# Abstracts

## TREATEMENT WITH ISOPROTERENOL OF BUPIVACAINE TOXICITY

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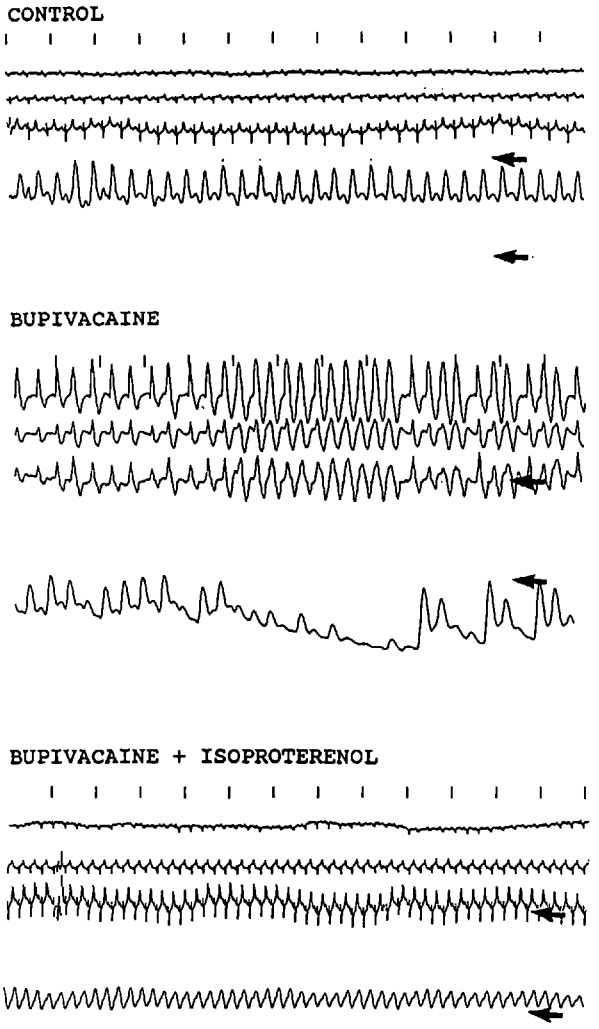
**Introduction:** Bupivacaine cardiovascular toxicity is well recognized. However, its mechanism of action is not completely agreed upon and the treatment on its toxicity is not well established. We have previously shown that in isolated perfused rabbit heart preparation, bupivacaine induced an increase in conduction time at auricular, AV junction, ventricular levels and some conduction defects (increased pacing thresholds and refractory periods) which were completely reversible by isoproterenol. This project was designed to verify if in vivo isoproterenol can also correct bupivacaine cardiovascular toxicity.

**Methods:** 7 pigs (15-20 Kg) were anesthetized with 10 mg/kg of IM Ketamine. They were trachetomized and ventilated with air and O2. Anesthesia was maintained with Na Pentobarbital. The femoral veins and arteries were dissected and catheterized. ECG (3 channels) and arterial blood pressure were continuosly recorded. After stabilization of the hemodynamic status, an arterial blood gas was measurement was done and bolus of 3 mg/kg IV of bupivacaine was then injected. If this injection did not induce dysrthmia or hypotention, a second injection of 2 mg/kg of bupivacaine was given. Isuprel was given intravenously at incremental doses of 0.2 mg to a maximum of 2 mg to correct bupivaciane induced toxicity (in 6 animals). We recorded the following parameters: heart rate, QRS duration , AV conduction; premature vantricular conduction and arterial pressure.

After the administration of bupivacaine, heart rate slowed by 10-50%; the QRS complex widened 50-200%. Frequent (>10/min) premature ventricular contractions (PVC's) occured in 6/7 animals (multifocal in 4/7, salvos of 2-4 in 4/7, sustained ventricular tachycardia in 2/7) and atrioventricular block was seen in 6/7 (first degree 1/7, second degree 4/7, third degree 1/7). Mean systolic and diastolic blood pressure decreased from 152.85/120 to 85/60.71. Six animals were given isoproterenol. PVC's were totally suppressed in all cases; atrioventricular block was corrected in all cases. QRS widening was corrected completely in 4/6 and partially in 2/6. Heart rate accelerated over baseline values in 5/6. Blood pressure was increased to basal values in 2/6 and to values lower than baseline in 3/6 (mean 132/102); one animal died of shock.




From top - Leads I, II,$V_1$, arterial blood pressure. Arrows indicate pressure levels of 100 and 200 mmHg.

**Discussion:** This in vivo study confirms our previous in vitro findings that isoproterenol, a pure beta-agonist, can reverse electrophysiologic and hemodynamic changes induced by bupivaciane. We strongly suggest that isoproterenol should be the first drug of choice to treat arrhythmias.

# EFFECTS OF HYPOXIA ON RELEASE OF AMINO ACID NEUROTRANSMITTERS FROM FETAL LAMB BRAIN IN VITRO

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## INTRODUCTION:

Selective neuronal necrosis, seen in the hippocampus and elsewhere in the brain, following periods of hypoxia/ischemia may be mediated by high concentrations of excitatory amino acid neurotransmitters such as glutamic acid [1]. Hippocampal slices are well suited to investigations into the mechanisms underlying hypoxic injury [2]. The slice incubating conditions (pH, glucose, gas tensions, $K^+$, $Ca_2^+$, temperature etc...) can be altered to study the importance of each in this injury. The neuroprotective properties of anaesthetics can be assessed in brain slices [3]. One of the goals of this study was to examine the role of excitatory amino acids in hypoxic brain injury using the fetal lamb as a model of human cerebral palsy. The fetal lamb has been extensively studied as a model of human pregnancy and, pertinent to this study, as a model of the fetal responses to hypoxia [4]. Knowledge of the ontogeny of amino acid efflux from the immature lamb brain during hypoxia will give important insights into the periods of development when the fetus may be most susceptible to this mechanism of injury.To achieve these goals, fetal lamb brain hippocampal slices were exposed to hypoxic conditions and the amino acid neurotransmitter efflux was assayed.

## METHODS:

Pregnant ewes (day 135-145, term-145 days) were euthanized and the fetal brain rapidly dissected and placed in cold artificial CSF (ACSF). The hippocampus was gently dissected free and transverse slices (400 μm) were made on a McIlwain tissue chopper. Slices were placed in a 4-pool static interface chamber (Stoelting). Composition of the ACSF (mM) was: $Na^+$ 143, $K^+$6.0, $Ca^{2+}$ 2.5, $Mg^{2+}$ 1.2, $SO_4^{2-}$ 1.2, $PO_4^{3-}$ 1.2, $HCO_3^-$ 25, Cl 127.8 and glucose 11. The ACSF was pre-equilibrated with 95% $O_2$ / 5% $CO_2$ . The gas was warmed to 38 C, humidified and passed over the slices which rested on nylon mesh at the interface of the ACSF and the gas. The slices were allowed to recover for 90 minutes. Thereafter the ACSF was collected and replaced with fresh ACSF at 10 minute intervals for 5 collection periods. The first two collections served as control periods. In the third collection period the 95% $O_2$ was switched to 95% $N_2$. At the same time, in pools 3 and 4, the $K^+$ was raised to 50 mM with a corresponding decrease in $Na^+$. In the fourth and fifth collection periods the $K^+$ and $O_2$ were returned to control values. The ACSF was frozen for later analysis by HPLC for glutamatic acid, aspartatic acid and glycine.

## RESULTS:

The ACSF pO2 in the control period was 601 +/- 11, decreased to 53 +/- 9 mmHg within one minute during hypoxia and increased back to control levels in periods 4 and 5. The pH, $pCO_2$ and $HCO_3^-$ were unchanged throughout the experiment. The figure summarizes the experimental results for pools 1 and 2. Values were recorded, in each collection period, as the mean of pools 1 and 2 (normal $K^+$) and 3 and 4 (high $K^+$) Reported values represent the means of all animals studied. Control period efflux of aspartate and glycine were stable while levels of glutamate were more variable. The efflux of each declined slightly during hypoxia but were elevated in the post hypoxic, reoxygenation period. This elevation was most marked with glycine and aspartic acid. Potassium stimulation caused a release of amino acids (data not shown).

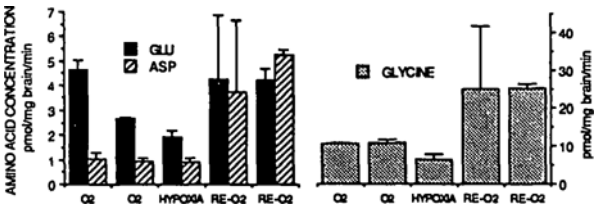


FIGURE ACSF levels of amino acids (+/- SEM)

## DISCUSSION:

Previous workers have shown, by microdialysis, a rise in extracellular glutamate in the brains of near-term fetal lambs during maternal aortic compression [5]. In contrast, our preliminary in vitro results show no change or a decrease in net glutamate efflux during hypoxia but a rise in the post-hypoxia period. This discrepancy could be due to a difference between in vivo and in vitro responses or a difference in the collection technique. The rise in amino acids may reflect delayed neuronal damage due to the hypoxia itself or a "reperfusion" type injury due, perhaps, to the generation of oxygen radicals. Work is ongoing examining the $Ca_2^+$ dependency of hypoxia induced amino acid release as well as extending the collection period to see if amino acid levels continue to rise or if they return to baseline following hypoxia. These experiments are being repeated in younger (80-85) day fetuses to assess the ontogeny of these excitotoxic processes. These studies will provide a basis for the understanding and assessment of neuroprotective drugs, including anaesthetics, on a model of fetal hypoxia.

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## CATION CHANNELS IN APICAL MEMBRANE OF FETAL ALVEOLAR EPITHELIUM

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Introduction: Resuscitation of the newborn requires adequate clearance of fetal lung fluid. One third of this fluid is removed mechanically as the fetus passes down the birth canal. The remaining two thirds moves across the pulmonary epithelium. The majority of transepithelial fluid movement results from active transport of $Na^+$ [1] and can be stimulated by epinephrine [2]. Failure to clear fluid results in neonatal hypoxemia and instability in the terminal lung units. The adult lung employ a similar mechanism to clear fluid following acute lung injury. The contribution made by the **alveolar** epithelium to the removal of fluid is unknown. Cultures of fetal alveolar epithelium have the bioelectric properties necessary to actively transport $Na^+$ and generate an osmotic gradient [3]. This transmembrane potential is sensitive to the $Na^+$ channel blocker amiloride and can be reduced by ouabain inhibition of Na/k ATPase [3,4,5]. We wish to further explore the mechanisms which regulate ion transport across alveolar epithelium using patch clamp electrophysiology. We have demonstrated a 25pS cation channel on the apical membrane of these cells [6].

By identifying the mechanisms which regulate cation channel expression, pharmacons can be developed to accelerate lung luid clearance.

Methods: Cultures of 20-day fetal rat alveolar epithelium were grown on collagen for 1 to 2 days prior to study. Inside-out excised patches were obtained from the apical surface of the cell following pre-treatment with isoproterenol 5 uM. Channel currents were recorded using an Axopatch amplifier. Data was filtered at 1kHz, and stored on a VCR tape following 12 bit A/D conversion. Electrodes were fabricated from boroscillicate glass and had a resistance of 5-10 Mohm when filled.

Results: Fig.1 illustrates single channel recordings in symmetrical NaCl (140 mM) bath and pipette solution. A downward deflection represents current moving from the intra to extracellular membrane. Similar current recordings symmetric around OmV were seen in multiple patches with linear slope conductances ranging from 16 to 26 ps. To assess the selective permeability of the channel, the bath solution was diluted 2:1 with isotonic sucrose (Fig 2)(bath mM NaCl 47 sucrose 145 pipette NaCl 140). This produced a rightward shift in the 1:E curve with a measured reversed potential ($E_R$) of +26mV. This is in agreement with the shift predicted by the Nernst Equation $E_R=(ZF/RT)\ln(C^+_{out}/C^+_{in})$ for a cation selective channel. Choline chloride dilution (140 mM) of the bath 2:1 produced a 25 mV shift in $E_R$ (bath control NaCl 140 pipette NaCl 140 choline substitution bath Na 47 choline 94).

Discussion: This data demonstrates a cation selective channel on the apical membrane of fetal alveolar epithelium. Opening of this channel in vivo would result in an inward $Na^+$ flux. Na could then be actively transported out of the basal lateral membrane via ouabain sensitive Na/K ATPase pump. Although this channel likely participates in fluid transport, the magnitude of its contribution to fetal lung liquid clearance remains to be determined.

FIG 1

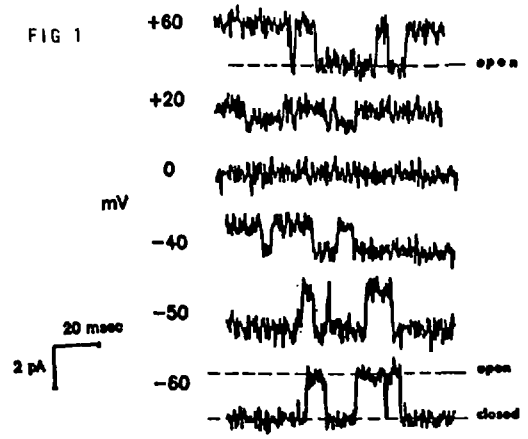



FIG 2

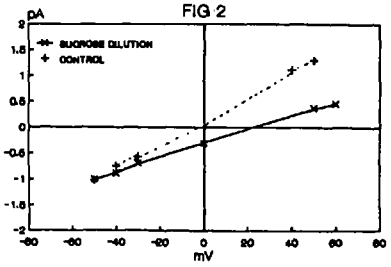
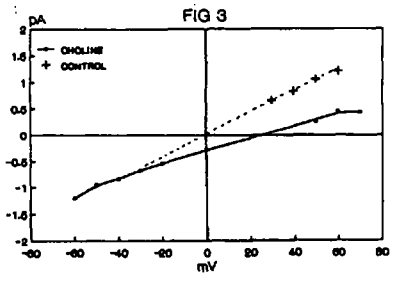



FIG 3

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# SERUM PROTEIN BINDING OF ROPIVACAINE IN NONPREGNANT AND PREGNANT EWES

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INTRODUCTION: Pregnancy enhances the cardiotoxicity of bupivacaine but not of mepivacaine (1,2). When bupivacaine was administered by a constant rate intravenous infusion, doses and plasma concentrations of the drug required to produce circulatory collapse were lower in pregnant than in nonpregnant ewes (1). In contrast, no pregnancy related differences were observed with infusion of mepivacaine(2). The difference between the two drugs has been attributed to gestational alterations in serum protein binding, resulting in increased availability of free bupivacaine but not of mepivacaine.
Ropivacaine is a new amide local anesthetic structurally related to mepivacaine and bupivacaine. Its potency and duration of action are similar to those of bupivacaine, however, its cardiotoxicity in sheep is not enhanced by pregnancy (3). The present study was undertaken to determine whether unaltered availability of free ropivacaine during pregnancy could be responsible for this finding.

METHOD: Four nonpregnant and 5 pregnant sheep, near term of gestation, were used according to a protocol approved by the Institutional Animal Care and Use Committee. Sheep unexposed to any drugs were obtained from the regular supplier. Blood was drawn by venipuncture and allowed to clot for approximately 30 min. Contact with polystyrene plastic or stoppers containing TBEP plasticizer was avoided. Serum rather than plasma was used in order to prevent the artifactual effect of in vitro lipolysis which is particularly significant during pregnancy. After centrifugation, all serum samples were frozen at -20°C until used within 1 week of collection.
On the day of study, serum was defrosted at room temperature and the pH adjusted to physiologic range for sheep, viz 7.50±0.02 pH units. Ropivacaine HCl (Astra) was added to 5 ml aliquots of serum resulting in drug concentrations found to be associated with systemic toxicity in sheep(3). Serum and drug were allowed to equilibrate for 1 hour. Thereafter, serum water was obtained from 1 ml samples after 45 min of centrifugation at 2000g, using an ultrafiltration system, Amicon MPS -1 with YMT membrane. Ropivacaine concentrations in serum and serum water were determined with gas chromatography (limit of sensitivity = 5 ng/ml). Unpaired Students t test was used to detect differences between pregnant and nonpregnant animals. A correction factor for repeated testing was applied, a p value of 0.017 was considered significant.All results are expressed as the mean ± SEM.

RESULTS: Seven studies were carried out in sera obtained from nonpregnant and 9 in sera from pregnant ewes. Mean ropivacaine concentrations studied were similar in both groups, 3.8 to 9.1 ug/ml (Table 1). No differences in the proportions of bound ropivacaine were detected between nonpregnant and pregnant ewes. These ranged from approximately 57% at the lowest drug concentrations tested to 48% at the highest. (Table 1).

DISCUSSION: These data indicate that ovine pregnancy is not associated with increased availability of free ropivacaine, and may explain why the cardiotoxicity of this drug is not enhanced during gestation.

Table 1

| Serum Conc (ug/ml) | | % Bound | |
|---|---|---|---|
| Nonpregnant | Pregnant | Nonpregnant | Pregnant |
| 3.8 ± 0.1 | 4.0 ± 0.2 | 57 ± 4 | 54 ± 5 |
| 6.4 ± 0.2 | 6.8 ± 0.5 | 52 ± 7 | 54 ± 4 |
| 8.6 ± 0.2 | 9.1 ± 0.4 | 48 ± 2 | 50 ± 4 |

Differences are not significant

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# EPIDURAL ALFENTANIL DURING LABOR, IN ASSOCIATION WITH A CONTINUOUS INFUSION OF BUPIVACAINE.

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**Introduction**: The first report of the use of epidural narcotics during labor dates back to 1979, when Dr. Perriss used epidural meperidine.[1] Our study was designed to evaluate epidural alfentanil during labor, using a single bolus of alfentanil with the first epidural injection, followed by the infusion of bupivacaine 0.125 %.

**Methods**: 40 patients were included in this double-blind study that was accepted by the Ethics and Research Committee. All patients had a pregnancy at term and a labour without serious complications. An epidural catheter was inserted into the lumbar region and the following drugs were injected: a test dose of lidocaine 1.5% with epinephrine 1 / 200,000 -3 cc, then bupivacaine 0.125 % - 8 cc mixed with either alfentanil 1 mg (0.5 mg / 1 cc) or saline (2 cc). Following that, an infusion of bupivacaine 0.125 % - 6 cc / hr was started. Whenever a patient complained of pain afterward, she was given a small bolus of bupivacaine 0.125 % and the infusion was increased by 2 cc / hr every time.

Parameters mesured in the maternal groups were the following: (1) the degree of pain using the visual analogue scale (VAS) mesured before, immediately after and every hour after the completion of the epidural; (2) the degree of pain of the epidural technique; (3) the time delay between the epidural completion and the first painfree contraction; (4) the time delay between the epidural completion and the return of a painful contraction; (5) the sensory level as well as the motor impairment immediately after the completion of the epidural as well as every hour thereafter; (6) the amount of bupivacaine used every hour as well as the total amount at the delivery; Parameters measured in the foetus were the Apgar scores at 1, 5 and 10 minutes as well as umbilical arterial and venous blood gases.

The results were analysed using the Student's t test and the Mann-Whitney U test where applicable.

**Results**: The demographic data regarding our two groups of 20 patients did not show any significant difference.

The time delay between epidural completion and the first painfree contraction were statistically similar in the alfentanil group (8.3 ± 4.8 min.) and the placebo group (12.4 ± 9.3 min.). However, there was a significant difference ($p < 0.05$) in the time delays between the epidural completion and the return of painful contractions in the alfentanil group (188.9 ± 65.7 min.) and the placebo group (119.1 ± 58.4 min.). The VAS results showed no significant difference at any time between the two groups, although there was less and less data to analyse after two hours of epidural infusion. There was also no significant difference in the total amount of bupivacaine used in the alfentanil group (12.7 ml / hr for a total duration of 4.7 hr) and the placebo group (12.3 ml / hr for a total duration of 4.6 hr). There was no significant difference between the two groups for the superior or inferior sensory levels as well as for the motor inpairment which was minimal in both groups. Superior sensory levels showed a mode of $T_{10}$ in the Alfentanil group and $T_8$ in the placebo group and inferior levels showed a mode of $L_5$ in both groups. There was no significant difference between the groups for the use of a perineal dose or for the use of local infiltrations, pudendal blocks or forceps. The durations of the first and second stages were also similar in the alfentanil (597 ± 341 min. for stage 1 and 45 ± 33 min. for stage 2) and placebo groups (691 ± 396 min. for stage 1 and 65 ± 57 min. for stage 2).

The results for the foetus showed modal Apgar scores at 1, 5 and 10 minutes of 9, 10, 10 in the alfentanil group and 9, 9. 10 in the placebo group. The umbilical cord blood gases showed a pH of 7.31 ± 0.06 in the alfentanil group and 7.34 ± 0.03 in the placebo group. All these, statistically showed no significant difference.

**Discussion**: The use of epidural narcotics in combination with local anesthetics during labor have been shown to decrease the total dose of local anesthetics, increase the duration and quality of analgesia, decrease the use of perineal doses and use of forceps as well as decrease motor impairment. This enhanced analgesia could be explained by a dual mode of action: at the axon as well as at the opiate receptor site.[2] However, one of the drawbacks for the use of epidural narcotics during labor is the possibility of neonatal hypotonia and respiratory depression secondary to placental transfer of narcotics. For that reason we used alfentanil in our study which would be expected to be eliminated much faster than other narcotics in the event of transplacental transfer and rapid delivery after the completion of the epidural.

Our results showed that the main advantage of epidural alfentanil is the prolonged duration of complete analgesia compared to the placebo group (189 vs 119 min.) and it appears to have no adverse effect on the neonate. However, using a single bolus of alfentanil at the beginning of the epidural infusion did not produce any other significant advantage over the use of plain bupivacaine during labor.

