $\mu g\,ml^{-1}$) were used to test 12 SIMS Portex epidural filters (0.2 µm, polysulphone membrane filter). A sample (60 ml) of each solution in a BD Plastipak syringe was infused through a single filter at 10 ml h^{-1} using an IVAC P1000 syringe pump. Drug concentrations, sampled both before and after the epidural filter at

Table 17 Drug absorption time course

Drug (% mean (SD))	0 min	15 min	30 min	45 min	60 min
$Bupivacaine_{pre\text{-}filter}$	100	99.71 (0.56)	100.07 (0.56)	100.37 (0.12)	100.36 (0.12)
$Bupivacaine_{post\text{-}filter}$	–	100.46 (0.29)	100.46 (0.28)	99.99 (0.94)	100.21 (0.46)
$Ropivacaine_{pre\text{-}filter}$	100	100.22 (0.23)	100.21 (0.13)	100.14 (0.06)	100.01 (0.09)
$Ropivacaine_{post\text{-}filter}$	–	100.03 (0.90)	100.15 (0.45)	99.84 (0.25)	100.01 (0.11)
$Fentanyl_{pre\text{-}filter}$	100	98.79 (0.54)	99.80 (0.41)	100.33 (0.73)	99.74 (1.06)
$Fentanyl_{post\text{-}filter}$	–	100.57 (0.72)	100.56 (0.72)	98.97 (0.59)	100.09 (0.22)
$Diamorphine_{pre\text{-}filter}$	100	99.69 (0.27)	99.92 (0.08)	100.17 (0.68)	100.26 (0.39)
$Diamorphine_{post\text{-}filter}$	–	99.96 (0.74)	99.96 (0.74)	100.33 (1.19)	99.49 (0.09)

predetermined time intervals (0, 15, 30, 45, 60, 120, 180, and 240 min), were measured using HPLC (high performance liquid chromatography) with a diode array detector. Samples were assayed in triplicate against a freshly prepared drug reference solution. Data were expressed as mean (SD) percentage (%) drug concentration with each pre-filter value compared with pre-filter at time, 0 min (control) and each post-filter value compared with its corresponding pre-filter value. A saline infusion through a test filter was also included in the procedure as a negative control. Statistical analysis included the Shapiro–Wilk test and repeated measures ANOVA using a general linear model ($P<0.05$).

No statistically significant differences ($P=0.998$) were observed in mean % drug concentration, for all drugs, over the initial 60 min-testing period (Table 17), when empirically maximal initial drug absorption would be expected to occur. No further significant differences were observed up to the total testing period of 240 min.

These experiments demonstrate no drug absorption by the epidural filter membrane over the 240 min test period.

Acknowledgements: SIMS Portex Ltd for study funding and Research Fellowship (VS).

Keywords: equipment, epidural filter membrane

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Are training standards for general anaesthesia in obstetrics impossible to meet?

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In the year 2000, there were 860 Caesarean sections at Northwick Park Hospital. General anaesthesia was used in 124 cases and they were classified[1] into 53, 38, 20, and 13 for types 1, 2, 3, and 4 Caesarean section, respectively. Eighty-four operations were outside normal operating hours. Analysis of the grades of the principal anaesthetist for general anaesthesia were consultant (19 cases), staff grade (eight), year 1–2 SPR (93), and year 3–4 SPR (four). Twenty-one cases had two or more anaesthetists present. Year 1–2 SPRs were with a senior anaesthetist for 16 Caesarean sections and performed 93 alone or with an SHO. During 2000, eight year 3–4 SPRs were in the department—six performed no general anaesthetics for Caesarean section, one performed two, and one performed 1. There were 12 year 1–2 SPRs. All 12 performed between two and 13 general anaesthetic Caesarean sections (mean 8). There were six anaesthetists at SHO level—four were present at six general anaesthetics whilst two did not see any. There were 102 grade 1, 15 grade 2, seven grade 3, zero grade 4, and no failed intubations.

The OAA recommends a minimum experience of 20 obstetric general anaesthetics in training and that training should primarily take place in the SHO grade and be of 8 weeks duration. These current recommendations are impossible to meet and the guidelines should be amended. Training takes place primarily in the year 1–2 SPR grade and supervised training is difficult. It is important that trainees be given adequate training in all theatre situations so that laryngoscopy grade 3 and failed intubation can be managed successfully. Grade 3 intubations are generally reported as 1.7% and in our unit are 1.6%. Failure of expertise has accounted for both of the failed intubations that have occurred in our unit over the past 5 yr. Will the incidence of general anaesthesia mortality increase from zero as in the last Confidential Enquiry into Maternal Mortality (1994–1996) report as a result of less experienced trainees and consultants emerging from training?