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# CONTINUOUS INFUSION EPIDURAL ANAESTHESIA FOR OBSTETRICS BUPIVACAINE VS BUPIVACAINE-FENTANYL

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INTRODUCTION: Since 1983, our institution has used Bupivacaine 0.25% for continuous infusion epidural anaesthesia (EA) in Obstetrics.[1] To minimize motor block (MB) at delivery, the pump rate is often lowered from the standard 7ml/hr (17.5mg/hr), based on nursing assessment at full dilation (FD) of patient leg strength and analgesia. Only rarely is the infusion ever stopped completely. Recent reports have suggested that a lower concentration of Bupivacaine (B) combined with a small amount of Fentanyl (F) offers equivalent analgesia with a lower incidence of MB without detectable neonatal depression.[2,3] The purpose of this study was to compare B-0.125% with F-4μg/ml (½B-F) with our standard B-0.25% (B-S) and to a 3rd group, B-0.125% plain (½B-P).

METHODS: The protocol was approved by the institutional review board for human research. Informed consent was obtained from 90 nulliparous women with singleton fetuses in vertex presentation and gestation greater than 36 weeks. Cervical dilation was between 3 and 7 cm. Patients were allocated randomly to one of the three groups (B-S, ½B-P, and ½B-F) in a double-blind manner using sequentially numbered sets of syringes prepared by a colleague. Each patient was asked to score her pain on a Visual Analog Scale (VAS 0-100) before EA was administered. All groups received the same test dose (TD) of 3ml Lidocaine 1.5% with epinephrine 1:200,000. To establish EA 5 min post-TD, groups B-S and ½B-P both received 6ml of B-0.25% while group ½B-F received 6ml of B-0.125% and F-50μg. If at 20 min post-TD the VAS score was 50% or less than the initial score, then placement of the catheter was considered successful and EA infusion was begun. Three different infusion protocols were used, all set at 7ml/hr. Group B-S received B-0.25% (17.5mg/hr); group ½B-P received B-0.125% (8.75mg/hr); and group ½B-F received B-0.125% (8.75mg/hr) with F-4μg/ml (28μg/hr). Every 30 min VAS scores, MB scores (0-3), vital signs, adverse effects and level of sensory block were recorded. Based on these observations, the pump rate could be lowered if necessary, but if analgesia was inadequate, 3ml of B-0.25% was given as a bolus. At FD and again at delivery, the patient was asked to rate the analgesia provided as either (E)xcellent, (G)ood, (F)air or (P)oor. Data were analysed by ANOVA, t-test, chi-square and Fisher exact tests where appropriate, with statistical significance assumed when $P < 0.05$ (except for Bonferroni-corrected t-tests when $P < 0.03$)

RESULTS: The rate of successful EA in each group was not significantly different. Demographic data including age, weight, height and gestational age were not significantly different between groups. Tables 1 to 4 summarize data concerning labour outcomes, analgesia, drug administration and motor block. No adverse effects, either maternal or neonatal, were documented.

| TABLE 1. | B-S | ½B-P | ½B-F | P |
|---|---|---|---|---|
| No. EA Successful | 24 | 27 | 24 | NS(0.49) |
| Duration (min) | | | | |
| 1st Stage | 448±279 | 495±331 | 463±272 | NS |
| 2nd Stage | 92±76 | 91±76 | 95±58 | NS |
| Epidural Infusion | 349±172 | 364±203 | 355±207 | NS |
| Mode of Delivery | | | | |
| Vaginal-Spontaneous | 15(62%) | 16(59%) | 19(79%) | |
| (95% conf. interval) | (42-82%) | (40-78%) | (63-95%) | NS |
| Vaginal-Forceps/Vacuum | 5(21%) | 9(34%) | 2( 8%) | (0.28) |
| Caesarean | 4(17%) | 2( 7%) | 3(13%) | |

| TABLE 2. | B-S | ½B-P | ½B-F | P |
|---|---|---|---|---|
| Analgesia - VAS Score | | | | |
| Establish Epidural | | | | |
| Time 0 min | 82±14 | 82±16 | 79±15 | |
| Time 20 min | 17±16 | 12±16 | 11±12 | NS |
| 1st Stage (avg) | 20±24 | 28±27 | 19±27 | 0.003 |
| (t-test: ½B-P vs ½B-F = 0.001; B-S vs ½B-F = NS) | | | | |
| 2nd Stage (avg) | 33±28 | 40±33 | 28±30 | 0.04 |
| (t-test: ½B-P vs ½B-F = 0.03; B-S vs ½B-F = NS) | | | | |
| Analgesia - Rated E/G | | | | |
| 1st Stage | 22(92%) | 16(59%) | 21(88%) | 0.008 |
| (Fisher exact test: ½B-P vs ½B-F = 0.025) | | | | |
| 2nd Stage | 15(63%) | 17(63%) | 14(58%) | NS |

| TABLE 3. | B-S | ½B-P | ½B-F | P |
|---|---|---|---|---|
| Bupivacaine (mg) - Total | | | | |
| - to Full Dilation | 84±46 | 60±35 | 45±32 | 0.003 |
| - to Delivery | 107±47 | 71±41 | 54±36 | <0.001 |
| (t-test: ½B-P vs ½B-F = NS; B-S vs ½B-F = <0.001) | | | | |
| Bupivacaine (mg) - Added to Basic Infusion | | | | |
| - to Full Dilation | 6.0±8.6 | 8.6±13.5 | 3.8±7.3 | 0.003 |
| (t-test: ½B-P vs ½B-F = <0.001; B-S vs ½B-F = 0.01) | | | | |
| - to Delivery | 7.3±13.4 | 13.8±17.0 | 6.1±9.6 | 0.003 |
| (t-test: ½B-P vs ½B-F = <0.001; B-S vs ½B-F = NS) | | | | |
| Fentanyl (μg) - Total | - | - | 166±97 | - |

| TABLE 4. | B-S | ½B-P | ½B-F | P |
|---|---|---|---|---|
| Motor Block Score = 0 | | | | |
| Time 30 min | 22(92%) | 27(100%) | 22(92%) | NS |
| Fully Dilated | 17(71%) | 23(85%) | 21(88%) | NS(0.27) |
| (95% conf. interval) | (56-89%) | (71-99%) | (75-100%) | |

DISCUSSION: The data supported our null hypothesis that there would be no difference in the total analgesia provided in the B-S and ½B-F groups. F was shown to be an effective adjuvant when comparing the ½B-F and ½B-P groups; by VAS and rating scores during 1st stage and by VAS in 2nd stage, ½B-F provided better analgesia than ½B-P. Total B (both predetermined infusion plus added top-ups or rate alterations) given in the ½B-F group was significantly less than in the B-S group. To achieve equivalent analgesia during 1st stage, ½B-F required significantly less additional B than B-S. There were no significant differences in the incidences of motor block or spontaneous vaginal births. Because less additional B was needed over and above the basic infusion rates, we conclude that ½B-F performed better than B-S.

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# PREOPERATIVE HEMOGLOBIN VALUES IN MINOR PAEDIATRIC SURGERY

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Introduction: The minimum preoperative hemoglobin (Hg) level necessary for the safe administration of anaesthesia has long been an issue for debate.[1] Some provincial laws dictate preoperative hemoglobin assessment.[2] This study was undertaken to determine the value of routine preoperative hemoglobin testing, and to establish how these results influence the conduct of anaesthesia and surgery in an ambulatory day surgery unit.
Methods: With institutional approval, 2,000 patients ASA I and II, aged one month to nineteen years who presented for minor surgery in the ambulatory day unit were studied. Patients requiring sickle cell screening were not included in the cohort. Patients scheduled for cystoscopy, lumbar puncture, bone marrow, or administration of chemotherapy were excluded from the study. Those patients who presented for anaesthesia and surgery with a Hg result from another laboratory were excluded from the study. Patients' capillary blood samples were analyzed the morning of surgery using a Coulter Counter®. The arbitrary level of < 100 gm/L was selected, as this value has been widely accepted as the minimum requirement for anaesthesia and surgery.[3,4] The charts of those patients with a Hg < 100 gm/L were reviewed at a later date to determine management (deferral or outcome). Most anaesthetists in this day surgery unit were unaware of the study in progress.
Results: The mean Hg value for the 2,000 patients was 128.6 gm/L with a standard deviation of ±11.1 gm/L (see Figure). One patient was noted preoperatively to have thalassemia minor while another had a known history of pyruvate kinase deficiency. Eleven patients (0.5%) were found to have a hemoglobin < 100 gm/L. Three of these eleven patients had their surgery deferred (see Table). These three patients received iron therapy over an interval of three to seven months and returned for uneventful anaesthesia and surgery at a later date. All patients with a Hg < 100 gm/L who underwent anaesthesia and surgery did so without complications.
Discussion: The value of preoperative assessment for anaemia and subsequent selective Hg analysis has recently been questioned.[5] We have observed that routine preoperative Hg testing produces considerable discomfort that is particularly upsetting for young children, may unnecessarily delay surgery and will certainly generate additional expenses ($10 per test)[6] that exceed any direct beneficial effects for the patients. Only eleven patients (0.5%) had a Hg of < 100 gm/L in this study cohort. Moreover, these results altered the conduct of anaesthesia in only 0.015% of cases reviewed. We conclude that healthy paediatric patients scheduled for minor surgery do not require routine Hg determinations. We propose that selective Hg testing may be a more effective screening test. Further studies are required to assess the effectiveness of selective Hg testing in the healthy paediatric age group.

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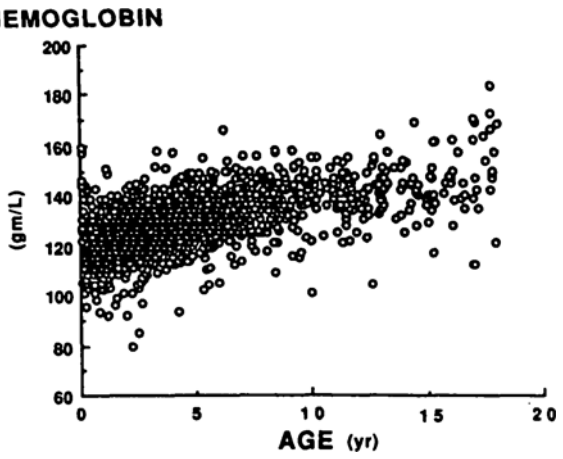
FIGURE




TABLE

| PATIENT | SEX | AGE (months) | Hg (gm/L) | ACTION TAKEN | COMMENTS - DIAGNOSIS |
|---|---|---|---|---|---|
| 1 | M | 51 | 93 | uneventful surgery | pyruvate kinase deficiency |
| 2 | M | 32 | 97 | uneventful surgery | thalassemia minor |
| 3 | M | 30 | 85 | case deferred | iron deficient anaemia |
| 4 | F | 19 | 99 | uneventful surgery | iron deficient anaemia |
| 5 | M | 24 | 92 | uneventful surgery | iron deficient anaemia |
| 6 | F | 18 | 96 | uneventful surgery | iron deficient anaemia |
| 7 | M | 14 | 92 | case deferred | iron deficient anaemia |
| 8 | M | 10 | 93 | uneventful surgery | iron deficient anaemia |
| 9 | M | 27 | 80 | case deferred | iron deficient anaemia |
| 10 | M | 8 | 98 | uneventful surgery | iron deficient anaemia |
| 11 | M | 3 | 95 | uneventful surgery | no diagnosis |

# AMBULATORY SURGERY QUESTIONNAIRE

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Outpatient surgery may improve the efficiency of medical care delivery. It is predicted that by the end of this decade, 60% of some hospitals' surgical caseload may be performed on an outpatient basis. With this group of patients, preoperative contact with the anesthetist tends to be brief and patients are not premedicated and may be quite anxious. The goal of this study was to : a)assess this population's knowledge of anesthesia and anesthetists b)identify their common fears and anxieties about anesthesia and c) evaluate the quality of the anesthetist-outpatient relationship.

## METHODS

A multiple-choice questionnaire was given to day surgery patients undergoing general anesthesia at two hospitals in Kingston, Ont. over a one week period. The form was either filled out post-operatively when the patient felt well enough or the patient was interviewed by telephone within a week of the surgery. Results of the questionnaire were analyzed using the Pearson chi-squared test.

## RESULTS

A total of 97 patients had GA's through the day surgery unit during the study period; of these 94 questionnaires were completed, 69 in the day surgery unit before discharge and 25 by telephone interview.

The results are as follows:

I. Patient Information

| SEX | | EDUCATION FINISHED | |
|---|---|---|---|
| F | 73% | public school | 18% |
| M | 27% | high school | 48% |
| | | college | 15% |
| | AGE | university | 15% |
| <20 | 6.4% | post-graduate | 3% |
| 20-65 | 85% | | |
| >65 | 8.5% | | |

80% of this group had undergone at least one GA in a hospital before and 16% had not.

II. Knowledge re: Anesthetist

| | yes | no | not intro |
|---|---|---|---|
| remembered anesthetist's name | 34% | 55% | 10% |

| | very | reasonable | not |
|---|---|---|---|
| confident in anesthetist | 67% | 33% | 0% |

| | yes | no | don't know |
|---|---|---|---|
| anesthetists qualified M.D. | 52% | 6.5% | 41.5% |

| | yes | no | don't know |
|---|---|---|---|
| certified specialist | 67% | 0% | 31% |

| | leaves room | stays-checks V/S | ? |
|---|---|---|---|
| what they do during surgery | 1% | 92.5% | 5.3% |

III. About the anesthetic

| | very | little | not at all |
|---|---|---|---|
| worried about surgery | 16% | 46% | 37% |
| worried about anesthetic | 19% | 28% | 52% |

| | anesthesia |
|---|---|
| there are no risks | 15% |
| are risks, don't know what they are | 47% |
| aware of risks | 35% |

The major worries that people had about the anesthetic in order of frequency were:

a) being sick to their stomach after
b) getting needles
c) not waking up after the surgery
d) losing control of what they say and do
e) waking up during the surgery

Other less common concerns included having their caps broken, the possibility of mistakes being made and being unable to breathe when they woke up (which happened to this patient last GA).

Analysis of these results showed that females (mostly gynecology patients) were more anxious about having surgery ($p=0.03$) and a GA ($p=0.01$) than males, the older age groups (ie.>40) tended to worry less and knew more about the risks than the other age groups. Also, patients who had previous GA's were less worried about having an anesthetic than those who had not ($p=0.05$) though some present worries had arisen from previous experiences. Patients with college education or higher tended to know that anesthetists are M.D.'s and specialists, but there was no correlation between education and knowing the risks of anesthesia. There was no correlation between knowing the anesthetist's name and the amount of confidence in him/her, or the degree of worry regarding having a GA.

## DISCUSSION

This survey reveals that the day surgery population has concerns about both the surgery and the anesthetic, but over half were not concerned about their anesthetic at all. Patients do know that their anesthetist stays in the room to monitor them during the surgery and have a high degree of confidence in him/her despite the rather superficial relationship. From this survey, we conclude that these patients do not know much about anesthetists and even less about the risks of anesthesia. Teaching could be done either through a day surgery anesthetic clinic or the distribution of a pamphlet about anesthesia pre-operatively. Further studies need to be done to determine whether this would increase or decrease the anxiety level of this group. Studies comparing inpatients with this group may also elucidate whether pre-op visits and premedications are truly beneficial.

## FORMALIZATION AND IMPLEMENTATION OF AN INSTITUTIONAL PREANAESTHETIC CHECKLIST

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Introduction: The introduction of a pre-anaesthetic checklist may; prevent equipment related morbidity and mortality, improve preventative maintenance programs and educate the anesthetist about equipment. There are several recommendations for the utilization of a pre-anaesthetic checklist [1, 2]. In 1984 a report prepared by a joint committee of the Ontario Medical Association and College of Physicians and Surgeons of Ontario stated that "each department of anaesthesia must ensure that appropriate equipment has been provided by the health care facility, and that each member of the department are aware of the requirements for a pre-anaesthetic checklist[2]. Based on this report, our institution formalized and implemented a pre-anaesthetic checklist. A review system of anaesthesia equipment faults was then incorporated into the departmental quality assurance program. Frequency and nature of equipment faults were reviewed for recurrent problems.

Methods: The department of anaesthesia agreed upon a standard mandatory checklist which was then placed with each anaesthesia machine. The checklist consisted of an initial version which was completed at the start of each day and an abbreviated version which was completed prior to starting subsequent cases. The checklist was submitted at the end of the day and was entered into database. Major and minor gas machine faults were collected. Major faults were defined as those leading to a potential disaster if the equipment was used without correction and minor faults were defined as those requiring non-urgent corrective action. Data was collected over a one year period. Gas machine faults were subdivided into the following categories; (1) Electrical system which included wall outlet, reserve battery and alarms, (ii) High pressure system which included gas circuitry from the cylinders, through the check valves to the regulators, (iii) Intermediate pressure system which included gas circuitry from the pipelines to the flowmeter controls, (iv) Low pressure system which included gas circuitry from the vaporizers to the patient and (v) Scavenging system which included the adjustable relief valve, the ventilator relief valve and the rest of the scavenging system to the scavenging outlet.

Results: The study took place over a one year period from the beginning of January to the end of December 1988. 2147 completed checklists were submitted while 2529 checklists were expected, resulting in a overall compliance rate of 84.8%. The total number of equipment faults identified were 115. There were 36 major gas machine faults and 79 minor gas machine faults. The location of faults within the gas machine are identified in table 1. Examples of major equipment faults include ventilator alarm failure, vaporizer window gasket leak or large breathing circuit leaks while examples of minor faults included low cylinder supply pressure or low batteries. There were no deaths related to equipment failure during the study period.

Table 1
Location of Anaesthetic Equipment Faults

| Location | | Major | Minor |
|---|---|---|---|
| (i) | Electrical System | 2 | 7 |
| (ii) | High Pres. System | 2 | 5 |
| (iii) | Intermed. Pres. System | 9 | 6 |
| (iv) | Low Pres. System | 23 | 58 |
| (v) | Scavenging System | - | 3 |

Discussion: The implementation of this program resulted in compliance with the recommendations of the joint committee of the Ontario Medical Association and the College of Physicians and Surgeons of Ontario[2]. This survey discovered, in the pre-anaesthetic period 36 major equipment faults any one of which could have resulted in significant morbidity and mortality. The program improved our preventative maintenance program by identifying recurring problems. A side benefit, was that the program had an educational value familiarizing anesthetists with their equipment so that weaknesses, potential problems and limitations of basic anaesthetic equipment were better understood. The lack of anaesthetic equipment related deaths over the study period suggest a desirable effect of implementation of this policy. Based on our experience we recommend that all anaesthesia departments formalize and implement a pre-anaesthetic checklist.

References:

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# HYPOXEMIA IN THE POST-ANAESTHESIA CARE UNIT

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INTRODUCTION: Due to the risk of hypoxemia, supplemental oxygen is used routinely in the initial post-anaesthesia care unit (PACU) stay in many hospitals. However, it is usually discontinued before discharge to the ward, based on clinical criteria without objective measurement of oxygenation. In this study we monitored a diverse group of adults having general anaesthesia for elective inpatient surgery throughout their PACU stay with continuous pulse oximetry. The incidence and magnitude of hypoxemia and relationship to possible associated factors was examined.

METHODS: The study was performed in accordance with our institutional review board. Informed consent was obtained from 131 ASA I-III patients who were ≥40 yr old having elective inpatient surgery with general anaesthesia (intubation and positive pressure ventilation). The exclusion criteria were: airway, thoracic, intracranial, aortic or cardiac surgery; severe cardiopulmonary disease; or anemia. The anaesthetic management was left to the discretion of the anaesthesiologist. The PACU staff were blinded to the results unless there was severe hypoxemia (= oxyhemoglobin saturation ≤90% for ≥2 min or ≤85%, whichever occurred first). All patients received oxygen by face mask at ≥10 lpm on arrival in the PACU. It was removed after at least 30 min at the nurse's discretion using our usual PACU criteria (awake; normal strength and vital signs). Discharge was also determined by the PACU staff but required at least 45 min since removing the oxygen. Continuous pulse oximetry (Nellcor N-100) began 5 min after arrival in the PACU and ended at discharge. An investigator constantly observed the oxyhemoglobin saturation ($SpO_2$) to eliminate artifacts and record the $SpO_2$ every 5 min and anytime it fell below the preceding 5 min value. The 5 min values were used to calculate the mean $SpO_2$ and all were used to determine the minimum $SpO_2$. During hypoxemic episodes (= $SpO_2$ ≤90% for ≥15 sec) the respiratory rate (RR), minimum $SpO_2$ and duration were recorded. Oxygen was administered on discharge if it had been resumed due to a severe hypoxemic episode or if, in the 10 min before discharge, any hypoxemic episode occurred or the $SpO_2$ was generally ≤92%. Pulse oximetry was performed the night before surgery on 106 patients for 15 min while resting quietly. The $SpO_2$ was recorded every 1 min and anytime it fell below the preceding 1 min value. The mean was determined from the 1 min values and the minimum using all values. If any preoperative $SpO_2$ was <91% the patient was excluded. The data are presented as mean±1 SD. Chi-square and Student's t-tests were used where appropriate. Significant p values were <0.05 for the $SpO_2$ comparisons and <0.005 for the associated factor analysis.

RESULTS: The 131 subjects (58 male; 73 female) had a mean age of 59±11 yr and % ideal body weight (IBW) of 120±25%. Table 1 shows the $SpO_2$ preoperatively and while in the PACU. The minimum $SpO_2$ on oxygen occurred at 21±22 min after arrival in the PACU, and the minimum off oxygen was at 81±33 min after arrival and 27±18 min after discontinuing oxygen. At least 1 hypoxemic episode occurred in 40.5% of the subjects, a severe episode in 23.7% and 32.8% required oxygen on discharge. Hypoxemia only occurred while off oxygen. All severe episodes were managed successfully by resuming the oxygen. For those who desaturated, the number of episodes per patient was 5±5, with mean and maximum durations of 77±69 and 128±94 sec and minimum $SpO_2$ of 87.1±2.0%. They began at 81±33 min after entering the PACU and 22±21 min after discontinuing oxygen. When hypoxemic, the RR was <10bpm (6-8) in 6 patients; abnormal breathing was present in 26 (18 had mild upper airway obstruction, 5 had shallow respirations and 3 had Cheyne-Stokes breathing); and cyanosis was noted in only 2. There was no association between the occurrence of ≥1 hypoxemic episode and age (40-64yr=39/89; ≥65yr=14/42); sex (M=24/58; F=29/73); %IBW (<120%=25/75; ≥120%=28/56); smoking (current=10/21; past=19/38; never=24/69); preoperative minimum $SpO_2$ (≥95%=18/63; <95%=23/43); premedication (narcotic=31/70; benzodiazepine=3/27; none=14/34); surgery duration (<60min=6/25; ≥60min=47/106); or surgical site (upper abdominal=19/37; lower abdominal=10/24; peripheral=24/70). TABLE 2 shows the factors that were associated with hypoxemia.

DISCUSSION: This study documents that supplemental oxygen is effective in preventing hypoxemia in the PACU period. However, hypoxemia occurred in 41% of our patients when the oxygen was discontinued. In more than half of these (24% of all patients) it was considered severe. These percentages are alarmingly high, especially since patients usually considered at risk were excluded from the study and cyanosis was detected in only 2 of the hypoxemic patients. Our incidence is higher than most previous reports[1], possibly due to our intensive continuous monitoring; blinding of the PACU personnel; and examining only the ≥40 yr age group. The only predictive factors reaching statistical significance were ASA class III and preoperative mean $SpO_2$ <95%, although a larger study size may identify others. We suggest that either all patients should have pulse oximetry for at least 45 min after discontinuing oxygen or the oxygen should not be removed and all patients should be sent to the ward with supplemental oxygen.

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TABLE 1: Preoperative and PACU $SpO_2$

| | Preoperative | PACU-on $O_2$ | PACU-off $O_2$ |
|---|---|---|---|
| Mean $SpO_2$(%) | 96.2±1.6* | 99.5±0.8+ | 94.7±2.1 |
| Minimum $SpO_2$(%) | 94.9±1.8* | 98.5±1.7+ | 90.9±3.9 |

$O_2$ = oxygen mask * p<0.001 *vs* PACU on and off $O_2$
+ p<0.001 *vs* PACU off $O_2$

TABLE 2: Factors Associated with Hypoxemia

| | | |
|---|---|---|
| ASA Class | I | 7/32 (21.9%) |
| | II | 30/73 (41.1%) |
| | III | 15/20 (75%)* |
| Preoperative Mean $SpO_2$ | ≥ 95% | 30/93 (32.3%)+ |
| | < 95% | 11/13 (84.6%) |

* p<0.001 *vs* I + p<0.001 *vs* <95%

# PERIOPERATIVE RESPIRATORY MANAGEMENT: DO RESPIROLOGISTS AND ANAESTHETISTS AGREE ?

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## Introduction

The perioperative management of patients with respiratory disease is often shared by respirologists and anaesthetists. A questionnaire was used to determine whether or not these two groups, with different backgrounds, training, and experience, had the same opinions about preoperative assessment, about the role and value of respiratory consults, and about perioperative management. This has not been studied previously.

## Methods

A questionnaire was prepared, and distributed to all nine of the staff and fellows in the respirology department of a large teaching hospital, and to a random selection of twelve of the staff anaesthetists from the same hospital. Questions were asked about preoperative tests, the assessment of risk factors, the role of respirology consults, attitudes to various controversial statements, and about the value of some respiratory treatment modalities. Non-responders were given one personal reminder.
Willcoxon's rank sum test was used for statistical analysis.

## Results

All nine of the respirologists, and eight of the twelve anaesthetists replied.
Preoperative tests: Respirologists felt that significantly more patients needed pulmonary function tests (PFTs) (median 20% compared with 7.5% for anaesthetists $P<0.5$). They also felt more patients needed chest X-rays (median 50% compared to 25%) arterial blood gases (15% v. 7.5%) and respirology consults (10% v. 7.5%).
Risk factors: There were no significant differences in the assessment of risk between the two groups. However, the respirologists tended to rate smokers and patients with chronic obstructive lung disease (COLD) as greater risks than did the anaesthetists, who were more concerned about patients with obesity or asthma. The interpretation of the risk associated with abnormal PFTs was similar, but the respirologists put hypoxaemic patients in a lower risk category than the anaesthetists did. Both groups labelled a patient with a slightly elevated CO2 as high risk.
Role and value of Respirology consults: The respirologists placed a higher value on quantifying risk than the anaesthetists, who were more concerned about acquiring data. Both groups felt they were valuable.
Attitudes: In both groups, half the respondents felt that spinal anaesthesia and good postoperative analgesia decreased respiratory complications, and half disagreed. Respirologists were more likely than anaesthetists to agree that too many preoperative tests are done, but this was not statistically significant.
Treatment Modalities: Given a patient with COLD undergoing gastric surgery, all the respondents replied that early ambulation and incentive spirometry were of moderate or great importance. Both groups gave equal, but lesser, importance to chest physiotherapy and breathing exercises. Both groups felt that ventolin was useful, and that ipratropium bromide ("atrovent") was of less benefit, but more useful than theophylline, antibiotics or steroids. Anaesthetists valued theophylline significantly more than respirologists ($p<0.5$).

## Discussion

This survey showed that in general the respirologists and anaesthetists surveyed had remarkably similar views about perioperative respiratory management, especially in situations in which hard data is available (1) (2). The respirologists may have ordered more preoperative test because they only see the higher risk patients preoperatively. Most anaesthetists have experienced a case of severe bronchospasm during anaesthesia, which may explain why they are more concerned about anaesthetising asthmatics, and why they value aminophylline (which can be given IV) more than did the respirologists.

## References

1) Med Clin N Amer 1987; 71 (3): 399
2) J Gen Int Med 1988; 3: 277

# THE NIGHT OF INTENSE REM SLEEP AFTER ANAESTHESIA AND SURGERY INCREASES URINARY CATECHOLAMINES

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Certain important complications of anaesthesia and major surgery peak in incidence on the 2nd to 4th postoperative days. These include acute myocardial infarction, stroke and delayed delirium. The specific factors that trigger each of these complications are unclear. We have observed that anaesthesia and abdominal surgery often lead to a night of highly intense REM sleep accompanied by unusually vivid nightmares about the 2nd to 4th postop days. We hypothesized that this night of intense REM sleep could produce additional neurohumoral activity that might contribute to the genesis of these complications. The purpose of this study was to see if this night of active REM sleep has an effect on sympathoadrenal function as reflected by the excretion of free catecholamines.

## Methods:

The subjects were sixteen adult patients undergoing upper abdominal surgery, either cholecystectomy (n=8, age 34±8 yrs, wt 70±10kg) or gastroplasty (n=8, age 34±11 yrs, wt 131±18 kgs). Anaesthesia was produced with a standard vapour and relaxant technique. Surgery was performed through an upper mid-line incision. Postoperative pain was treated with intramuscular opioid.

On the day before surgery, on the operative day and on each of the first 5 postop days, all urine was collected in two 12 hr periods, in the daytime from 0800 to 2000 hr and in the nighttime from 2000 to 0800 hr. Free norepinephrine, dopamine and epinephrine were extracted and measured with an HPLC/electrochemical detector system. To identify the nights of intense REM sleep, patients were asked each morning about their recollection of dreams. The nighttime catecholamine outputs of patients reporting nightmares on any night were compared to the outputs of the remaining patients the same night, using the Wilcoxon-Mann-Whitney test.

## Results:

There were no major anaesthetic nor surgical complications. Since neither catecholamine outputs nor reports of nightmares were detectably different between the cholecystectomy and gastroplasty groups, their results were combined for analysis.

Norepinephrine outputs during the daytime decreased on the day of operation, increased on postop day 1 and then declined (Figure). Outputs in the nighttime of patients who did not report nightmares were less than in the daytime, except on the night of operation ($p < 0.05$).

There were 9 nights of frightening nightmares reported among 8 patients. Nightmares appeared on postop night 2 (n=3), night 3, (n=4) or night 4 (n=2). The nighttime norepinephrine outputs of patients who reported nightmares on postop nights 2 and 3 were substantially greater than the outputs of the remaining patients these nights ($p < 0.05$). The outputs with nightmares on night 4 tended to be greater as well (N.S.). In 3 patients, a night of nightmares produced the greatest 12 hr norephinephrine output of the perioperative period.

Excretions of dopamine, but not of epinephrine, followed the same pattern of change.

## Discussion:

The postoperative nights of intense REM sleep, as identified by nightmares, bring about increments in the excretions of free norepinephrine and dopamine, indicating an augmentation of sympathetic nervous system activity during these nights. If these added excretions were generated during periods of intense REM sleep only (which would make up 10-15% of the 12 hr urine collection period), they would represent an enormous surge of sympathetic activity within this sleep state.

We conclude that the nights of intense REM sleep associated with vivid nightmares after anaesthesia and surgery produce a substantial increase in sympathetic neural activity. In some patients, this added activity results in the greatest 12 hr period of sympathetic activity in the entire perioperative course. This neurohumoral response of the 2nd to 4th days after operation may play a role in the genesis of one or more of the postoperative complications noted above.

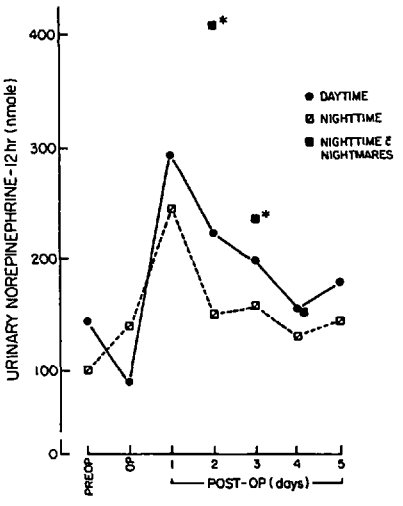


Figure. 12 hr urinary norepinephrine excretions (mean values only). "*" indicates the nighttime values associated with nightmares that exceeded the remaining nighttime values of the same night.

(Supported by MRC of Canada)

# VECURONIUM NEUROMUSCULAR BLOCKADE AT THE DIAPHRAGM, ORBICULARIS OCULI AND ADDUCTOR POLLICIS MUSCLES

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INTRODUCTION. When compared with the adductor pollicis, the diaphragm requires a larger dose of vecuronium for a similar intensity of neuromuscular blockade(1), but diaphragmatic blockade occurs sooner(2). Thus, monitoring adductor pollicis blockade is a poor indicator of diaphragmatic paralysis. The orbicularis oculi has been shown to recover from neuromuscular blockade earlier than the adductor pollicis (3). However, comparisons with the diaphragm have not been made, and the onset characteristics of orbicularis oculi blockade have not been measured. The purpose of this study was to determine the usefulness of orbicularis oculi monitoring as an indicator of diaphragmatic paralysis.

METHODS. After institutional approval and informed consent were obtained, sixteen ASA I and II adults were studied under propofol-alfentanil-oxygen anaesthesia. Nitrous oxide and inhalational agents were avoided. Supramaximal train-of-four stimulation was applied to the left ulnar, right phrenic, and right facial nerves. The force of contraction of the adductor pollicis muscle was measured, and the electromyographic responses of the diaphragm and orbicularis muscles were amplified and recorded. Vecuronium, 0.04 or 0.07 mg/kg (8 patients for each dose) was administered. Time to maximal blockade, intensity of maximal blockade, and time to 25 and 75% recovery were measured at each muscle for first twitch response (T1) and train-of-four ratio (T4/T1). Comparisons were made between the diaphragm and each of the other two muscles. A P value of 0.05 or less was considered to indicate statistically significant differences.

RESULTS. For each dose given, there was no statistically significant difference in the maximum T1 blockade achieved (Table I). However, time to maximal blockade was significantly longer for the adductor pollicis than for the diaphragm. Onset of blockade at the orbicularis oculi was much closer to that of the diaphragm (Table II). Recovery of the orbicularis oculi parallelled that of the diaphragm, but that of the adductor pollicis was much slower (Table III). At each muscle, for similar levels of T1, T4/T1 was less during recovery than during onset. The T4/T1 of the adductor pollicis recovered later than that of the diaphragm, but the time course of T4/T1 recovery was similar at the orbicularis oculi and the diaphragm.

DISCUSSION. This study showed that the time course of orbicularis oculi blockade is similar to that of the diaphragm for the two doses of vecuronium given. Thus, it appears to be a better indicator of diaphragmatic blockade than the adductor pollicis. The intensity of blockade was the same at the adductor pollicis and the diaphragm, because maximum effect occurs sooner at the diaphragm, at a time when plasma concentrations are greater than at the time of maximum adductor pollicis blockade. Thus, the results are consistent with the hypothesis that both the diaphragm and the orbicularis oculi require higher concentrations of vecuronium than the adductor pollicis for a similar degree of blockade. It is concluded that monitoring deep vecuronium blockade can be achieved better with train-of-four stimulation of the orbicularis oculi than the adductor pollicis.

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TABLE I

Intensity of Blockade (%; mean ± SEM)

| Dose | Orbicularis | Diaphragm | Adductor |
|---|---|---|---|
| 0.04 | 62 ± 11 | 98 ± 8 | 84 ± 3 |
| 0.07 | 82 ± 11 | 95 ± 3 | 95 ± 2 |

TABLE II

Time to Maximum Blockade (min; mean ± SEM)

| Dose | Orbicularis | Diaphragm | Adductor |
|---|---|---|---|
| 0.04 | 3.7 ± 0.5 | 2.9 ± 0.3 | 6.6 ± 0.6* |
| 0.07 | 3.4 ± 0.5* | 2.2 ± 0.3 | 6.3 ± 0.6* |

* : P < 0.05 compared with diaphragm

TABLE III

Time to 75% Recovery (min; mean ± SEM)

| Dose | Orbicularis | Diaphragm | Adductor |
|---|---|---|---|
| 0.04 | 18 ± 5 | 15 ± 2 | 24 ± 3* |
| 0.07 | 29 ± 4 | 26 ± 4 | 35 ± 4* |

* : P < 0.05 compared with diaphragm

# DDAVP DOES NOT REDUCE BLEEDING DURING SPINAL FUSION FOR IDIOPATHIC SCOLIOSIS.

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Introduction: DDAVP (1-desamino-8-arginine vasopressin) has been reported to reduced bleeding after cardiac surgery and during spinal fusion by 30 to 40% [1,2]. However, in the latter situation the authors suggested that it might be more helpful in patients with underlying neuromuscular disorders. This study was undertaken to determine the efficacy of DDAVP in patients undergoing spinal fusion for idiopathic scoliosis.

Methods: This double-blinded protocol was accepted by the ethics committee of our institution and informed consent was obtained for each patient. Thirty healthy (ASA 1 or 2) patients were divided at random into two groups and received at the time of cutaneous incision either 100 ml of physiologic saline (Group 1) or DDAVP 10 ug/$M^2$ S.A in the same amount of saline (Group 2) infused in 20 min. Patients were excluded if the bleeding time (B.T.) was longer than nine minutes or if they had bleeding diathesis or were taking drugs associated with abnormal coagulation. A balanced anesthesia technique with normotension using $N_2O$, isoflurane, fentanyl and pancuronium was used in all patients. If the patient was obese (>20% Ideal Body Weight (IBW) all drugs and estimated blood volume (EBV) were calculated using the IBW. The skin was infiltrated with 20 to 250 ml of a solution of epinephrin 1:500,000 and all patients were submitted to a Cotrel-Dubousset technique executed by the same surgeon. Pulse and blood pressure were measured every 5 minutes, central venous pressure (CVP), temperature and diuresis every hour. Blood samples were taken for PT, PTT, TT, BT, Platelets counts, Factors V, VIII, Von Willebrand (VW), euglobulin lysis time and fibrin plate lysis the day before the surgery and 20 min after DDAVP. Hemoglobin, hematocrit, blood and urinary sodium and osmolarity were measured before DDAVP, and at 1, 8, 14 and 24 hours after the cutaneous incision. Intraoperative blood loss was measured by weighing sponges and suction drainage, and post-operative bleeding by Hemovac drainage. Comparison of the mean age, minimal temperature observed, S.A, sex distibution, prevalence of obesity, were analysed by a Chi-square test with the Yate's correction and the other parameters by a multivariate analysis with repeated measures if indicated.

Results: The two groups were comparable for: Sex distribution (Group 1 14 F:1 M vs Group 2 14 F:1 M), age (15.1±1.9 yr vs 13.5±1.9), S.A.(1.4±0.1 $m^2$ vs 1.5±0.1), minimal temperature (34.7±0.7 C vs 34.9±0.7), number of fused vertebrae (9±1.6 vs 9.7±2.3), length of surgery (3.7±0.7 hrs vs 4.1±1.2). There was no obese patient in Group 1 compared to 6 in Group 2. There were no differences between the two groups for mean pulse and CVP. The mean arterial pressure (MAP) was lower in Group 2 for up to 45 min with the largest difference at 30 min (79.3±7.4 torr vs 67.6±9.3). All hematologic parameters were in the normal ranges and similar in both groups before the intervention. After DDAVP, there were significant increases in F VIII (119% vs 167% $p<0.001$) and in VWF (81% vs 144% $p<0.02$). The amount of blood loss in % of EBV per fused vertebra was similar in both groups for the intraoperative period (7.3±2.6% vs 5.9±2.2%), the postoperative period up to 24 hrs (3.7±0.8% vs 3.9±1.4%) and both periods (9.2±3.0% vs 10.5±2.6%). The strength of the tests was close to 1 for each of these three tests. The total amount of blood loss for the obese patients in Group 2 was similar to that of the non obese patients of the same group (2,886 ml=74.7% of EBV vs 2,879 ml= 89% of EBV). There was a significant difference in the diuresis during the first (5.1±0.6 ml/kg/hr vs 1.2±1.2 $p<0.05$) and the second hr (1.6±2.4 vs 0.4±0.3 $p<0.05$) and both groups had a low value for the third (0.9±1.0 vs 0.6±0.5) and the fourth hr (0.7±0.6 vs 0.7±0.5). Variations of blood and urinary sodium and osmolarity were similar in both groups and stayed in the normal range except for one patient of Group 2 who had a sodium of 128 mEq/L 8 hrs after DDAVP and two patients of both groups who had serum osmolarity <270 mosm/kg $H_2O$ at 8, 14 or 24 hrs after the cutaneous incision.

Discussion: In this study, although DDAVP significantly increased both F VIII and VW F, it did not reduce the surgical blood loss. The decrease in MAP caused by DDAVP was not clinically significant. The diuresis was very low in the two groups and both had patients with low serum osmolarity. This was probably due to the inappropriate secretion of antidiuretic hormone often seen in patients undergoing spinal fusion [3].

In conclusion DDAVP DOES NOT reduce the surgical bleeding in normal patients undergoing spinal fusion for idiopathic scoliosis.

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# INFLUENCE OF MEMBRANE BINDING IN THE ACCURATE MEASUREMENT OF EQUILIBRIUM DIALYSIS OF PLASMA FREE FENTANYL CONCENTRATIONS.

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**INTRODUCTION:** Equilibrium dialysis (EQD) is capable of separating the plasma free fentanyl concentration ([FREE] - the active moiety) from the total plasma fentanyl concentration ([FEN]).(1) Factors known to influence the measurement of the true [FREE] have been described and include membrane binding of the drug and impurities in the radioactive ligand.(1-7) For fentanyl EQD, some factors require more specific description. This study examined the role that dialysis temperature, duration, and [FEN] play in altering loss of fentanyl to the membrane, measurement of [FREE], magnitude of effects due to plasma alone (blank effects), and the time needed to reach equilibrium using a radioimmunoassay technique (RIA)(8). A model was developed to predict [FREE] given [FEN].

**METHODS:** Pooled dog plasma was spiked with fentanyl citrate to produce [FEN] (as the base) of 0, 1.6, 3.1, 6.3 or 11 ng/ml. Using a Spectrum® Equilibrium Dialyser and a Spectra/Por 2® membrane, 1 ml samples from each concentration were prepared and dialysed against 1 ml of an ionic phosphate buffer pH 7.3 (9) for a duration of 4, 8 or 12 hours, and at a temperature of 37, 33 or 28°C (n=180). [FEN] before and after EQD and [FREE] in the dialysate were measured with (RIA) (within assay variation = 3.5 ± 1.0%; between assay variation = 8.2 ± 3.1%). The loss of fentanyl to the membrane was calculated as the difference between [FEN] before EQD and [FEN] in the half cell after EQD. The after-dialysis ratio of free to total fentanyl concentration was multiplied by the total lost to the membrane to achieve the free fraction lost to the membrane. This loss was added to the measured free fentanyl concentration in the dialysate to give a "corrected" [FREE] value. Protein bound fentanyl was the difference between the [FEN] before EQD and the value for the corrected [FREE]. Equilibrium was considered complete when [FREE] first achieved maximum values and remained constant with subsequent dialysis times. Predictive equations for determining [FREE] and amount lost to the membrane were derived by linear regression. One way ANOVA and paired t-tests determined statistical differences ($p<0.05$).

**RESULTS:** Temperature and [FEN] at which dialysis was performed did not alter blank effect, proportional [FREE] or proportional loss of fentanyl to the membrane. Equilibrium was reached at 4 hrs and was independent of dialysis time, temperature, and [FEN]. To determine whether dialysis time affected the proportion of [FREE], proportional loss to the membrane, or blank effect, the data were pooled for all temperatures (n=12) (Table). [FEN] after EQD was significantly lower than [FEN] before EQD ($p<0.05$). At the three highest doses, loss of fentanyl to the membrane was significantly greater at 12 hours than at 4 or 8 hours ($p<0.05$). The mean percent loss to the membrane was 30±7%, and the mean percent [FREE] was 35 ± 5%. The following regression equations were developed:

Membrane Loss=0.25(Fen preEQD)+0.25 ng/ml.
[FREE] = 0.42(Fen preEQD)-0.25 ng/ml.