Keywords: anaesthesia, obstetric; education

Reference

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Dural puncture and subsequent blood patches in the obstetric population

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Post-dural puncture headache is a recognised complication of spinal and epidural anaesthesia. Epidural blood patch is the accepted treatment of persistent headache though debate exists as to its success.[1 2] A retrospective audit of all epidural blood patches performed in the Rotunda Hospital over a 4-yr period from 1996 to 2000 was perfomed. The aim was to examine the efficacy of epidural blood patches in the management of post-dural puncture headache and to identify any risk factors to the development of severe post-dural puncture headache.

Theatre records for the 4-yr period were examined and the charts of all patients who had blood patches performed during this period were reviewed. Date, time, seniority of anaesthetist, patient characteristics, position and size of needle used were recorded. In addition, time to onset of symptoms, time to blood patch insertion, symptom relief, need for subsequent blood patch, and symptoms on discharge were all noted. Patients were then sent a questionnaire to complete and return enquiring about symptoms on their return home and whether they would have a repeat epidural for subsequent deliveries. Non-responders were subsequently contacted by phone.

During the study period 15 088 epidurals and 3622 spinals were performed. Eighty-seven patients required blood patches, 61 (70.11%) after accidental dural puncture and 26 (29.88%) after spinal anaesthesia. Of these 11 (12.64%) needed repeat blood patches. The combined response rate was 72.09%. The majority of the procedures were performed by junior anaesthetists (SHO 75.86%). Headache reoccurred in 33 patients (53.22%) on discharge and new backache was present in 33 (53.22%) of patients questioned. The majority of patients would not have a repeat epidural (50 *vs* 33.87%) while 16.13% were unsure.

Epidural blood patches are not as effective in the long-term treatment of post-dural puncture headaches as thought. Dural puncture headache causes considerable morbidity in the obstetric patient, leading to long-term symptoms in a large proportion of the patients surveyed. The majority of those surveyed would not have an epidural again.

Keywords: complications, dural puncture headache; complications, epidural blood patch

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Diagnosis of occiput-posterior position from failure of epidural analgesia in the first stage of labour

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Occiput-posterior (OP) position of the fetus is associated with long, difficult labours, and with failure of epidural analgesia.[1] In early labour, OP position can be difficult to diagnose, but becomes easier with descent of the head. In the majority, the fetal head rotates via occiput-transverse (OT) to an occiput-anterior (OA) position, but the malposition may persist in 6–8%.[2] The aim of this study was to assess if the pattern of pain distribution in women, whose epidural analgesia was inadequate, could be used to diagnose OP fetal position.

A 3-month prospective observational study was designed to identify labouring women with failure of epidural analgesia and the associated fetal position. Failure of epidural analgesia was defined as unacceptable pain, as assessed by the attending midwife, at least 30 min after an initial bolus of 20 ml of 0.06, 0.08, or 0.1% bupivacaine plus 20 $\mu g\,ml^{-1}$ alfentanil, followed by a 12 $ml\,h^{-1}$ infusion. An epidural failure was, therefore, one that required a concentration of bupivacaine greater than 0.1% at any time throughout its use. The anaesthetist assessed the pain distribution pattern as either abdominal or lower back, rectal, with premature pushing urge, and decided on the pain rescue options: increased concentration of local anaesthetic bolus, re-site the epidural or combined spinal epidural anaesthesia. The fetal position was assessed by a midwife using vaginal examination or abdominal palpation. The duration of epidural analgesia was calculated.

Twenty-six women with failure of epidural analgesia were identified from a total of 462 (5.6%). Three women had incomplete data, leaving 23 for analysis. Nineteen women were nulliparous. The initial rescue medication administered was stronger local anaesthetic bolus +/– opioid in 22 cases, one epidural was re-sited immediately for a unilateral block. Four epidurals subsequently required re-siting after ineffective rescue medication, including two in combination with a spinal anaesthetic. All re-sites were effective. The pain distribution pattern, fetal position, and duration of epidural analgesia are recorded in Table 18. Back pain, as a test of OP position is 86% sensitive, but only 69% specific. Its negative predictive value is 92%.

We conclude that, in women requiring rescue medication for inadequate pain relief in the first stage of labour, OP position of the fetus is significantly associated with back pain, rectal pressure and prolonged epidural analgesia. Clinically, abdominal pain in a woman with inadequate epidural analgesia is unlikely to be associated with OP position of the fetus, and may be useful for its negative predictive value.

Keywords: anaesthesia, obstetric; complications, fetal position

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An audit of high dependency care for obstetric patients in the Yorkshire region

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The latest Confidential Enquiry into Maternal Deaths[1] recommended the establishment of High Dependency Units (HDUs) for the care of the high-risk obstetric patient. Before an Obstetric HDU course being held at Leeds General Infirmary in November 2000, an audit was conducted to gain a picture of HDU provision and midwife training in the Yorkshire region. Participants at the course were then asked about their own training and practical experience in the management of the high-risk obstetric patient and their confidence in the management of various situations.

A questionnaire was sent to the midwife-in-charge of each delivery unit in the Yorkshire region. Thirty questions were asked regarding the availability of HDU facilities at their unit and training provided for midwives in HDU care. Participants attending a local HDU course were also asked to complete a two-part questionnaire at the start of the first session; the first part questioned their background experience and the second asked midwives to complete a 1–10 visual analogue rating of their subjective confidence in the management of eight common situations.