**TABLE:** Values for [FEN] before (Pre EQD) and after (Post EQD) dialysis: Free Corrected Fentanyl Concentration [FREE,COR (ng/ml)] and as a percent [Free,Cor(%)]; Fentanyl Bound to Plasma Protein (Bound (%)) and lost to the membrane (Loss (%)) for each Dose and Duration of EQD. Mean±STD (n=12).

| DURATION (hours) | PRE EQD (ng/ml) | POST EQD (ng/ml) | FREE,COR (ng/ml) | FREE,COR (%) | BOUND (%) | LOSS (%) |
|---|---|---|---|---|---|---|
| 4 | 1.6±0.1 | 1.3±0.2$ | 0.5±0.1 | 29±7 | 71±7 | 28±12 |
| 4 | 3.1±0.2 | 2.6±0.1$ | 0.9±0.2 | 28±8 | 71±8 | 22±4 |
| 4 | 6.3±0.5 | 5.0±0.3$ | 2.0±0.5 | 32±8 | 68±8 | 22±4 |
| 4 | 11.0±0.9 | 8.7±0.7$ | 3.9±1.0 | 35±9 | 65±9 | 22±7 |
| 8 | 1.6±0.1 | 1.2±0.2$ | 0.5±0.1 | 31±9 | 69±9 | 33±11 |
| 8 | 3.1±0.2 | 2.4±0.2$ | 1.1±0.3 | 35±9 | 64±9 | 26±6 |
| 8 | 6.3±0.5 | 4.8±0.3$ | 2.5±0.4 | 39±7 | 61±7 | 26±5 |
| 8 | 11.0±0.9 | 8.8±0.9$ | 4.4±0.8 | 40±8 | 60±8 | 22±8 |
| 12 | 1.6±0.1 | 1.1±0.2$ | 0.5±0.1 | 31±7 | 69±7 | 38±13 |
| 12 | 3.1±0.2 | 1.9±0.3$ | 1.1±0.2 | 34±7 | 65±7 | 44±9* |
| 12 | 6.3±0.5 | 4.0±0.6$ | 2.5±0.6 | 40±9 | 60±9 | 39±9* |
| 12 | 11.0±0.9 | 7.5±0.9$ | 4.8±1.0 | 44±9 | 56±9 | 33±8* |
| | | | Mean % | 35±5 | 65±5 | 30±7 |

$p<0.05 versus Fentanyl (pre EQD) *p<0.05 versus 4 and 8 hours

**DISCUSSION:** There was an average 30% loss of fentanyl to the membrane. Failure to account for the loss to the membrane during EQD may introduce an under- estimation of [FREE] if only the value for post-dialysis [FEN] is utilised. It is important to measure the [FEN] both before and after EQD to correct for loss of fentanyl to the membrane. Since equilibrium is achieved in 4 hours, longer durations of dialysis are unnecessary.

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# CONTINUOUS INFUSIONS OF LUMBAR EPIDURAL FENTANYL AND INTRAVENOUS FENTANYL FOR POST-THORACOTOMY PAIN RELIEF. II: RESPIRATORY EFFECTS

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Respiratory depression in patients receiving epidural fentanyl is reported to be uncommon. This prospective double-blind randomized study compares the effects of continuous lumbar epidural and intravenous fentanyl infusions on postoperative respiratory function.

**Methods:** With institutional approval and informed consent fourteen patients undergoing thoracotomy were studied. The night prior to surgery respiratory pattern was monitored using respiratory inductive plethysmography (RIP), allowing detection of apneas (AP=tidal volume less than 100 ml for >15 sec) and slow respiratory rate (SRR=respiratory rate less than 10/min). Spirometry and repeat arterial blood gases (ABGs) were also obtained. No premedication was given. Immediately prior to surgery a lumbar epidural catheter was inserted, and anaesthesia was induced and maintained without narcotics. The patients were randomly allocated to one of two groups: Group Epi=lumbar epidural infusion of fentanyl and intravenous infusion of normal saline, or Group IV=lumbar epidural infusion of normal saline and intravenous infusion of fentanyl. One hour after induction a 1.5 ug/kg bolus of fentanyl was administered via the allocated route and an infusion of 1.0 ug/kg/hr was begun. Upon arrival in the recovery room RIP monitoring was resumed and ABGs were collected at regular intervals. Somnolence was scored hourly from 1 to 5 (1=oriented and conversant, 5=unresponsive). Infusion rates were adjusted according to patient pain. Spirometry was performed 2 to 3 times during the first postop day. Results were analyzed using t-tests and repeated measures analysis of variance and covariance, as applicable. $p < 0.05$ was considered significant.

**Results:** There were no significant between group differences for both pre and post-operative AP episodes, SRR, somnolence, pH, $pCO_2$, $pO_2$, $FEV_1$, and FVC (table). However, within both groups there was a significant increase postop in SRR episodes and $pCO_2$ and significant decreases in pH and $FEV_1$. Only the IV group experienced a significant drop in FVC. Mean $pO_2$ increased postop in both groups due to supplemental $O_2$. Although there was a marked increase in mean AP/hr postop, particularly in the Epi group between 12-20 hr (fig.1), this did not reach significance due the small sample size and large within group variability.

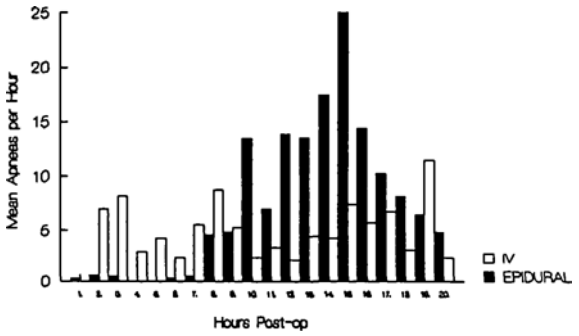
**Discussion:** Overall, there was no difference between the continuous epidural and i.v. fentanyl groups in postoperative respiratory parameters. Both experienced a late increase in SRR (15 to 20 hours postop). This suggests the need for close monitoring during the first postop night. Although statistically significant increases in $pCO_2$ and decreases in pH were found, these were of no clinical consequence.

Table of group means ± sem

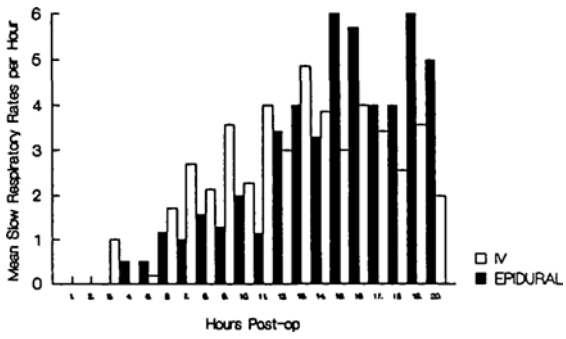
| | EPIDURAL | | INTRAVENOUS | |
|---|---|---|---|---|
| | Preop | Postop | Preop | Postop |
| pH | 7.44 ±.01 | 7.35 ±.01 | 7.42 ±.01 | 7.33 ±.01 |
| PCO2 | 38 ± 1 | 45 ± 1* | 40 ± 2 | 47 ± 2* |
| pO2 | 83 ± 4 | 108 ± 4* | 81 ± 5 | 117 ± 5* |
| Somn. | N/A | 1.6 ± 0.2 | N/A | 1.5 ± 0.1 |
| AP | 1.4 ± 0 | 2.5 ± 1.0 | 1.3 ± 0.4 | 3.8 ± 2.3 |
| SRR | 0 | 1.3 ± 0.4 | 0 | 1.3 ± 0.5 |
| FEV1(L) | 1.9 ± 0.3 | 1.4 ± 0.2* | 1.7 ± 0.3 | 1.1 ± 0.3* |
| FVC(L) | 2.6 ± 0.3 | 2.1 ± 0.1 | 2.4 ± 0.5 | 1.5 ± 0.4* |

Somn = somnolence
* $P < 0.05$ postop vs. preop
N/A = Not applicable

APNEIC EPISODES PER HOUR fig.1




SLOW RESPIRATORY RATE EPISODES PER HOUR fig.2



# NITROUS OXIDE POTENTIATES VECURONIUM

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## INTRODUCTION:

In a recent study, Szalados et al. (1) found that nitrous oxide 70% in oxygen potentiated succinylcholine neuromuscular blockade. The present study was designed to determine if $N_2O$ has the same potentiating effect on vecuronium blockade.

## METHODS:

Thirty-eight ASA I and II adult patients, within 15% of their ideal body weight were randomly divided into two groups. Anesthesia was induced with thiopentone and fentanyl and was maintained in patients in group I with intermittent boluses of thiopentone and fentanyl while breathing 100% $O_2$ and in group II with $N_2O$ 70%. Supramaximal stimulation of the ulnar nerve at the forearm with trains-of-four was performed every 20 seconds with a Datex 221 NMT Monitor and the force of contraction of the adductor pollicis was measured. The stimulation commenced four minutes after the induction of anaesthesia. One minute later, vecuronium in doses of 0.02, 0.03 or 0.04 $mg.kg^{-1}$ was administered. The twitch tension was measured until maximal depression was achieved. Dose-response curves were constructed of the log of the dose received versus the logit transformation of twitch depression. The curves were compared with analysis of covariance.

## RESULTS:

The administration of $N_2O$ was associated with potentiation of vecuronium blockade. The difference between the two dose-response curves were statistically significant ($P=0.05$). The ED50 and ED95 values derived from the dose-response curves are given in the Table.

## DISCUSSION:

In this study, $N_2O$ 70% (0.7 MAC) was found to potentiate the neuromuscular blocking effect of vecuronium, so that the ED95 was decreased by 30% in the presence of $N_2O$. This is a statistically significant but small effect. This small effect may be due to the low potency (0.7 MAC) of the $N_2O$-$O_2$ mixture. In previous studies (2,3), volatile-$N_2O$-$O_2$ mixtures of 1 to 2 MAC were used, resulting in greater potentiation. The influence of $N_2O$ should thus be taken into account when determining the dose-response curves of vecuronium.

**Table**

| | $O_2$ | $N_2O$ |
|---|---|---|
| ED50 | 0.0297 ± 0.0023 | 0.0260 ± 0.0014 |
| ED95 | 0.0670 ± 0.0052 | 0.0442 ± 0.0025 |

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# Quantitation of thiopental anesthetic depth with clinical stimuli.

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**Introduction:**
Anaesthetic "depth" can be interpreted as the presence or absence of response to a specific stimulus during surgical anaesthesia. The probability of a response to a stimulus is a function of the anaesthetic drug concentration in the brain and the intensity of the stimulus. Many measures of response have been studied, including movement, hemodynamics, and intraoperative recall. Previous pharmacodynamic studies of thiopental were done under non-steady-state condition in which the measured plasma thiopental concentrations (TC) did not reflect the concentrations at the site of action (1,2). Using a pharmacokinetic model, a Computer Control Infusion Pump (CCIP) can rapidly achieve and maintain a stable TC (3). When sufficient time is allowed for thiopental to equilibrate between the plasma and the brain, this stable TC can be used to quantitate thiopental anesthetic depth. Our study determines the relationship between stable TC and the depth of thiopental anesthesia as assessed by several clinically relevant noxious stimuli.

**Methods:**
We studied 26 unpremedicated healthy ASA I or II male surgical patients. Their mean (+SD) age was 45.4 ± 11 yrs and weight was 87.5 ± 14.8 kg. Exclusion criteria include cardiovascular, CNS diseases or concomitant use of cardiovascular and CNS drugs. Upon arrival in the O.R., a radial arterial catheter was placed for continuous hemodynamic monitoring and blood sampling. During the study, frequent blood samples were collected for drug assay and arterial blood gases to ensure adequate ventilation and oxygenation. Two stable TCs were studied in each patient. After baseline recording of the hemodynamics, the CCIP rapidly achieved and maintained the first target stable TC (10 to 30 ug/ml) for 5 minutes to allow the blood-brain equilibration. The following stimuli were applied sequentially at 1 minute intervals: verbal command, 50 Hz tetanus to the forearm, trapezius muscle squeeze and direct laryngoscopy. Movement, blood pressure and heart rate response to the stimuli were recorded. A second target stable TC (40 to 90 ug/ml) was then achieved and maintained by the CCIP for 5 minutes. The same stimuli were repeated and followed by intubation. No other anesthetic drugs were administered during the study. Any purposeful movement was considered a positive movement response. A 15% increase of mean arterial pressure (MAP) or heart rate (HR) from pre-stimulation was considered a positive hemodynamic response. Using these quantal responses and the stable TC, the probability of no response to each stimulus was modelled by the logistic regression.

**Results:**
None of the subjects had post-operative recall of the stimuli. The curves describing the probability of no movement for all the stimuli are shown in Figure 1. $Cp_{50}$s (the stable TC which will produce 50% probability of no responses) for all stimuli were estimated and shown in Table 1.

**Discussion:**
The steady state concentrations which produce an effect (response) in 50% of the patients are commonly used to compare relative drug potency. In this study, the estimated $Cp_{50}$ can be used as a measure of stimulus "potency" (intensity). Our results have demonstrated a gradation of stimulus intensity. Intubation appears to be the most noxious stimulus. Movement was the most consistent clinical response that separated the different clinical noxious stimuli applied. MAP and HR responses were consistent measures of anesthetic depth only for the more noxious stimuli (laryngoscopy and intubation). HR response is attenuated at a lower TC compared to movement and MAP. The $Cp_{50}$ for different stimuli is analogous to the MAC concept for inhalational agents. Using a CCIP and gradation of clinically relevant noxious stimuli, this study demonstrates a new conceptual approach to quantitate concentration effect relationship and also brain sensitivity of intravenous anesthetics. This method should prove useful for identifying determinants of intravenous anesthetic brain response (sensitivity) and interactions with other anesthetic drugs such N2O and narcotics.

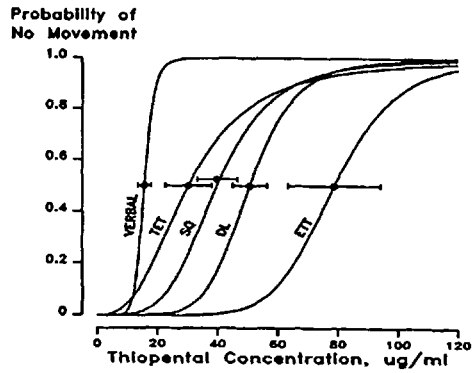


Figure 1. The probability of no movement curves to verbal command(VERBAL), tetanus (TET), trapezius squeeze (SQ), laryngoscopy (DL), and intubation (ETT). The $Cp_{50}$ of these stmuli with 95% confidence bounds are shown.

Table 1: Cp50 of the clinical responses for all stimuli.

| RESPONSES | STIMULUS | $CP_{50}$(ug/ml) | S.E. |
|---|---|---|---|
| MOVEMENT | VERBAL | 15.6 | 1.11 |
| | TETANUS | 30.3 | 3.83 |
| | MUSCLE SQUEEZE | 39.8 | 3.33 |
| | LARYNGOSCOPY | 50.7 | 2.87 |
| | INTUBATION | 78.8 | 7.41 |
| MAP | TETANUS | ND | ND |
| | MUSCLE SQUEEZE | ND | ND |
| | LARYNGOSCOPY | 56.4 | 9.78 |
| | INTUBATION | 65.5 | 6.10 |
| HR | TETANUS | ND | ND |
| | MUSCLE SQUEEZE | ND | ND |
| | LARNGOSCOPY | 33.5 | 4.35 |
| | INTUBATION | 59.8 | 6.29 |

S.E. = Standard Error
ND = Not able to determine due to inconsistent concentration/responsse relationship

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## SYSTEMIC HEMODYNAMICS AND ORGAN BLOOD FLOW DURING ADENOSINE-INDUCED HYPOTENSION: EFFECTS OF HALOTHANE AND SEVOFLURANE ANAESTHESIA

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**Introduction**: Adenosine (AD), a short acting purine vasodilator, has been shown to be a safe and effective agent for inducing hypotension during anaesthesia.[1] Although the effects of AD on systemic haemodynamics and organ blood flow have been studied, the interaction between AD and potent inhalational agents has not been thoroughly investigated. The purpose of this study was to compare the effects of halothane (H) and sevoflurane (S) anaesthesia on systemic haemodynamics and organ blood flow (OBF) during AD-induced hypotension.

**Methods**: With approval from the animal care committee, fasted adult Sprague-Dawley rats, weighing 260-320 g were studied. During brief ether anaesthesia, three sites were cannulated: (1) the left femoral artery, for systemic blood pressure monitoring, blood sampling, and reference sample withdrawal, (2) the right internal jugular vein, for intravenous infusions, and (3) the left ventricle via the right common carotid artery, for injection of radioactive microspheres. Placement of the catheter in the left ventricle was verified by monitoring the blood pressure waveform. After recovering for 4 hours, the rats were placed in plexiglas chambers and given 100% $O_2$ to breathe. Systemic haemodynamics and OBF were determined in 3 groups of rats: (1) awake (control) (2) anaesthetized with 1.0 MAC H and (3) anaesthetized with 1.0 MAC S. The rats were infused with saline for initial cardiac output (CO) and OBF measurements and then with AD for repeat measurements. The AD was infused at a rate sufficient to reduce the mean arterial pressure (MAP) by 30-35% and determinations were made after 20 mins of stable haemodynamic recordings. To determine CO and OBF, microspheres 16 ± 0.1 μm in diameter, and labelled with either $^{57}Co$ (for pre-AD measurements) or $^{46}Sc$ (for post-AD measurements) were infused into the left ventricle. A reference sample (0.6 ml) was simultaneously withdrawn. Blood samples were replaced with Ficoll (0.6 ml, 13% w/v). The following organs were then removed for gamma scintillation counting: brain, spinal cord, lungs, heart, liver, kidneys, spleen, stomach, omentum, pancreas, small intestine and large intestine. CO, systemic vascular resistance (SVR) and OBF were calculated using standard formulae.[2] Arterial blood gases (ABG's) were determined immediately before and 30 mins after exposure to the anaesthetic agents at the time of initial OBF determination. The inspired anaesthetic concentrations were monitored using a Beckman LB-2 analyzer. Throughout the experiments the rats breathed spontaneously. Normothermia was maintained with overhead radiant heaters. MAC for H and S was determined using standard tail clamp techniques. Data are presented as mean values ± SEM. Statistical significance ($p < 0.05$) was determined using analysis of variance.

**Results**: MAC for H and S was 1.10 ± 0.05% and 2.30 ± 0.05%, respectively. ABG's in awake rats were: pH = 7.41 ± 0.04, $pCO_2$ = 38 ± 4; in the H group were: pH = 7.38 ± 0.03, $pCO_2$ = 50 ± 5 and in the S group were: pH =7.35 ± 0.02, $pCO_2$ = 56 ± 5 mmHg. There were no significant differences in $pO_2$. The dose of AD required to reduce MAP by 30-35% in awake rats was 1.2 ± 0.1 μg/kg/min and in rats anaesthetized with H and S was 0.45 ± 0.05 and 0.57 ± 0.05 μg/kg/min, respectively.

AD, in awake rats, significantly decreased SVR and heart rate (HR) but did not change CO. In addition, AD increased coronary, hepatic arterial (HABF) and portal venous (PVBF) blood flows but did not change cerebral (CBF), spinal cord and renal blood flows (Table).

H significantly decreased HR, MAP, CO, coronary and PVBF, but increased CBF compared to awake rats. The addition of AD to rats anaesthetized with H did not change HR but increased CO above that observed with H alone. Also, AD increased coronary and HABF and restored PVBF to that observed in awake AD-treated rats.

S did not affect systemic haemodynamics. Furthermore, S did not affect OBF except for an increase in HABF. The addition of AD to rats anaesthetized with S yielded similar effects on systemic haemodynamics as those observed in awake AD-treated rats. The effects on OBF were also similar except that AD did not increase HABF above that observed with S alone.

**Discussion**: H and S differ in their effects on systemic haemodynamics and OBF. In spontaneously breathing rats, the effect of AD on systemic haemodynamics and organ blood flow predominates when this drug is given in combination with either H or S.

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TABLE

| | CONTROL (n = 16) | AD (n = 16) | H (n = 10) | H + AD (n = 10) | S (n = 10) | S + AD (n = 10) |
|---|---|---|---|---|---|---|
| MAP | 105 ± 2.3 | 68* ±3.0 | 91* ±5.3 | 65+ ±3.3 | 107 ± 4.4 | 67† ±2.9 |
| HR | 360 ±15 | 302* ±10 | 320* ± 8 | 307 ±11 | 352 ± 7 | 311† ± 6 |
| CO | 244 ±12.1 | 261 ±18.6 | 173* ±11.2 | 234 ±12.5 | 244 ± 8.3 | 241 ±22.8 |
| SVR | 0.46 ±0.02 | 0.28* ±0.02 | 0.53 ±0.04 | 0.28 ±0.01 | 0.44 ±0.03 | 0.29† ±0.03 |
| CARDIAC | 7.4 ±0.7 | 17.0 ±2.3 | 405* ±0.4 | 15.9† ±2.1 | 9.0 ±0.4 | 15.53† ±1.7 |
| CBF | 3.5 ±0.3 | 3.2 ±0.3 | 5.06 ±0.4 | 6.8* ±1.1 | 4.0 ±0.4 | 4.5 ±0.9 |
| SPINAL | 0.9 ±0.1 | 0.8 ±0.1 | 1.3 ±0.2 | 1.5 ±0.3 | 1.3 ±0.1 | 1.4 ±0.4 |
| RENAL | 42.2 ±1.6 | 43.4 ±1.9 | 33.2 ±1.6 | 40.8 ±1.5 | 40.6 ±4.4 | 48.6 ±3.1 |
| HABV | 9.2 ±1.1 | 13.7* ±1.3 | 11.5 ±1.2 | 15.8† ±1.5 | 12.5* ±1.2 | 14.4 ±1.5 |
| PVBF | 40.6 ±2.2 | 59.4* ±4.5 | 29.9* ±1.6 | 57.1+ ±3.6 | 39.8 ±3.4 | 59.0† ±10.7 |

Values (ml/kg/min) are presented as means ± SD
*p < 0.05 compared to controls
+p < 0.05 compared to halothane
†p < 0.05 compared to sevoflurane

# ALFENTANIL INFUSION FOR INTRA-ABDOMINAL SURGERY

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**INTRODUCTION:** Although alfentanil may be considered especially suited for brief surgical procedures, it has been used for longer operations using a bolus injection followed by an infusion at a rate sufficient to compensate for redistribution and elimination (1). Its small volume of distribution limits accumulation and allows for rapid elimination from tissue storage sites. This accounts for the rapid recovery seen following both bolus intravenous injection and continuous infusion (2). The aim of this study was to evaluate the efficacy and safety of a bolus/infusion technique of administration of alfentanil as an adjunct to $N_2O/O_2$/isoflurane anaesthesia in patients undergoing intra-abdominal surgery. Furthermore, we wished to evaluate the rate of recovery and incidence of side effects associated with this technique.

**METHODS:** 107 ASA 1-3 patients scheduled for elective intra-abdominal surgery expected to last > 45 min were entered into this multicentre study (five centres). Concurrent medications were continued perioperatively and all patients received diazepam 0.15 mg/kg po 1 hr preoperatively. During a 3-min period of preoxygenation, patients received droperidol 0.0175 mg/kg plus DTC 0.05 mg/kg, then a bolus of alfentanil 50 or 75 mcg/kg at a rate of 50 mcg/kg/min using the Harvard Mini-Infuser pump. One min after this infusion, thiopental was given to loss of consciousness, then succinylcholine 1.5 mg/kg. Maintenance of anaesthesia was with $N_2O/O_2$ (70%/30%) with 0.5% inspired isoflurane plus an alfentanil infusion (0.5-1.5 mcg/kg/min) adjusted to maintain cardiovascular stability. If the highest infusion rate did not provide suitable conditions, a bolus of 7.5 mcg/kg was given. The infusion was stopped 10-15 min prior to the end of surgery and the isoflurane tapered. Pancuronium was given for muscle relaxation. HR,SBP,DBP and MAP were recorded on arrival in OR, 1 min after: alfentanil bolus, intubation and first surgical stimulus, at 3 min intervals thereafter for first 30 min, then every 5 min. At the end of surgery, time to: awakening, response to verbal commands, extubation and full alertness were recorded. The presence or absence of side effects and the anaesthetist's assessment were also recorded. All patients were given a PARR score on arrival in the recovery room (RR) and thereafter at selected intervals, dependent on motor performance, respiration, consciousness and pain.

**RESULTS:** There were 13(12%) males and 94(88%) females with a mean age of 41.3±1.2 yrs. The total dose of alfentanil was 154.4±5.1 mcg/kg for a mean surgical time of 95.3±3.7 min and total anaesthesia time of 116.5±4.0 min. Surgical procedures included cholecystectomy(29%), hysterectomy(43%), gastroduodenal(9%), bowel resection(5%) and tuboplasty(14%). 53% of the total infusion time was at 1 mcg/kg/min, 20% at 0.5 mcg/kg/min and 12% at 1.5 mcg/kg/min.

There was a significant decrease in mean SBP of 26.5% during induction/intubation (128.4±1.9 to 101.1±1.7 mmHg) which returned to control value by 12th min of surgery and was then maintained at ± 5% of control. Mean HR also decreased significantly by 10.6% during induction/intubation (77.2±1.4 to 69.8±1.1 bpm), returned to control value by 15th min of surgery, gradually decreased over the next 30 min, thereafter remaining between 65-75 bpm. MAP and DBP followed similar pattern to SBP. Table 1 shows the response times recorded at the end of surgery. Table 2 lists the incidence of the most frequent side effects and the percentage recorded as disturbing and possibly related to alfentanil. The incidence of all other side effects was < 1% and none were attributed to alfentanil. Anaesthetist assessment of induction, maintenance and recovery was good or satisfactory in 94.3%, 97.1% and 97.1% of cases, respectively. On arrival in RR, 40% of patients were fully awake, 46% arousable and only 16% not responding. By 15 min, 70% were fully awake and 30% arousable. On arrival in RR, 60% of patients had no pain with < 10% with severe pain. However, by 30 min, only 15% had no pain, although > 45% of patients had only mild pain not requiring analgesia in the RR. No patient was aware during surgery.

**CONCLUSION:** The technique of bolus/infusion of alfentanil provided good hemodynamic control during intra-abdominal surgery with rapid recovery. Although there was a significant fall in SBP after induction, this was not clinically significant as indicated by the low incidence of disturbing hypotension reported. Furthermore, the doses used in this study successfully obtunded any hemodynamic response to intubation. The low incidence of reported side effects attributed to alfentanil confirms the safety of this technique. Where the length of surgery is uncertain, this adjustable method of anaesthesia may be an attractive alternative. The absence of response to intubation, stable intra-operative hemodynamics, rapid recovery and residual post-operative analgesia make this technique suitable for a wide variety of intra-abdominal procedures. Future studies will be required to determine if patients with coronary artery disease may benefit from this technique.

**Table 1 : Postoperative Data (Mean ± SEM)**

| | |
|---|---|
| Time to awakening | 6.2 ± 0.8 min |
| Time to response to verbal commands | 8.4 ± 1.0 min |
| Time to extubation | 11.0 ± 1.4 min |
| Time to alertness | 21.5 ± 1.8 min |

**Table 2 : Incidence of Side Effects**

| Side Effect | Total Incidence | Disturbing/Poss. Alf. Related |
|---|---|---|
| Hypotension | 26.2% | 4.7% |
| Hypertension | 20.6% | 1.9% |
| Bradycardia | 14.9% | 2.8% |
| Tachycardia | 12.1% | 0% |
| Chest Wall Rigidity | 8.4% | 1.9% |
| Nausea | 13.1% | 0% |
| Vomiting | 4.7% | 0% |

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## A COMPARISON OF SEDATION FOR UPPER GI ENDOSCOPY USING DIAZEPAM with DEMEROL or MIDAZOLAM with ALFENTANIL

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Introduction Complications of sedation for upper GI endoscopy using diazepam are rare, but midazolam has been shown in a large number of studies to provide improved sedation and amnesia without impaired recovery. In our clinic meperidine is used in addition to diazepam. This has been found to reduce gagging during endoscope insertion and enhance the sedation of diazepam. The present study was designed to compare the effectiveness and safety of combining midazolam and alfentanil, a potent and rapid-acting narcotic analgesic, with the established regimen.

Methods With hospital ethical committee approval, informed consent was obtained from 60 patients requiring upper GI endoscopy. Subjects who were pregnant, suffering from chronic obstructive pulmonary disease or cirrhosis of the liver were excluded. Before endoscopy subjects completed two serial four-choice reaction time tests (4CRT) each of five minutes duration[1]. Subjects were randomly divided into two groups, group D received meperidine 50 mg then diazepam while group M received alfentanil 250 μg then midazolam according to scale (table 1). Lidocaine 10% spray < was used to provide topical anaesthesia. Subjects breathed air, $O_2$ saturation was monitored using a pulse oximeter (Nellcor N-100) and $O_2$ was given only if $O_2$ saturation fell below 90% for 15 secs. The drugs were administered by the endoscopist who was blinded and each procedure was observed by an anaesthetist who noted these times :- drugs injected, endoscope inserted, endoscopy completed and subject oriented. Every 30 seconds during endoscopy, the pulse rate, $O_2$ saturation, any aversive movements or apnoeic episodes were noted. 30 and 60 minutes after the endoscopy the subjects were asked to sit, complete a 5-minute 4CRT then stand and walk and were asked whether they felt nauseous or dizzy. 4CRT's were recorded on tape and analysed after the study was completed[2]. The effect of treatments on 4CRT's were compared using repeated measures ANOVA with the control preoperative test as a covariate. Other variables were compared using Student's t or $Chi^2$ test as appropriate.

| Wt(kg) | M(mg) | D(mg) |
|---|---|---|
| < 50 | 2.5 | 5.0 |
| 50-99 | 3.75 | 7.5 |
| > 99 | 5.0 | 10.0 |

Table 1 Dose of Benzodiazepine

Results Valid 4CRT results were obtained for 58 subjects (29 each group). The age of group M was 51.6±13.2 (mean±sd) years slightly though not significantly higher than group D 46±16.6. There were no significant differences between groups in mean weight, numbers currently taking cimetidine or benzodiazepines, male/ female ratio or control pulse or $O_2$ saturation. The average dose of diazepam used was 91±12 and of midazolam 47±6 μg/kg. During endoscopy, insertion time was shorter (p=0.023) and the number of aversive movements (p=0.004) less in group M. No apnoeas were recorded in either group nor were there differences in highest pulse rate. Lowest $O_2$ saturation (LOSAT) was correlated with age. If subjects are grouped according to age there is no difference between LOSAT of group D. However in group M, age <= 45 LOSAT was 96±1.9 (n=9) while age > 45 was 90±3.9 (n=21) (p<0.0001). Endoscopy conditions were rated only fair in 5 of group D and none of group M but this just failed (p=0.0525) to differ significantly. During recovery there were no differences at 30 or 60 minutes in subjects ablity to stand and walk or complaints of nausea or dizzyness (Table 2). There was a tendency for control 4CRT to be higher in group M (p=.07) therefore values quoted are adjusted mean values from the covariance analysis. Control 4CRT was 563 msec and this rose to 611 msec at 30 min in group M but was unchanged at 565 msec in group D. After 60 minutes median 4CRT's were unchanged from control at 539 and 524 msec in group D and M respectively. There were no differences in the number of error responses.

| | 30 mins | | | | 60 mins | |
|---|---|---|---|---|---|---|
| | std | wlk | ns | diz | std | wlk |
| gp D | 26 | 24 | 4 | 6 | 27 | 27 |
| gp M | 30 | 24 | 2 | 4 | 30 | 30 |

Table 2 Incidence of Postoperative Findings.

Discussion Better endoscopy conditions were achieved more quickly in group M without an increase incidence of adverse effects or longer recovery. This was due to the relatively larger dose of benzodiazepine (dose ratio 1:2 vs potency ratio 3-4:1). Although there was no evidence of psychomotor impairment in group D 30 min after endoscopy, fewer group D subjects were ready to leave after 60 min. Although supplemental $O_2$ was not required by anyone there was a lower $O_2$ saturation in older subjects in group M. Midazolam / alfentanil may be used to achieve improved sedation for endoscopy in younger subjects without prolonged recovery.

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# RANDOM DOUBLE-BLIND COMPARISON OF NIZATIDINE, FAMOTIDINE, RANITIDINE AND PLACEBO

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## Introduction:

Aspiration of gastric contents remains a potentially lethal complication of general anæsthesia. Premedication with H2 antagonists can minimize this risk by increasing the pH and consequently reducing gastric volume. Currently, ranitidine is the most favoured drug for this purpose. The present study compares oral administration, of two newer H2 antagonists; nizatidine and famotidine, with ranitidine and placebo to determine their relative effectiveness in prophylaxis for acid aspiration pneumonitis.

## Methods:

After approval from the institutional ethics review board, informed written consent was obtained from 40 healthy, ASA I or II, patients, scheduled for elective surgery. All patients were within 20% of ideal body weight, had no history of gastrointestinal disease, and were not on medication known to affect gastric pH or motility. This was a random double-blind study. Randomization and blinding were performed by the hospital pharmacy. Patients received either; nizatidine 300 mg, famotidine 40 mg, ranitidine 300 mg or placebo. The pill was given by mouth with a sip of water two hours prior to surgery. No other premedication was given. Patients were fasting for a minimum of eight hours prior to the induction of anæsthesia. Anæsthesia was induced with fentanyl and pentothal. Intubation was facilitated using succinylcholine. Anæsthesia was maintained with nitrous oxide and isoflurane. After the patient's condition was stabilized, an 18 gauge orogastric tube was inserted and the gastric contents were aspirated. A second sample was collected at the conclusion of surgery (approximately two hours later). Gastric volume was determined using a calibrated syringe. Gastric pH was measured using a calibrated, Corning pH meter. Samples were analyzed as soon as possible after collection. Statistical assessment of the data was performed using ANOVA and $\chi$-square analysis for parametric and nonparametric data respectively. A value of $p<0.05$ was considered statistically significant.

## Results:

We studied 40 subjects, 10 per group. Patients in each group were similar with respect to age, sex, height and weight. No adverse effects were noted. Results are shown in the tables. Compared to placebo all treatments markedly increased gastric pH. Compared to placebo, both nizatidine and ranitidine reduced gastric volume. The effect of famotidine in reducing gastric volume was not detectably different from the placebo group due to the large standard deviation. Despite confirmation that the orogastric tube was correctly positioned in the stomach, (by auscultation during air insufflation), in some subjects no gastric sample could be obtained. Using standard criteria that gastric volume of >25 ml and pH of <2.5 represents a patient "at risk" of acid aspiration pneumonitis, not a single subject was "at risk" following pretreatment with nizatidine. In contrast, one patient from each of the famotidine and ranitidine groups and six patients from the placebo group, remained in the "at risk" category. The second sample did not identify any patient "at risk".

**Table 1 Gastric Volume and pH**

| | Nizatidine | Famotidine | Ranitidine | Placebo |
|---|---|---|---|---|
| **Sample 1** | | | | |
| pH | 7.44±.33* | 5.75±1.95* | 6.57±1.88* | 2.96±2.67 |
| Volume (ml) | 6±6* | 18±25 | 14±20* | 33±18 |
| **Sample 2** | | | | |
| pH | 7.73±.43 | 7.39±.47 | 7.47±.90 | 5.18±2.25 |
| Volume (ml) | 5±7 | 2±2 | 9±11 | 8±7 |

**Table 2 Patients "At Risk"**

| | Nizatidine | Famotidine | Ranitidine | Placebo |
|---|---|---|---|---|
| **Sample 1** | | | | |
| pH<2.5 | 0* | 1* | 1* | 7 |
| Volume>25 ml | 0* | 2* | 1* | 8 |
| At Risk | 0* | 1* | 1* | 6 |
| **Sample 2** | | | | |
| pH<2.5 | 0 | 0 | 0 | 2 |
| Volume>25 | 0 | 0 | 1 | 0 |
| At Risk | 0 | 0 | 0 | 0 |

* different from placebo $p<0.05$

## Discussion:

We conclude that nizatidine, famotidine and ranitidine are effective in reducing gastric acidity and volume. Only patients receiving nizatidine had consistent acid aspiration prophylaxis. In addition patients in the nizatidine group had the lowest values for gastric acidity and volume. At the doses we studied nizatidine is the least expensive and the most cost effective agent. Although pretreatment with an H2 antagonist reduced gastric volume and acidity in most patients, it is unsafe to assume that H2 antagonists will ***always*** eliminate the risk of acid aspiration pneumonitis.

# MONITORING OF BRAIN STEM FUNCTION DURING POSTERIOR FOSSA SURGERY

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During posterior fossa surgery, blood supply to the vital areas of the brainstem may be compromised by retraction of the brainstem. During the clipping of vertebral-basilar artery aneurysms this may also occur with the temporary or permanent occlusion of the feeding artery. Monitoring of cardiovascular (CVS) changes is the most common method used for detecting such compromise. Spontaneous respiration (spont resp) has also been recommended, as well as monitoring of brain stem auditory evoked potentials (BAEP).1,2 In this study we examined the value of spont resp as a monitor of brain stem function in comparison to CVS changes and evoked potential (EP) monitoring during vertebral-basilar aneurysm surgery.

## Methods

In 44 patients with vertebral-basilar aneurysms spont resp under general anaesthesia was used during the clipping of the aneurysm or permanent occlusion of the feeding artery. Anaesthesia records were examined for documented evidence of changes in respiratory pattern and changes in blood pressure and heart rate. EP monitoring was used in 20 patients. All significant changes in latency or amplitude of BAEP or somatosensory evoked potential (SSEP) were documented.

## Result

The mean (± SD) age of the patients was 46 ± 14 years. All patients had aneurysms of the vertebral artery or of the vertebral-basilar junction; 31 had ruptured and 13 intact. Forty-two procedures were performed in the park bench position and two in the sitting position. Patients received total means of 3.2 mcg/kg fentanyl (n = 43) or 1.3 mcg/kg sufentanil (n = 1), 1.2% isoflurane (n = 40) or 0.6% halothane (n = 4) with or without nitrous oxide prior to spont resp. Spont resp was instituted at a mean time of 184 minutes after induction with reversal neuromuscular blockage and administration of naloxone where appropriate. Nine patients received a mean dose of 156 mcg of naloxone.

Thirteen patients experienced breathing abnormalities or apnea during retraction (n = 6) or occlusion of the artery (n = 7) (Table). This resulted in the surgeon removing (n = 5) or repositioning (n = 2) the clip in a location that did not alter breathing. Retractor changes reversed with repositioning of the retractor.

EP monitoring was useful in 17 patients. In three other patients the initial EP was very abnormal as these patients had major preoperative neurological deficits, thus the EP was not useful intraoperatively. All patients with EP monitoring had BAEPs and in 4 patients SSEPs were also used. Seven patients had EP changes. In 3 of these patients the EP changes occurred at the same time as a change in the respiratory pattern and then an increase in blood pressure and heart rate. CVS changes alone occurred in only one patient.

## Discussion

The areas of the brainstem where hemodynamic and respiratory control and conduction of EP take place are adjacent but anatomically discrete. An enlarging ischemic area or edema may ultimately derange all three functions. To prevent ischemia that results in neurological deficits, monitoring that allows early detection is needed. In our study CVS changes did not occur as frequently or as early as respiratory changes. If good quality EP can be obtained, they may substitute for spont resp. If they are abnormal preoperatively, or as an additional monitor to EP, the institution of spont resp during vertebral-basilar aneurysm surgery allows for better monitoring of brainstem function.

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## Table

| Changes | Number of Patients With EP (n = 17) | Number of Patients Without EP (n = 27) |
|---|---|---|
| No change | 9 | 18 |
| Resp only | 1 | 6 |
| CVS only | - | 1 |
| Resp & CVS | - | 2 |
| EP only | 3 | |
| EP & Resp | 1 | |
| EP & CVS | - | |
| EP & Resp & CVS | 3 | |

# CRANIAL DUPLEX SONOGRAPHY: DOES HALOTHANE AFFECT THE CEREBROVASCULAR RESPONSE TO CARBON DIOXIDE IN ANAESTHETIZED CHILDREN?

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**INTRODUCTION:** Halothane(H) is the oldest of the inhalational agents in current use. Long before isoflurane (I) was available H was used in patients for neurosurgery. It is now evident that H causes the most vasodilation of all the inhalational agents.[1] Moderate decreases in carbon dioxide ($CO_2$) can be expected to counteract increases in cerebral blood flow (CBF) more effficiently with I than with H.[2,3] A recent study using transcranial doppler (TCD) has shown that when H concentration is decreased there is a delay in return of CBF to baseline, a hystereisis type effect.[4] Studies on the effect of $CO_2$ on CBF have shown that $CO_2$ causes a linear increase in CBF between 20-60 mmHg.[5,6] It is the practice with raised intracranial pressure to use hyperventilation to attenuate any increase in CBF. Hyperventilation in adults and pediatric patients have demonstrated that the $PaCO_2$ directly affects the caliber of the resistance vessels in the cerebral vasculature and therefore CBF.[7]

**METHODS:** With approval of this institutions Human Ethics Committee,15 healthy infants and children for elective urological or orthopedic procedures were studied. All patients were ASA Physical Status I and II, fasting and unpremedicated. Anesthesia was induced with thiopentone 5mg/kg, fentanyl 2mcg/kg, and vecuronium 0.1 mg/kg. After the trachea was intubated, anesthesia was maintained with H, 75% air in $O_2$ and vecuronium 0.05mg/kg. All patients received a continuous caudal or lumbar epidural block performed with 0.25% bupivacaine prior to incision. Ventilation was adjusted to achieve an end tidal $CO_2$ ($PE'CO_2$) of 20 mmHg at the same time that H equilibrium was being established. Fresh gas flows were maintained constant throughout the study to avoid any variation in intrathoracic pressure. Normothermia was maintained. $PE'CO_2$ was randomly equilibrated to 20, 40, or 60 mmHg with an exogenous source of $CO_2$. Patients were non- randomly started at either 0.5 MAC or 1.0 MAC H concentration. A time interval of five minutes was allowed between $CO_2$ changes and fifteen minutes was allowed between H changes to achieve steady-state. SAP, HR , oxygen saturation, end-tidal H and inspired $O_2$ were recorded within the range of $PCO_2$ values investigated. Cerebral Blood Flow Velocity (CBFV) and resistance index (RI+) in the middle cerebral artery (MCA) was measured through the temporal window with a TCD. CBFV, RI+, and $PE'CO_2$ were analyzed using logarithmic regression and $r^2$ value. Statistical significance ($p<0.05$) was determined with student's paired t-test, ANOVA and the Tukey test for multiple comparisons.

**RESULTS:** The mean (±S.D.) age and weight was 46.1 ±30.2 mo and 17.0±6.1 kg. The CBFV increased logarithmically as $PE'CO_2$ increased during both 0.5 MAC ($r^2$=0.99) and 1.0 MAC ($r^2$= 0.95 ) H. The RI+ showed an inverse log relationship with $PE'CO_2$ at 0.5 MAC ($r^2$= 0.99) and 1.0 MAC ($r^2$=0.53) H (fig 1). There was a statistically significant difference between CBFV at all $CO_2$ levels when comparing 0.5 MAC and 1.0 MAC H concentrations ($p<0.05$) (fig 2). HR, SAP, temperature and $O_2$ stauration did not change significantly during the study.