Questionnaires were sent to 18 units and 16 forms were returned (89% response rate). The majority of units (14/16) nursed patients requiring HDU care on the delivery suite, but only four units (22%) had a dedicated HDU and only five units (28%) made specific reference to the availability of basic monitoring facilities. HDU training was provided by only a minority of units; two units had an HDU training programme and six units had a study day or an HDU/ITU experience day. Midwives in half of the units felt they would benefit from more training in the care of HDU patients, with anaesthetic department input being specifically mentioned. The HDU course participants' confidence ratings were higher in areas that specifically related to obstetric problems (median (range)VAS: epidural complications 9 (2–10) and pre-eclampsia 9 (1–9)) and lower in those relating to monitoring of the mother (basic monitoring 6 (1–10) and invasive monitoring 4 (1–10)), major haemorrhage 7 (1–10) and management of the collapsed mother 6 (1–10). Despite limited exposure to patients recovering from general anaesthesia, with the greater use of regional techniques for operative delivery, midwives felt confident with postoperative recovery 9 (2–10). As regards their training and experience, although many of the course participants (77%) had nursed mothers requiring high dependency care on a delivery suite, the majority (92%) had never worked in a general HDU or ITU or received formal HDU training. Anaesthetic-led teaching for midwives is uncommon on either HDU issues or even routine anaesthetic techniques and their complications.

It is evident that the majority of units in our region are managing high-risk obstetric patients with inadequate facilities,

Table 18 Pain distribution pattern and duration of epidural analgesia

Fetal position	Pain distribution pattern		Mean duration of epidural analgesia in min (SD)
	Back or rectal pain/pushing urge	Abdominal pain only	
OP	6	1	451 (104)
OA/OT	5	11	312 (150)
	Fisher's exact test P=0.027		Student t-test P=0.038

Table 19 Mean or median anxiety scores (range). *P<0.0001 Mann–Whitney (paired), each group, between admission and anaes rm. **P=0.057 (ns) Mann–Whitney (paired), group 1, between admission and anaesthetic room. Admiss., admission; Anaes. rm, anaesthetic room

	Group 1		Group 2		Group 3	
	Admiss.	**Anaes. rm**	**Admiss.**	**Anaes. rm**	**Admiss.**	**Anaes. rm**
Number	44		45		35	
Mean LAAS	4.32	5.53*	3.79	5.88*	4.42	6.59*
(0–10) (range)	(0–9.5)	(0–10)	(0–9.8)	(0.2–10)	(1–8.5)	(2.2–10)
Median HAD	8	9**	–	7.5	8	–
(0–21) (range)	(0–18)	(0–21)	–	(0–20)	(1–17)	–

staffed by midwives with inadequate training and clinical experience in HDU care. It is also evident that although anaesthetists are increasingly involved in the peripartum care of sick mothers, midwives are not receiving the benefit of our knowledge and expertise. There is, therefore, an urgent need for increased anaesthetic input into the training of midwives generally and HDU care specifically.

Keywords: anaesthesia, obstetric; high dependency care

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Linear analogue anxiety scale or hospital anxiety and depression score to assess preoperative anxiety in day case surgery

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In a previous study presented to the Society, we used a Linear Analogue Anxiety Scale (LAAS) to measure preoperative anxiety.[1] However, a more established measure is the questionnaire-based Hospital Anxiety and Depression Score (HAD).[2 3] LAAS and HAD have been compared preoperatively,[3 4] but not immediately before induction of anaesthesia. We used only the seven anxiety-orientated questions of the HAD,[3] which gives a maximum possible score of 21.

We recruited day case gynaecological patients as a model of increasing stress, randomized into three groups. Group 1 were given both tests on admission and in the anaesthetic room, group 2 only LAAS on admission but both in the anaesthetic room, and group 3 both tests on admission but only LAAS in the anaesthetic room. This allocation was intended to identify any learning component of the HAD questions. One hundred and twenty nine patients were recruited; 124 had sufficient data completed to be included in the analysis.

As in our previous study, virtually all LAAS scores increased between admission and the anaesthetic room. This increase was highly significant in all three groups (P<0.0001, paired Mann–Whitney). However, in group 1 (the only group to have HAD on both occasions) the HAD score increased in only 26 of 35 patients who completed both tests, and the increased median score did not reach statistical significance. Several patients did not in fact complete the HAD in the anaesthetic room as they were too anxious! There was however a statistically significant but weak correlation between LAAS and HAD for all groups combined (Spearman r=0.48 95% CI 0.32–0.61, P<0.0001) (Table 19).

We suggest that LAAS is a more reliable and sensitive tool for measurement of anxiety than HAD in a preoperative day case setting, particularly when more than one assessment needs to be made in quick succession.

Keywords: psychological responses, preoperative anxiety

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