**DISCUSSION:** H partially blunts cerebrovascular reactivity to $CO_2$. H has been shown to dilate the cerebrovasculature but have a delayed return to baseline upon decreasing the concentration.[4] It is known that if one hyperventilates a patient and then introduces H then there is a blunting of cerebrovascular reactivity to $CO_2$.[8] At $PE'CO_2$ of 60 mmHg the arterioles appear to be fully vasodilated since the CBFV is nearly identical at both 0.5 and 1.0 MAC and RI+ seems to have plateaued at a low value. There is a partial cerebrovascular response tat all $CO_2$. Vasomotor paralysis secondary to H may play a part. Since there is no change in the diameter of the basal cerebral vessels in the pediatric population with changes in $CO_2$ we can assume that changes in CBFV are proportional to changes in CBF.[9,10] We interpret these observations to indicate that with hyperventilation and H anesthesia there is blunted cerebrovascular reactivity to $CO_2$, but one quickly reaches maximal arteriolar vasodilation at normo and hypercapnia.

**ACKNOWLEDGMENTS:** We thank Medasonics Transpect TCD,Canada for providing the TCD

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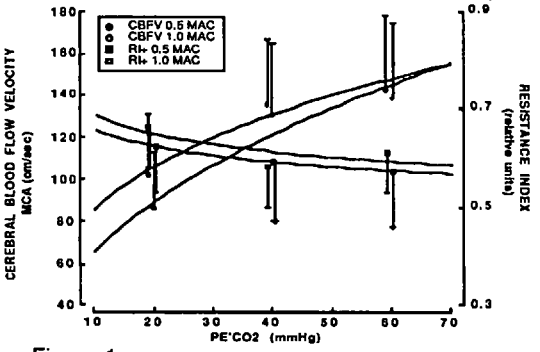


Figure 1

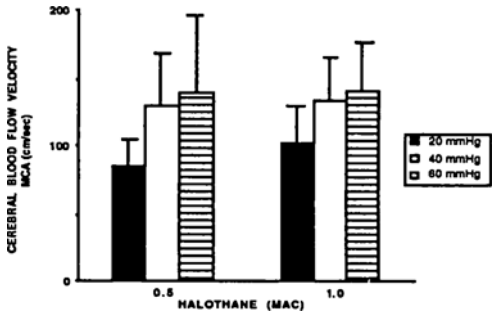


Figure 2

# A COMPARISON OF ELECTROCARDIOGRAPHIC AND ECHOCARDIOGRAPHIC ABNORMALITIES IN SUBARACHNOID HEMORRHAGE

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**Introduction:** Electrocardiographic(EKG) changes following subarachnoid haemorrhage (SAH) have been well documented. In addition to T wave abnormalities, changes in QRS or P wave configuration as well as arrhythmias may be found. However,the functional significance of these changes has not been assessed, thus creating a dilemma for the anaesthetist. The aim of this study was to correlate the EKG changes with echocardiographic (ECHO) assessment of cardiac function in SAH patients .

**Methods:**
Twenty four patients with intracranial aneurysms were studied within ten days of admission. Two dimensional ECHOs were obtained and wall motion was visually classified as normal, hypokinetic, akinetic or dyskinetic. A 12 lead EKG was recorded in close temporal proximity to the ECHO study. Patient age, sex, neurological disease, BOTTRELL neurological grade, cardiovascular disease, and electrolytes were documented. Hospital course and clinical status at discharge were obtained from the chart.

EKG AND ECHO RESULTS

| NEUROLOGICAL GRADE | NL EKG NL ECHO | ABN EKG NL ECHO | ABN EKG ABN ECHO |
|---|---|---|---|
| 0 | 2 | 2 | 1* |
| 1 | 4 | 7 | 1* |
| 2 | 3 | 1 | |
| 3 | | 2 | $1^{+}$ |
| 4 | | | $1^{+}$ |

NL = Normal ABN = Abnormal

* = Chronic heart disease $^{+}$ = Died

**Results:**
Nineteen patients (15 female, 4 male; age 18-71 years) had a SAH and 5 (2 female, 3 male; age 40-63) had not bled but had a local mass effect from the aneurysm.
Two patients with abnormal ECHO had a history of heart disease. Both SAH patients with EKG and ECHO changes but no previous heart disease died from complications of the SAH while there were no deaths among the patients without ECHO abnormalities($P< 0.05$). These two patients with abnormal ECHO had only minor EKG changes (T wave flattening and sinus tachycardia) while those patients with the most prominent T wave changes had normal ECHO studies. However no patient had an ECHO abnormality without any, albeit minor, EKG change. None of the EKG changes were associated with abnormal electrolytes and no patient suffered a myocardial infarction.
Seven patients with no previous history of hypertension were found on admission to have elevated blood pressure. Both patients with EKG and ECHO abnormalities developed severe hypertension ( > 200/100 mmHg ).

**Conclusion:**
From this ongoing study and previous publications, we conclude that (1) myocardial dysfunction is related to a worse neurological grade (2) an abnormal EKG is not an accurate predictor of myocardial dysfunction. (3) more extensive cardiac monitoring is indicated in neurologically sicker patients.

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# DOES INHIBITION OF $K^+$ TRANSPORT IN GLIAL CELLS BY LOCAL ANAESTHETICS CONTRIBUTE TO SEIZURES?

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**INTRODUCTION:** One of the most important toxic effects of local anaesthetics is convulsions, secondary to high serum concentrations of local anaesthetics.[1] Traditionally, this adverse effect has been attributed to suppression of inhibitory cortical pathways.[2]

It has recently been shown that several anticonvulsant drugs exert effects on astrocytes.[3] One important process of astrocytes is regulation of the extracellular K+ concentration in the brain, at least partly by a channel mediated redistribution of extracellular K+.[4] Since the extracellular K+ concentration has a major effect on neuronal output this mechanism is probably of importance in seizure formation. In the present work we have studied the effects of three commonly used local anaesthetics, lidocaine, procaine and tetracaine on unidirectional (mainly channel mediated) $K^+$ uptake by primary cultures of murine cerebral cortical astrocytes.

**METHODS:** Primary cultures of astrocytes were prepared from the neopallium of the cerebral hemispheres of newborn Swiss mice (0-24 hr old) and grown in a slightly modified Dulbecco's tissue culture medium with horse serum. After two weeks, the cultures reached confluency and were then grown for at least one week in the additional presence of 0.25 mM dibutyryl cyclic AMP, which induces a morphological and functional differentiation. Analysis of such cultures has shown that 95% of the cells obtain an unquestionable astrocytic morphology and stain for astrocytic markers, such as glial fibrillary acidic protein and glutamine synthetase. Furthermore these cultures contain no neurons and less than 1% macrophages. Uptake rates for $K^+$ were measured as previously described[3] incubation of intact cultures in tissue culture medium containing radioactively labelled potassium ($^{42}K$) and determination of accumulated radioactivity. They were expressed per mg protein as determined by the Lowry technique. Owing to a rapid $K^+$ exchange uptake of $^{42}K$ is rectilinear for only a very short period. $^{42}K$ uptake was therefore calculated during the initial 10 seconds of exposure to $^{42}K$.

**RESULTS AND DISCUSSION:** In the absence of any drug, $K^+$ uptake was calculated to be 2093 ± 116 (n=14) nmol/min per mg protein. Each of the local anaesthetics was able to reduce the initial uptake rate as shown in Fig. 1. The potency of the three drugs differed, with tetracaine being the most potent ($IC_{50}$ 0.41 mM), procaine the least potent ($IC_{50}$ 20.5 mM) and lidocaine ($IC_{50}$ 3.4 mM) intermediate.

Computer analysis of these results demonstrated that the difference in $IC_{50}$ values are highly significant. The "Hill coefficients" (slope factors) were not significantly different from 1, suggesting that only one binding site is involved and that no cooperativity exists between individual drug molecules.[5]

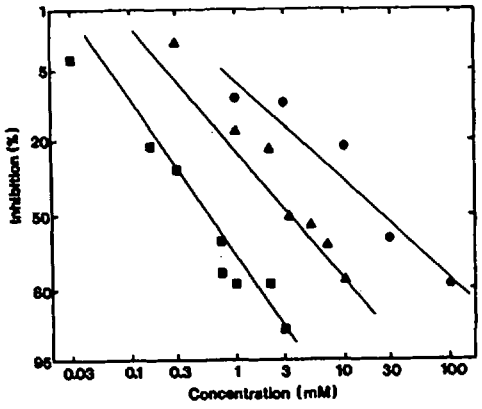


Fig. 1. Log-probit analysis of inhibition of channel mediated $K^+$ uptake into mouse astrocytes in primary cultures by tetracaine (■), lidocaine (▲), or procaine (●). The fully drawn lines were obtained by weighted computer analyses of all the individual values and therefore may not appear to be the best fit.

Inhibition of channel mediated $K^+$ uptake by local anaesthetics has not previously been described in astrocytes, but it is well known that several local anaestetics inhibit $K^+$ channels in nerve fibres. Our results suggest similarities of $K^+$ channels in the two cell types, but it is unknown which specific $K^+$ channel is affected. Further work will elucidate the possible significance of this effect to local anesthetic toxicity.

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## MIDAZOLAM POTENTLY AFFECTS FREE CALCIUM CONCENTRATION IN ASTROCYTES

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Introduction:

The benzodiazepine midazolam is used in anaesthesia as an adjunct together with, e.g., opiates, primarily on account of its amnestic properties. Like many other clinically used benzodiazepines, midazolam binds with high affinity not only to neurons, but also to astrocytes (1). Evidence has previously been obtained that the astrocytic benzodiazepine binding site, but probably not the neuronal benzodiazepine binding site, interacts with a calcium channel (2). Astrocytes in primary cultures display voltage-sensitive calcium channels and a potassium induced uptake of calcium, which is inhibited by dihydropyridine antagonists of the voltage-sensitive L-channel for calcium (3).

It has repeatedly been shown in many different cell types that the concentration of free intracellular calcium (0.1 μM) serves as an essential intracellular messenger. This concentration is 10,000 times lower than the extracellular calcium concentration (1 mM). The steep gradient across the cell membrane is maintained by control of calcium entry through channels (including the L-channel and transmitter operated channels), active carrier-mediated transport of calcium out of the cell and sequestration of calcium in the cell interior by binding to or release from intracellular organelles. Release of calcium from the intracellular calcium-binding organelles can be achieved by transmitter stimulation.

Methods

In the present work we have investigated the effect on the free intracellular concentration of calcium (measured by the aid of the fluorescent dye ENDO-2 (4) in primary cultures of mouse astrocytes. Such cultures constitute a reliable model for their counterparts in the mature brain. Individual cultures were continuously superfused with a physiological, saline medium with glucose. At selected periods during the superfusion the potassium concentration was increased from 5.4 to 20 mM. The drugs midazolam and/or the astrocyte-specific benzodiazepine antagonist PK 11195 were added either alone or together with the elevated potassium concentration.

Results

A typical result is illustrated in Fig. 1 which shows the free intracellular calcium concentration in arbitrary units. Exposure to the increased potassium concentration is indicated by $K^+$, to midazolam by Mid and to PK 11195 by PK. It can be seen that the free intracellular calcium concentration is increased by an elevation of the potassium concentration and that a low concentration of midazolam (0.01 μM) greatly enhances the potassium effect. When given alone, midazolam had no effect (results not presented). Addition of PK 11195 (1 μM) had a large inhibitory effect both on the midazolam/$K^+$ stimulated increase in calcium concentration and on the increase evoked by excess potassium alone. The effects of PK 11195 were reversible since re-exposure to a control medium for a couple of minutes lead to the return to a normal (or almost normal) response to elevated potassium concentrations both with and without midazolam.

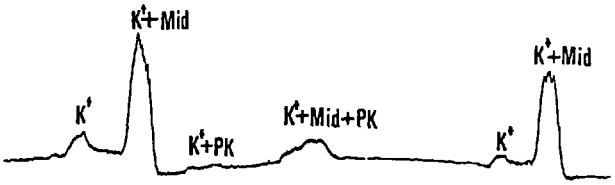


Fig. 1

The alterations in intracellular calcium concentration described above do not necessarily indicate that midazolam enhances channel mediated influx of calcium. It can not be excluded that at least part of the effect could result from a release of calcium from intracellular organelles. A large transmitter-mediated increase in free calcium concentration has been observed in astrocytes (5). However, at least some of the calcium ions contributing to the elevation of the calcium concentration must have entered the cells through L-channels, since the dihydropyridine nimodipine abolished the response. On the other hand, exposure to 20 mM potassium plus midazolam caused an increase in the intracellular free concentration of calcium even during superfusion in a calcium free medium, which furthermore contained EGTA to bind traces of calcium which might still be present.

Discussion

The calcium signal is involved in regulation of many cellular properties. In astrocytes, one of these appears to be the closing of calcium- sensitive potassium channels. It is likely (but has not yet been determined) that the high potassium conductance in astrocytes might be severely decreased by midazolam in combination with an elevated potassium concentration (resulting from neuronal function) or by midazolam in combination with an elevated potassium concentration and simultaneous or previous exposure to a transmitter. This would, in turn, affect the extracellular potassium concentration and thus neuronal output. Such an effect could contribute to amnesia. The midazolam effect on free intracellular calcium in astrocytes is very potent (the effects described in the Fig. was obtained with 0.01 μM). This is less than the plasma concentration of midazolam during anaesthesia. However, benzodiazepines, including midazolam, are protein-bound so that only a minor part of the total plasma concentration is free. It is, therefore, likely that some of the effects by midazolam as an amnestic adjunct are exerted on astrocytes.

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# *IN VIVO* CATECHOL ACTIVITY IN THE LOCUS COERULEUS FOLLOWING NOCICEPTION, NALOXONE, AND YOHIMBINE

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## Introduction

The nucleus locus coeruleus (LC), a major noradrenergic brain centre rich in opioid receptors[1], is thought to participate in the response to environmental stressors and the processing of spinal reflexes following nociceptive stimuli[2]. While it is generally accepted that antinociception is partly dependent upon noradrenergic relays in the brainstem[3], the role of the LC in antinociception is not clearly defined. Little is known about the conditions that influence LC activity, but it may involve activation of endogenous opioid systems. LC activity can be reliably measured by monitoring catechol metabolism using *in vivo* voltammetry[4]. The objective was to examine, using *in vivo* voltammetry, the effects of nociceptive stimuli (chemical and mechanical), naloxone (opioid receptor antagonist), and yohimbine (alpha$_2$ adrenoceptor antagonist) on LC activity.

## Methods

Rats (350-400 g, male), anaesthetized under halothane (1.0%) and vecuronium (50 µg/kg), were stereotaxically implanted with carbon fibre microelectrodes in the LC. Using differential normal pulse voltammetry (DNPV), catechol oxidation current (CA•OC, % baseline) was used as a measure of LC catechol neuronal activity. Blood pressure was continuously monitored via a femoral arterial catheter. Groups of animals (n = 4 each) were treated as follows: (1A) cotton swabbing of the hindpaw for 60 s; (1B) 100 µl formalin (5%) injected in the hindpaw; (1C) tailclamp for 30 min; (2A) naloxone (1 mg/kg iv); or (2B) yohimbine (0.5 mg/kg iv). Significance was assessed at $p < 0.05$, ANOVA.

## Results

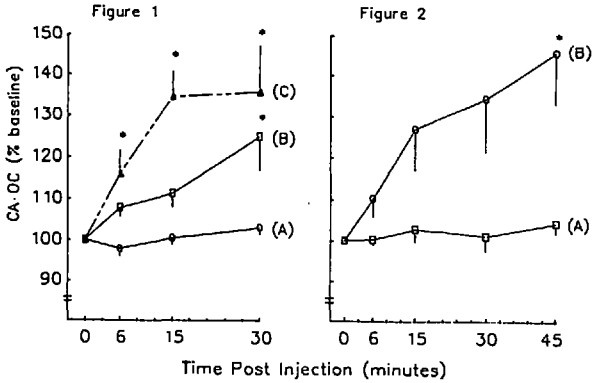


FIG 1. Change in CA·OC (% baseline) following different stimuli: (A) cotton swab, (B) formalin, (C) tailclamp. Mean ± S.E., * $p < 0.05$ compared to control.

FIG 2. Change in CA·OC (% baseline) following different treatments: (A) naloxone, (B) yohimbine. Mean ± S.E., * $p < 0.05$ compared to pretreatment.

Swabbing of the hindpaw for 60 s produced no significant change in CA•OC (Fig. 1A), while formalin produced a significant increase in CA•OC 30 min post injection (Fig. 1B) and the tailclamp significantly increased CA•OC 15 min after clamping (peak 30 min, 135.8 ± 11.3% baseline) (Fig. 1C). Systemic naloxone (1 mg/kg) failed to change CA•OC (Fig. 2A), while yohimbine (0.5 mg/kg) significantly increased CA•OC 45 min post injection (145.63 ± 12.5% baseline) (Fig. 2B). The tailclamp increased blood pressure (BP), while yohimbine decreased BP immediately following treatment (1 min). The BP quickly returned to resting BP levels and did not correlate with changes in CA•OC.

## Discussion

These data show that exposure to chemical and mechanical nociceptive (formalin and tailclamp) but not to non-nociceptive (cotton swab) stimuli produce increases in catechol oxidation current indicative of increased LC neuronal activity. The delay in the change in CA•OC following formalin suggests that a temporal relationship exists between the onset and duration of the nociceptive stimulus and the activation of LC neurons. Further studies are necessary to examine this relationship. Despite the presence of opioid receptors in the LC, naloxone failed to alter CA•OC. This finding suggests that the LC is not under tonic opioid influence. The dose of naloxone (1.0 mg/kg) used in this study exceeds that shown to block morphine-induced inhibition of LC discharge[5]. Consistent with the existence of an auto feedback mechanism of noradrenergic neurons[6], yohimbine increased CA•OC. The lack of a temporal correlate between the drop in blood pressure and the increase in CA•OC suggests that the yohimbine-induced effect involves blockade of central alpha$_2$ adrenoceptors and that the maintenance of blood pressure does not depend upon activation of LC noradrenergic neurons. The present study clearly demonstrates that activation of LC noradrenergic neurons occurs following exposure to nociceptive stimuli and an alpha$_2$ adrenoceptor antagonist. There does not appear to be a tonic opioid influence on LC noradrenergic neurons, but opioids may be important modulators during a nociceptive response.

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# CEREBRAL BLOOD FLOW VELOCITY FOLLOWING TOURNIQUET RELEASE IN HUMANS

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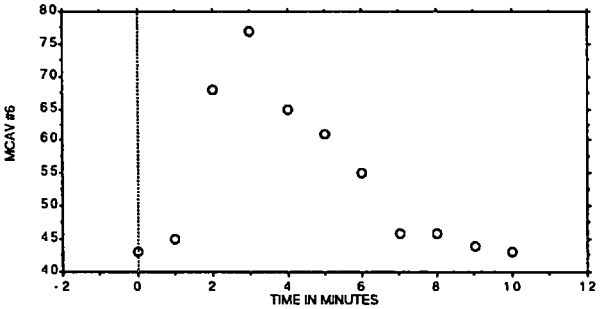
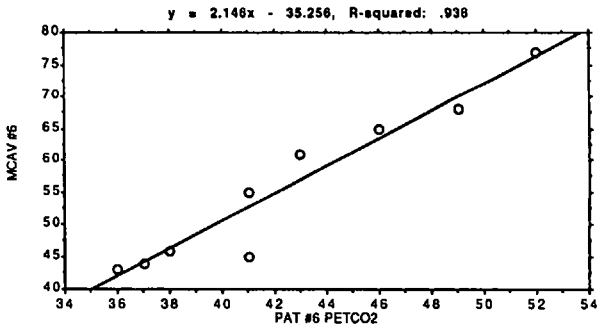
**Introduction**: Pneumatic tourniquets are used routinely to create a bloodless surgical field during surgery on the extremities. The advantages are gained, however, at the expense of tissue hypoxia from tourniquet ischemia. Subsequent deflation of the tourniquet results in release of lactic acid, potassium, a decrease in arterial pH and an increase in $P_aCO_2$.[1] While these metabolic and respiratory changes have been well documented[2], the change in cerebral blood flow (CBF) following tourniquet release has not been studied. The purpose of this study is to examine the change in CBF by measuring middle cerebral artery velocity (MCAV) following tourniquet release using transcranial ultrasonography(TCD) which allows noninvasive and continuous measurements.

**Methods**: With the approval of the Institutional Human Subjects Review Committee we studied 9 healthy patients, free of neurological disease, undergoing general anesthesia for orthopedic procedures in the lower extremity necessitating the use of tourniquets. Anesthesia was induced in a standard fashion using fentanyl, thiopental and vecuronium in appropriate doses. During stable anesthesia maintained with a continuous infusion of fentanyl (2-3µg/kg/hr) , nitrous oxide(50% inspired) and isoflurane (0.5%-0.8% inspired), and prior to the release of the tourniquet, the transcranial doppler probe was placed over the left temporal window to locate the left middle cerebral artery. Subsequently, the probe was anchored in this position using a head harness so that the angle of insonation, as well as the position of the probe, remained constant throughout the study periods. Measurement of MCAV, end-tidal CO2($P_{ET}CO_2$), systemic blood pressure, and heart rate were recorded just before release of tourniquet and then at 1 minute intervals for 10 minutes following deflation of the tourniquet. One subject was studied twice during the same anesthetic, 90 minutes apart, due to the use of bilateral tourniquets consecutively. Because of the difference in tourniquet time, they were treated as separate data. Changes in MCAV with $P_{ET}CO_2$ were assessed with linear regression analysis and a $p<0.05$ was considered significant.

**Results**: The mean age of the 9 subjects was 40±9(SD), and the weight was 71±15(SD). The tourniquet was always inflated to 300 mmHg, and the ischemic time ranged from to 60 to 121 min with a mean of 93±27(SD). As expected, there was a rapid rise in PETCO2 accompanied by a corresponding increase in MCAV. Both peaked at between 2-4 min. but not always coincide, returning towards control values by 8-10 minutes. A transient decrease in BP was noted in all patients between 1-3 minutes. A typical response is shown in Fig 1. Linear regression analysis of MCAV and $P_{ET}CO_2$ yielded a highly significant correlation (R value between 0.7 and 0.95) between the two variables in all patients except one who had a flat $CO_2$ response. Expressing the slope as a percentage of MCAV at $P_{ET}CO_2$ of 40 mmHg yielded a value of 3.14±0.5% per mmHg change in $P_{ET}CO_2$. Plotting this slope against the tourniquet time yielde
sugge
to the ischemic time.




**Discussion**: Our results confirmed that the metabolic changes following tourniquet release is accompanied by corresponding changes in MCAV. Although the absolute CBF cannot be derived from the MCAV, previous investigations have demonstrated that CBF corresponds closely with MCAV within any given individual, and that the $CO_2$ reactivity measured by TCD closely parallels CBF measurements[3]. Although these changes are transient and of no consequence in otherwise healthy patients, the sudden rise in CBF following tourniquet release is potentially detrimental in neurologically impaired patients with increased intracranial pressure. Although the increase in $CO_2$ is clearly the major factor, the fact that the reactivity , as expressed in % change per mmHG rise in $P_{ET}CO_2$, varies inversely with tourniquet time suggests that other factors may also be involved. Further investigation, including the efficacy of prior hyperventilation to prevent the rise in CBF, are indicated.

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# NARCOTIC INFUSIONS FACILITATE EMERGENCE FOLLOWING NEUROSURGERY: A DOUBLE BLIND COMPARISON OF FENTANYL AND ALFENTANIL INFUSIONS

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**Introduction:** At emergence following neurosurgery, the neurosurgeon desires hemodynamic stability, no bucking on the endotracheal tube (ETT), an aware and oriented patient and a normal or low $PaCO_2$. Narcotics may provide a smoother emergence, with less response to the endotracheal tube, decreased requirement for vasoactive agents, and a more rapid emergence due to volatile agent sparing. Negative consequences of narcotic administration are respiratory depression, miotic pupils and delayed emergence if there is a narcotic overdose. To permit a prompt emergence associated with narcotic administration steady state plasma concentrations should not exceed threshold concentrations i.e. that concentration associated with adequate minute ventilation (1-2 ng/ml for fentanyl and 100-200 ng/ml for alfentanil)[1]. In this study we compared our standard fentanyl-based infusion protocol (Group F; n=8) with 3 different concentrations of alfentanil (low dose alfentanil where the steady state concentration of alfentanil was less that the threshold concentration, approximately 60 ng/ml (Group L; n=8), mid dose where the alfentanil concentration was at the lower end of the threshold concentration 120 ng/ml (Group M; n=8) and high dose alfentanil where the alfentanil concentration was at the higher end of the threshold concentration 180 ng/ml (Group H; n=7)) to determine if narcotic infusions facilitated emergence following neurosurgery, as assessed by emergence times, requirement for vasoactive agents, and acceptable extubation $PaCO_2$.

**Methods:** Thirty-one patients undergoing supratentorial craniotomy for brain tumour were studied. Exclusion criteria included evidence of expressive or receptive aphasia, untreated hypertension, age $\geq$ 70 years or $\leq$ 18 years and weight $\geq$ 100 kg. The evening prior to surgery, blood pressure was determined times three. The average of these values served as the baseline mean arterial pressure (MAP) to determine treatment of hypertension during that study. Patients were unpremedicated. Upon arrival in the operating room, under local anesthesia, a large bore intravenous cannula and radial arterial cannula were placed. After baseline hemodynamic measurements the patients were induced with 4 mg/kg of thiopental and vecuronium 0.15 mg/kg. Ventilation was assisted manually prior to intubation. Following adequate muscle relaxation a bolus infusion of one of either fentanyl (Group F; 8.3 $\mu$g/kg) or three concentrations of alfentanil (Group L; 35.1 $\mu$g/kg: Group M; 70.2 $\mu$g/kg: and Group H; 105.3 $\mu$g/kg) was administered over 2 minutes from a 30 cc syringe. Following intubation a continuous infusion of narcotic was started at kg/10/hr by infusion pump (Group F; 1.56 $\mu$g/kg/hr: Group L; 16.2 $\mu$g/kg/hr: Group M; 32.4 $\mu$g/kg/hr: Group H; 48.6 $\mu$g/kg/hr). Maintenance anesthesia comprised isoflurane/$N_2O$/$O_2$ (50/50). Vecuronium or metubine/pancuronium 4:1 mixture was administered to maintain one muscle twitch by train-of-four monitoring. The isoflurane concentration was varied to maintain MAP at ward MAP $\pm$ 20%. Continuous end-tidal $CO_2$ and isoflurane were recorded throughout the procedure. Isoflurane was discontinued with closure of the dura (iso off). Mean arterial pressure + 20% above ward MAP was treated with 0.15 mg/kg boluses of labetalol to a total dose of 1.5 mg/kg. If not effective then 0.5-1.0 mg/kg boluses of diazoxide were administered. If hypertension persisted SNP was started, the dose titrated to control MAP. The narcotic infusion was continued until closure of the galea. Following application of the scalp bandage the muscle relaxants were reversed and the $N_2O$ discontinued. Extubation occurred with adequate minute ventilation and eye opening. Arterial blood gases were drawn 2 and 5 and 30 minutes post-extubation. Narcotic reversal by naloxone administration was done if adequate minute ventilation was not evident 10 minutes after reversal of the muscle relaxants. Statistical methods included repeated measures ANOVA for hemodynamic comparisons, ANOVA for comparison of emergence times, Chi square for comparison of requirement for vasoactive agents.

**Results:** No differences between groups were seen for patient age, weight, ward HR and MAP. No differences were seen between groups for hemodynamic measurements at control, 1-minute post induction, 1-minute post intubation, skull tongs on, isoflurane on, isoflurane off, skull tongs off, $N_2O$ off, 2 and 5-minute post extubation, admission to the recovery room. These results indicate that the anesthetist intervened appropriately to maintain MAP within the range desired in the study. Emergence $PaCO_2$ and times are shown in Table 1. Emergence time was determined as the difference from eye opening to $N_2O$ off. A significantly longer time until the patient could follow commands (request for hand grasp) was seen in Group L. The explanation for this seeming paradoxical response may be explained by examination of Table 1. This group required significantly higher concentrations of isoflurane to maintain MAP within range. End-tidal isoflurane was significantly higher at closure of dura (iso off) and with $N_2O$ off. Requirement for vasodilator therapy was 8/8 in Group L, 7/8 in Group M, 6/8 in Group F and 3/7 in Group H. Chi-square for this 2 x 4 contingency table was 7.61 (statistically significant results for a P-value $\leq$ 0.05 would require the Chi-square to be 7.81). No patient required SNP for control of elevated MAP. No intergroup difference was seen for naloxone requirements.

**Discussion:** Narcotics infused to provide an expected plasma concentration at the threshold level facilitate emergence from neurosurgery as evidenced by a slower emergence time until the patient could follow commands in Group L (low dose alfentanil) which probably relates to the isoflurane sparing effect of narcotics. In group H (high dose alfentanil) a trend to less vasodilator therapy was seen.

**Table 1:**

| | | Group F | Group L | Group M | Group H |
|---|---|---|---|---|---|
| $PaCO_2$(mmHg) | 2 min | 40.3±1.5 | 43.6±2.7 | 42.8±2.3 | 46.3±2.2 |
| | 5 min | 42.1±3.7 | 41.3±1.9 | 40.9±1.5 | 45.0±2.6 |
| | 30 min | 39.9±1.7 | 37.4±1.9 | 39.3±1.2 | 39.6±1.3 |
| Emergence times (min) | | | | | |
| Eyes open | | 2.3±1.0 | 5.1±0.9 | 4.5±0.9 | 2.9±0.7 |
| ETT out | | 3.6±0.8 | 6.3±0.9 | 6.1±1.2 | 4.1±0.4 |
| Follows Commands | | 4.0±0.8 | 8.6±1.4# | 6.3±0.8 | 4.0±1.0 |
| End tidal iso (v/v%) | | | | | |
| iso off | | .33±.11 | .64±.11* | .28±.05 | .28±.09 |
| $N_2O$ off | | .06±.04 | .14±.03* | .06±.02 | .07±.02 |

# P $\leq$ 0.05 vs Group F and H
* P $\leq$ 0.05 vs other groups

**Reference:**
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## Catecholamine Level and Plasma Renin Activity During Induced Hypotension - Adenosine vs Sodium Nitroprusside

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**Introduction**: Complications from the stress response to induced hypotension include reflex tachycardia and rebound hypertension. However, these responses are agent specific and significant differences have been demonstrated between sodium nitroprusside(SNP)- and isoflurane-induced hypotension.[1] Adenosine(ADO) is a potent systemic vasodilator and has been used as a hypotensive agent in clinical settings.[2] The theoretical advantages include maintenance of cardiac output and reduction of systemic oxygen consumption. Its effects on the stress response, however, have not been clearly defined. The purpose of this study is to compare the stress response during ADO-induced hypotension to SNP-induced hypotension.

**Methods**: The study was approved by the Institutional Human Subjects Review Committee. Using an open-label, randomized design, we administer either ADO or SNP to twenty patients undergoing cerebral aneurysm surgery to achieve hypotension during cerebral aneurysm clipping. Anesthesia was induced in a standardized manner with thiopental 3-5 mg/kg, fentanyl 2-3 µg/kg, vecuronium 1 mg/kg, and lidocaine 1mg/kg. Following tracheal intubation anesthesia was maintained with nitrous oxide/oxygen (50%) and isoflurane 0.5-1.0%, and mechanial ventilation was adjusted to achieve an end-tidal $CO_2$ of 30-35 mmHg. Monitors include direct arterial BP, pulmonary artery catheter, end-tidal capnometry and pulse oximetry. Lasix (20 mg) and 20% Mannitol (500 ml ) was given to every subject intraoperatively, at least 90 minutes prior to induction of hypotension. Intravenous fluid therapy consisted of plasmalyte adminstered at 3-4mlkg/hour and blood was given when the hematocrit fell below 30. When hypotension was required, ADO infusion (5.3 mg/ml, supplied by Astra Pharmaceuticals) or SNP (0.01% solution) was commenced. ADO was started at a rate of 20 µg/kg/min and increased in 20 µg/kg/min increments every 30 seconds and SNP was started at a rate of 1 µg/kg/min and incremented by 1µgkg/min every minute until the desired level of BP between 50 and 55 mmHg is achieved. Blood samples were drawn for determination of serum epinephrine(EPI), norepinephrine(NOREPI) and plasma renin activity(PRA) using HPLC immediately prior to hypotension, during stable hypotension and 30 minutes following return of normotension. Anesthesia was maintained as nearly constant as possible during the sampling periods. Two-way ANOVA and unpaired t-test were used for statistical analysis and a $p<0.05$ was considered significant.

**Results**: Blood samples were obtained in 7 ADO patients and 8 SNP patients. The target mean BP (MAP) achieved was similar in both groups, as was the duration of hypotension and amount of IV fluid given. No blood was administered to any patient. Table 1 summarizes the age and BP changes in the two groups. Control catecholamine levels and PRA prior to induced hypotension were similar in both groups. During induced hypotension, EPI and NOREPI levels rose in both groups, but the increase of NOREPI in SNP group was significantly higher than that in the ADO group. PRA rose significantly during SNP infusion and remained elevated in the posthypotensive period, whereas no increase was evident during ADO-induced hypotension. No reflex tachycardia was seen in either group but, BP was significantly higher in the SNP group after distinuation of the infusions. (Table II)

**Discussion**: Consistent with previous observations, SNP-induced hypotension is associated with significant increases in catecholamines and PRA. In contrast, adenosine-induced hypotension was only associated with a small increase in EPI and no increase in PRA. We conclude that the stress response is attenuated during A-induced hypotension and would be a preferred agent if obtundation of the stress response is considered important.

Table I

| | SNP(n=8) | ADO(n=7) |
|---|---|---|
| AGE (mean± SD) | 52 ± 14 | 48 ± 12 |
| MAP BEFORE (mmHg±SEM) HYPOTENSION | 80 ± 3 | 82 ± 3 |
| MAP DURING HYPOTENSION | 54 ± 2 | 50 ± 2 |
| MAP AFTER HYPOTENSION | 93 ± 4* | 81 ± 3 |

Table II

| | | SNP (mean ±sem) | ADO (mean ±sem) |
|---|---|---|---|
| EPI (pg/ml) | Before Hypotension | 295 ± 27 | 403 ± 59 |
| | During Hypotension | 614 ± 152 | 480 ± 101 |
| | After Hypotension | 353 ± 64 | 342 ± 68# |
| NOREPI (pg/ml) | Before Hypotension | 363 ± 56 | 328 ± 37 |
| | During Hypotension | 981 ± 203* | 598 ± 95 |
| | After Hypotension | 339 ± 46 | 378 ± 61 |
| PRA (ng%/3hr) | Before Hypotension | 532 ± 105 | 432 ± 117 |
| | During Hypotension | 1164 ± 183* | 394 ± 112 |
| | After Hypotension | 815 ± 187* | 358 ± 98 |

* $p \leq 0.05$ # n=6 because of contamination of 1 sample

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# CEREBRAL OXYGEN CONSUMPTION DURING SUFENTANIL ANESTHESIA: MEASUREMENT BY $N_2O$ UPTAKE VS $^{133}$ XENON CLEARANCE

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Introduction: The use of xenon clearance techniques has allowed the measurement of intraoperative cerebral blood flow (CBF)[1,2] and, in combination with sampling of cerebral jugular venous blood, has been used for determination of concomitant cerebral metabolic rate for oxygen ($CMRO_2$).[1,3] Because cerebral jugular venous blood is representative of the whole brain, while CBF via $^{133}$Xe clearance is cortically-weighted, this study was undertaken to assess the accuracy of the resultant $CMRO_2$ relative to that derived from the classical jugular venous sampling technique derived by Kety and Schmidt.

Methods: After obtaining institutional approval and written informed consent, 11 patients undergoing elective cardiac surgery were anesthetized with $O_2$-sufentanil without use of other inhalational agents. Prior to induction of anesthesia a 15cm 16 Fr catheter was inserted retrogradely into the jugular bulb as heralded by a complaint of transient discomfort in the ipsilateral ear.[1] Xenon CBF measurements were made after sternotomy by IV injection of 5-10 mCi of $^{133}$Xe in 5 ml NS using a 10 channel cerebrograph (Novo Diagnostics®) with compensation for changes in temperature and hematocrit and end-tidal respiratory gas sampling to correct for re-circulation. The resulting clearance curves were analyzed by noncompartmental height-over-area analysis and mean CBF calculated as the average of the regional CBF from all 10 detectors. Simultaneous with the injection of $^{133}$Xe, 10% $N_2O$ was added to the inspired gas and paired arterial and jugular venous blood samples withdrawn anaerobically every 1 min for 5 min and then every 2 min for 15 min. Samples were injected into a recirculating chamber and $N_2O$ content analyzed using a Vital Signs "Trace Test" infra-red $N_2O$ monitor.[3] The mean cerebral arterio-venous $N_2O$ concentration difference was obtained as the area between the arterial and venous curves and CBF calculated according to the equation of Kety and Schmidt.[3] $CMRO_2$ was calculated as the arterial and cerebral venous $O_2$ content difference. To assess the relationship between CBF and $CMRO_2$ measured by $N_2O$ uptake vs $^{133}$Xe clearance, Student's T-test and linear regression analysis using the method of least squares was used.

Results: Of the 11 patients enrolled, 2 were excluded from analysis because of elevated background counts or a poor air curve rendering $^{133}$Xe clearance uninterpretable. A third patient was excluded because the arterio-venous $N_2O$ curves had not converged at 20 min. Mean CBF via $N_2O$ uptake was 29 ± 8 ml.100g$^{-1}$.min$^{-1}$ and $CMRO_2$ was 1.97 ± 0.5 ml.100g$^{-1}$.min$^{-1}$ while $^{133}$Xe clearance CBF was 32 ± 8 ml. 100g$^{-1}$.min$^{-1}$ and $CMRO_2$ was 2.12 ± 0.4 ml. 100g$^{-1}$.min$^{-1}$ (N.S.). Correlation coefficient for regression of $CMRO_2$ via $N_2O$ uptake against $CMRO_2$ via $^{133}$Xe clearance was 0.824 ($p < 0.01$).

Discussion: CBF and $CMRO_2$ measured by $^{133}$Xe clearance were about 10% higher than simultaneous measurements using a modified Kety-Schmidt technique, presumably reflecting greater cortical weighting with the $^{133}$Xe method. Importantly, directional changes were similar with the two techniques.

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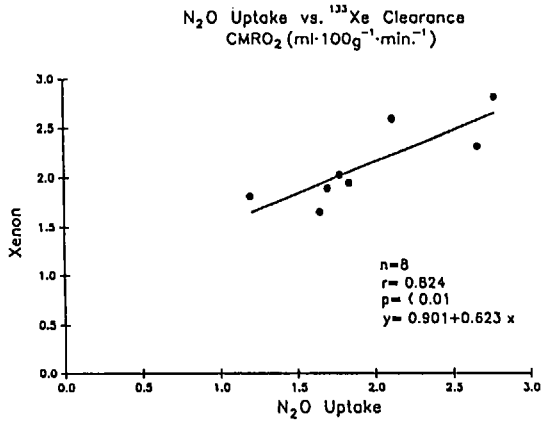

# CRANIAL DUPLEX SONOGRAPHY: DOES ISOFLURANE AFFECT THE CEREBROVASCULAR RESPONSE TO CARBON DIOXIDE IN ANAESTHETIZED CHILDREN?

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**INTRODUCTION:** It has been stated that isoflurane (I) is the inhalational agent of choice in neuroanesthesia because of its lesser cerebral vasodilatory properities as compared to halothane (H).[1] Although this statement has been supported by several adult studies, regional cerebral blood flow (CBF) investigations have shown an increase in CBF with stepwise increases in I concentrations.[2] In practice one uses hyperventilation to contravene this increase in CBF during procedures with raised intracranial pressure (ICP). Studies in adult and pediatric patients have demonstrated that the $PaCO_2$ directly affects the caliber of the resistance vessels in the cerebral vasculature and therefore CBF.[3] Alone, $PaCO_2$ causes a linear increase in CBF between 20-60 mmHg.[4,5] No studies to date have compared the effects of both $CO_2$ and I in varying concentrations on the cerebral blood flow velocity (CBFV) in healthy anesthetized infants and children.

**METHODS:** With approval of this institutions Human Ethics Committee, 14 healthy infants and children for elective urological procedures were studied. All patients were ASA Physical Status I and II, fasting and unpremedicated. Anesthesia was induced with thiopentone 5mg/kg, fentanyl 2mcg/kg, and vecuronium 0.1 mg/kg. After the trachea was intubated, anesthesia was maintained with isoflurane, 75% Air in $O_2$ and vecuronium 0.05mg/kg. All patients received a continuous caudal or lumbar epidural block performed with 0.25% bupivacaine prior to incision. Ventilation was adjusted to achieve an end tidal $CO_2$ ($PE'CO_2$) of 20 mmHg. Fresh gas flows were maintained constant throughout the study to avoid any variation in intrathoracic pressure. Normothermia was maintained. $PE'CO_2$ was randomly equilibrated to 20, 40, or 60 mmHg with an exogenous source of $CO_2$. Patients were randomized to begin either at 0.5 MAC or 1.0 MAC I. A time interval of five minutes was allowed between $CO_2$ changes and fifteen minutes was allowed between [I] changes to achieve steady state. SAP, HR , $O_2$ saturation, end-tidal isoflurane, and inspired $O_2$ were recorded within the range of $PCO_2$ values investigated. Cerebral Blood Flow Velocity (CBFV) and resistance index (RI+) in the Middle Cerebral Artery (MCA) was measured through the temporal window with the TCD. CBFV, RI+, and $PE'CO_2$ were analyzed using logarithmic regression and $r^2$ value. Statistical significance ($p<0.05$) was determined with paired t-test, ANOVA and Tukey test tor multiple comparisons.

**RESULTS:** The age range was from 16 months to 7.5 years old. The mean (±S.D.) age and weight was 39.4 ±27.2 mo and 15.5±6.2 kg. The CBFV increased logarithmically as $PE'CO_2$ increased during both 0.5 MAC ($r^2$=0.99) and 1.0 MAC ($r^2$= 0.96 ) I. The RI+ showed an inverse logarithmic relationship with $PE'CO_2$ at 0.5 MAC ($r^2$= 0.98% ) and 1.0 MAC ($r^2$ =0.76) I (fig 1). However, there was no statistical difference between CBFV at 20, 40, or 60 mmHg when comparing 0.5 MAC and 1.0 MAC I concentration (p=0.12) (fig 2). HR, SAP, temp and $O_2$ saturation did not change significantly during the study.

**DISCUSSION:** We showed that I does not effect cerebrovascular carbon dioxide reactivity. Recently, it has been suggested that there is an intrinsic effect of I anesthesia to decrease $CO_2$ reactivity.[6] Our data indicates that $CO_2$ reactivity is maintained in spite of changes in I concentration. Therefore, we have demonstrated an absence of a dose-dependent relationship between I and CBFV while hyperventilation is used. Because the caliber of the basal cerebral vessels do not change in the pediatric population with changes in the $CO_2$ tensions, we can assume that the changes in CBFV are proportional to changes in CBF.[7] This data indicates that $CO_2$ reactivity under I anesthesia is maintained in spite of increasing $CO_2$ concentrations. Patients with raised intracranial pressure undergoing general anesthesia would benefit from the association of hyperventilation and isoflurane.

**ACKNOWLEDGMENTS:** We thank Medasonics Transpect TCD,Canada for providing the TCD.

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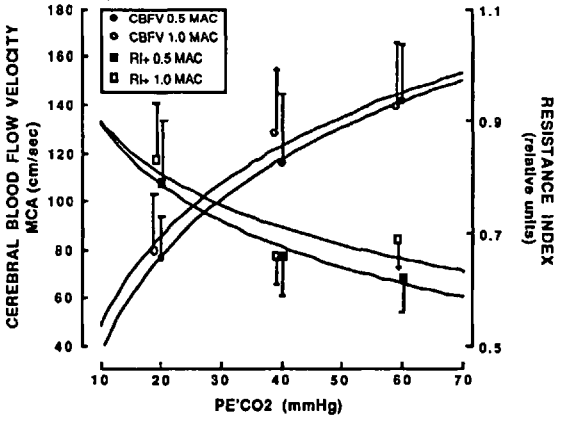


Figure 1

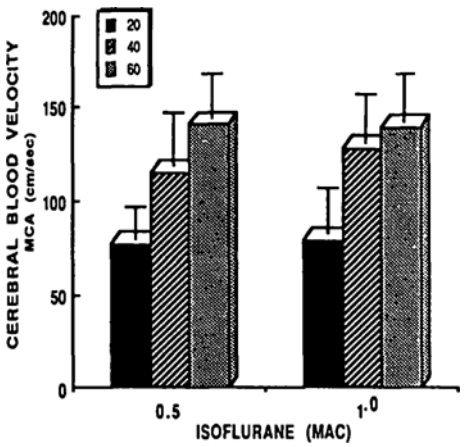


Figure 2

# "OFF THE WALL - JET" FOR TRANSTRACHEAL VENTILATION

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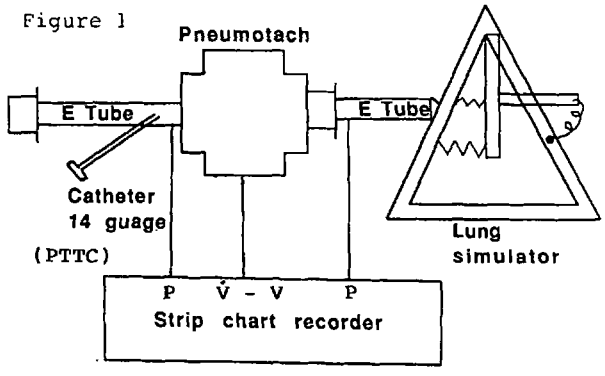
Introduction: Percutaneous transtracheal ventilation (PTTV) has been proposed as a potential lifesaving technique when conventional manoeuvres to establish an airway have failed.[1] Numerous techniques are described in the literature for connecting the tracheal catheter to a source of oxygen.[2,3,4] Most of the techniques described have used equipment available in the operating room, but not in the rest of the hospital. The purpose of this study was to examine the ability of two other techniques using equipment available in most areas of a medical establishment, to provide minute ventilation (rate x volume) in a test lung.

Methods: Two methods of PTTV were compared to a previously well described technique, the Flush Technique.[3,4] Methods tested were:
1. "Off the Wall - Jet". The tracheal catheter was connected to an oxygen flow regulator in the wall outlet via regular oxygen tubing and a 3 way stopcock. The oxygen was jetted into the PTTV by opening and closing the 3 way stopcock. Flows of oxygen used were 5, 10, 15 and 85 litres per minute (maximum flow).
2. Self-inflating bagging unit: The tracheal catheter was connected to a bagging unit via a 3 ml syringe barrel and a 7 mm ET tube connector.
The Flush Technique: The tracheal catheter was connected to the fresh gas outlet on the anaesthesia machine via a length of high pressure tubing and activated intermittently by depressing the oxygen flush button.
All three methods were tested using a mechanical upper airway lung model. The model consisted of a 9.5 endotracheal tube (ETT) with a PTTC (14 gauge) inserted through its side wall. The distal end of the ETT was connected to a pneumotachograph which in turn was connected to a bellows type of mechanical lung set at a compliance of 50 mls per cm of water.[Fig. 1] In line pressure measurements were carried out at the junction of the first ETT and the pneumotachograph. Flow, volume and pressure measurements were recorded using a strip chart recorder. All of the methods were tested with the ETT unobstructed. The "Off the Wall - Jet" method was also tested with the addition of a 2 1/2 mm internal diameter orifice (restricted exhalation).

Figure 1




Results: Utilizing the self-inflating bagging unit tidal volumes (VT) of 8 to 12 mls at a rate of 20 per minute were generated. User fatigue led to a decrease in rate very quickly. The Flush Technique generated VT of 300 to 500 mls per flush and rates of 80 flushes per minute were achieved without difficulty. The "Off the Wall - Jet" mode generated VT of 300 mls, 450 mls, 650 mls and 1,000 mls per jet at flows of 5, 10, 15 and 85 litres per minute respectively and rates of 70 to 80 jets per minute were achieved without difficulty. When expiration was restricted by the 2 1/2 mm orifice, VT generated was 250 mls, 700 mls and 850 mls using flows of 5, 10 and 15 litres per minute respectively, at a rate of 25 to 27 jets per minute. At faster rates a significant PEEP effect was obtained. At flows of 5 and 10 litres per minute, with expiratory resistance, inspiratory/expiratory (I:E) ratios were maintained at 1:3. However, at a flow of 15 litres per minute, in order to prevent a PEEP effect, an I:E ratio of 1:6 had to be used in order to be able to ventilate at a rate of 27 jets per minute.

Discussion: The data clearly demonstrates the ability to ventilate adequately using flows of 5, 10 and 15 litres per minute from a regular oxygen wall outlet. In the obstructed airway with resistance to expiration, VT could be maintained without PEEP by reducing the rate and at higher flows (15 litres per minute) by altering the I:E ratio (1:6). This technique is at least as good as, if not better than the "Flush Technique" for ventilation. The bagging mode was totally inadequate for ventilation via PTTC. This simple "Off the Wall - Jet" system may be used anywhere in the hospital for ventilation via a PTTC for a failed intubation.

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## ONSET OF SUBARACHNOID BUPIVACAINE IN CAESAREAN SECTION

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Introduction:
The proper composition of the test dose in epidural anaesthesia for the detection of inadvertent subarachnoid injection has been a point of controversy in the anaesthesia literature[1-3]. It should produce a rapid, easily detectable block both subjectively and objectively, and be predictable to prevent too high a block. In the past it has been suggested that lidocaine was superior in that it's onset was very rapid and that it produced a predictable block[4]. It has thus been adopted as the standard test dose in a number of institutions. Bupivacaine has been criticized for it's purported slow onset and unpredictable block[5-6], but the work done to support these ideas has been carried out in non-obstetric populations in poorly controlled studies. This is a study of the onset of intrathecal bupivacaine in Caesarean Section patients to demonstrate it's rapid onset and detectable block.

Methods:
This double blind, randomized, controlled trial involved measuring the onset of anaesthesia produced by bupivacaine either intrathecally (test group) or epidurally (control group) for elective Caesarean section. Fourteen ASA 1 or 2 patients undergoing elective Caesarean section with no contraindication to regional anaesthesia were studied. Seven spinal and seven epidural anaesthetics were randomly performed. The patients were monitored prior to the block with ECG, Pulse oximeter, blood pressure cuff and fetal heart monitor. Each patient received 1.5 ml of Lactated Ringer's solution to prevent hypotension associated with sympathetic blockade. 2.5cc of .5% isobaric bupivacaine was used in both forms of anaesthetic. Once the block was instilled, the patient was placed in the left lateral position with oxygen at 4 lpm. The subjective onset of sensory symptoms and the objective loss of pinprick and cold touch sensations were measured every minute by a blinded observer five minutes after the instillation of the block. Maternal blood pressure, heart rate and $SaO_2$ as well as fetal heart rate were also measured.

Results:
The mean time of subjective onset of sensory loss of paraesthesia in the spinal patients was 34+/- 2 sec. The control group (epidural) developed no subjective changes as well as no loss of pinprick or cold temperature sensation with this dose of bupivacaine. As well, all hemodynamic parameters remained unchanged. Figure 1 shows the onset of sensory loss from instillation of 12.5 mg of isobaric bupivacaine. As can be seen, pinprick and cold touch are lost between L1 and L5 after one minute. This progresses rapidly to T6 to S4 after three minutes and ultimately T5 at five minutes. The onset of anaesthesia was similar in all patients tested. There was little change in the systolic blood pressure over the first five minutes of the block, with values remaining above 100 mmHg and not requiring volume or inotropic support.

Discussion:
Abraham et al[4] displayed a sensory block at S2 within two minutes ascending ultimately to T6 after five minutes with lidocaine in a subarachnoid block. While bupivacaine has been criticized for a slower onset, our study has shown a rapid subjective and objective onset comparable to lidocaine. As well, the block peaked at T5 producing no discomfort to the patient. Both maternal and fetal parameters were stable requiring no intervention. Importantly, the control groups with 12.5 mg of bupivacaine in the epidural space, did not develop any subjective or objective symptoms. These results suggest that bupivacaine, which is used in epidural anaesthesia for labour, produces a rapid, predictable block when instilled intrathecally, making it acceptable for an epidural test dose.

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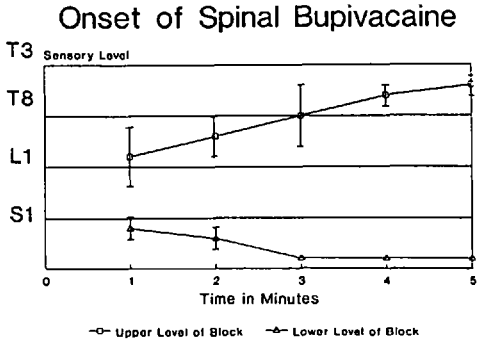
Figure 1



# THE USE OF NORMOSOL-R FOR DILUTION OF RED BLOOD CELL CONCENTRATES PRIOR TO TRANSFUSION

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Introduction:
ABO compatible plasma, 0.9% saline (NS) and 5% human albumin are the only solutions recommended for use by the Canadian Red Cross[1] and Canadian Association of Immunohematologists[2] for the dilution of packed red blood cells (PRBC). Ideal crystalloid solutions for the dilution of PRBC's must be free of calcium and glucose. Normosol-R (NR) is just such a solution, and although advocated for use[3], no studies have validated its safety and efficacy. We sought to compare the effect of dilution of PRBC with NR and NS.

Methods:
The study was conducted in 2 parts. In part 1 we assessed the in vitro stability of RBC's following equal volume dilution with NR and NS. The PRBC samples were pooled from volunteer group O donors. Separate samples were prepared from PRBC's stored for 7, 21 and 35 days. Undiluted PRBC served as controls. The effect of pre-incubation was assessed by sampling immediately following admixture and after 30 minutes incubation. The effect of temperature was assessed by studies at both 21° and 37°C. The in vitro assessment of hemolysis was performed by measurements of supernatant potassium ($K^+$) and free hemoglobin (Hb) following equal volume admixture with either NR or NS. In addition, an assessment of red blood cell (RBC) stability was performed by measuring osmotic fragility (OF) of the PRBC's following dilution with NR or NS. These studies were performed by routine methods.

Part 2 of the study involved an assessment of in vivo RBC survival following dilution with NR. Three healthy male volunteers donated one unit of PRBC stored in CPDA-1. After storage at 4°C for 14 days the blood was warmed to 37°C, an aliquot was labelled with $Cr^{51}$ and the blood diluted in equal volumes with NR at 37°C for 30 minutes. The PRBC's was then infused and RBC survival studies were performed by routine methods.

Results:
The control undiluted PRBC samples showed an increase in free Hb and $K^+$ with increasing storage date in vitro. This effect was increased slightly following incubation for 30 minutes at either room temperature or 37°C. Similar results were seen with both NS and NR with no statistically significant difference between these two groups.

OF increased in the control, NR and NS groups with increasing in vitro storage dates. An increase in OF was also noted in all 3 groups following incubation at both room temperature and 37°C. Importantly, no significant difference was noted in OF between NR and NS groups. Of interest, both NR and NS offered a slight protective effect as demonstrated by a decreased percent lysis of PRBC at all storage dates, compared with control samples. In vivo RBC survival studies for the 3 volunteers confirmed normal survival for PRBC's re-constituted with NR.

Discussion:
The dilution of PRBC can have significant advantages for the transfusionist. NS is the only crystalloid solution presently recommended for use, and in most clinical situations it is acceptable. However, there are settings in which the risk of electrolyte and acid-base disturbances, such as dilutional hyperchloremic acidosis, is appreciable. In these settings it would be desirable to have another crystalloid solution available. NR is an isosmolar, pH adjusted, balanced salt solution that contains no calcium or glucose, and is therefore a logical solution for re-constituting PRBC's.

This study compared the effects of NS and NR on PRBC following dilution at 21° and 37°C (with and without incubation). NS was used as the "gold standard". As previously documented, samples without diluent showed increasing concentrations of free Hb and $K^+$ with increasing storage dates[4]. Samples diluted either in NS or NR, whether incubated or unincubated, and at 21° and 37°C showed increasing values of free Hb and $K^+$. Importantly, there was no statistically significant difference between NS and NR. OF increased with increasing storage date and incubation but was the same for both NS and NR groups. Both NS and NR decreased OF compared with control samples, possibly due to a protective shrinkage effect of PRBC's in a hypo-osmolar solution.

Despite the lack of difference between NS and NR in vitro, it remained to be proven that PRBC's re-constituted with NR were not somehow altered, such that their in vivo survival would be compromised. The $Cr^{51}$ survival curves in our 3 healthy volunteers indicate that this is not the case; transfused cells had a half-life within normal limits.

In conclusion, our results indicate that PRBC's can be safely re-constituted with NR and there is no in vitro evidence of increased hemolysis using this solution. The in vivo survival studies confirmed this observation. We would recommend that NR be added to the list of safe solutions for re-constituting PRBC's and that it provdes an attractive alternative to NS, particularly in the massive transfusion setting.

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# EXPERIMENTAL AEROSOL DELIVERY BY METERED DOSE INHALER VIA PAEDIATRIC SIZE TRACHEAL TUBES

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## INTRODUCTION:

Selective beta$_2$-adrenergic drugs have been shown to attenuate histamine-induced bronchoconstriction during halothane anaesthesia in dogs.[1] Although the percent delivery efficiency (%DE) of beta$_2$-adrenergic drugs by metered dose inhaler (MDI) through tracheal tubes (ETT) > 6.0 mm internal diameter (ID) is low (between 3.0 and 30.0%),[2,3] the %DE in ETTs < 6.0 mm ID is undetermined. We investigated the %DE of salbutamol, a beta$_2$-adrenergic drug, through paediatric size ETTs with and without intraluminal catheters.

## METHODS:

The %DE of salbutamol by MDI was investigated using an in vitro model that consisted of an actuator swivel, 4 tracheal tubes (3.0, 4.0, 5.0 and 6.0 mm ID) 16 cm in length and 20 micron mesh filters after the methods of Kim et al[4] and Crogan et al.[2] A continuous flow of dry air at 30 L/min was used. In parallel experiments, 3 Deseret® catheters, 16, 19, and 22 SWG, each 16 cm in length were inserted through the actuator swivel and positioned with the distal end of the catheter at the tip of the ETT. The catheter hubs were shortened 4 mm in order to accomodate the actuator of the canister. To reduce the variability between experiments, 2 actuations from 3 different MDI canisters were used, i.e. 6 actuations per experiment. Each MDI canister was shaken before each actuation. The experiment was repeated 9 times for each tube size. Each component was dried between experiments. The %DE was calculated as the ratio of the increase in dry weight of the filter and the increase in dry weight of the entire apparatus.

To compare the efficiency of the 20 µm and 0.2 µm mesh filters to trap aerosol particles, two filters of the same pore size were placed in series and connected directly to the swivel actuator. The dry weight gain of the proximal filter was compared to that of the distal filter after actuation of the MDI, for both filter sizes. Each component was weighed using a calibrated Mettler 163 analytical balance (sensitivity at 30 mg was ± 10 mcg).

Statistical significance ($p < 0.05$) was accepted. ANOVA and the Neuman-Keuls test were used to analysze the increases in dry weight of the components of the apparatus.

## RESULTS:

The %DE of salbutamol was significantly less with a 3.0 mm ETT than it was with 4.0 mm, 5.0 mm and 6.0 mm ETTs ($p < 0.05$). However, the %DE increased from ≤12.3% when the MDI canister was discharged directly into an ETT to 96.7% when it was discharged through a 19 SWG catheter ($p < 0.001$) (Table 1). The increase in dry weight of the apparatus per dose was 176-202 µg (Table 1). This did not depend on the diameter of the ETT. The %DE with the 19 and 14 SWG catheters did not differ significantly, however, both were significantly greater than that with the 22 SWG catheter (Table 2). The dose per puff with the 19 SWG catheter was twice that of the 22 or 14 SWG catheters ($p < 0.001$) (Table 2). There was no difference in the effectiveness of the 20 µm filter to trap aerosol particles compared to the 0.2 µm filter.

## DISCUSSION:

The %DE of drugs by MDI administration is inefficient and highly variable in 3.0-6.0 mm tracheal tubes, but may be dramatically increased using a distally-placed catheter. The 19 SWG catheter is almost twice as effective at delivering the dose discharged from the canister as both the 22 and 14 SWG catheters. Nevertheless, all three catheters deliver substantially greater fractions of the dose discharged than no catheter at all. We found that for each puff, the increase in weight of the apparatus was 1.7-2.0 times that which the manufacturers claim is due to the salbutamol (100 µg). Other investigators have reported similar findings.[2,4] They attributed this discrepancy to a second constituent within the canister, "surfactant". Further studies are required to determine the net drug dose delivered using an intraluminal catheter in vivo, and the particle size of the aerosol as it exits from the catheter.

## REFERENCES:

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Table 1

| | Dry weight gain (%) | Weight gain/dose (µg) |
|---|---|---|
| 3.0 I.D. ETT | 45.7 | |
| Swivel | 51.7 | |
| Filter | 2.5* | 183 (± 35) |
| 4.0 I.D. ETT | 47.1 | |
| Swivel | 44.4 | |
| Filter | 10.8 | 176 (± 30) |
| 5.0 I.D. ETT | 47.5 | |
| Swivel | 42.0 | |
| Filter | 10.7 | 202 (± 70) |
| 6.0 I.D. ETT | 47.6 | |
| Swivel | 40.1 | |
| Filter | 12.3 | 198 (±32) |
| 19 SWG catheter | 3.3 | |
| Filter | 96.7** | 202 (± 40) |

Data are Means (± SD)
*p <0.05
**p < 0.001

Table 2

| | %DE | Dose/puff (µg) |
|---|---|---|
| 22 SWG | 77.7 ±16.5 | 105.2 ± 33.1 |
| 19 SWG | 96.7 ± 2.5** | 202.0 ± 40.0** |
| 14 SWG | 100.2±19.3* | 105.6 ± 29.7 |

Data are means ± SD
*p<0.005
**p<0.001

# Does Spinal Anaesthesia Interact with Sedation to Alter Ventilatory Responses?

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A recent review described several cases of cardiac arrest in healthy patients undergoing spinal anaesthesia.[1] Deafferentation of the chest wall with spinal anaesthesia results in an altered ventilatory response to carbon dioxide ($CO_2$).[2] We hypothesized that spinal anaesthesia and non-narcotic sedation may interact to cause a depressed response to $CO_2$ and subsequent respiratory compromise.

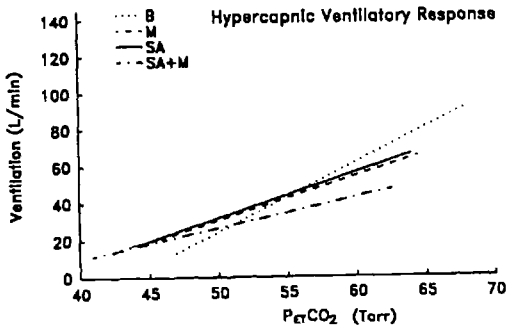
METHODS. With institutional approval, 10 ASA I subjects (5 F, 5 M) aged 23-33 completed $CO_2$ rebreathing experiments in the supine position under 4 conditions: Day 1 = baseline (B), midazolam (M); Day 2 = spinal anaesthesia (SA), spinal anaesthesia plus midazolam (SA + M).

Subjects wore nonrestrictive, respiratory inductance plethysmography (RIP) bands on the chest and abdomen to monitor ventilation noninvasively. Subjects were connected to a bag-in-box rebreathing circuit via an occlusive facemask and the circuit filled with an appropriate volume of 8% $CO_2$ balance oxygen ($O_2$). End-tidal $CO_2$ ($ETCO_2$) was monitored by infrared analyzer and $O_2$ saturation by pulse oximeter. The subject breathed the $CO_2/O_2$ mixture until 4 minutes or an $ETCO_2$ of 63 mm Hg was reached. The subject then breathed room air for 10 minutes while signals from the RIP were collected during quiet respiration for calibration (least squares technique) and evaluation of the thoracoabdominal motion. During SA, the subject received 50-85 mg (mean = 69) hyperbaric xylocaine into the subarachnoid space via a #25 spinal needle. Sensory levels were recorded until stable, the mask applied, and the rebreathing experiment conducted as above. Experiment B was followed on the same day by M. Midazolam 0.05 mg/kg was administered intravenously. If the subject was not sedated after 2 m, a further 0.025 mg/kg was given. Five m after the initial dose, the level of sedation was graded, the mask applied, and the rebreathing experiment repeated. The same dose of midazolam was administered in experiment SA + M, following SA on day 2.

Minute ventilation was plotted as a function of $ETCO_2$ on a breath by breath basis and regression analysis performed. The effects of midazolam and spinal anaesthesia, both singly and in combination, on hypercapnic ventilatory response slope, tidal volume (VT), breathing frequency (F), minute ventilation and the components of respiration were compared.

RESULTS. Three subjects required 0.075 mg/kg midazolam for sedation in M and SA + M. After sedation with midazolam on both days, 6 subjects responded to painful stimulation only and 4 responded to verbal command but did not initiate conversation. Mean anaesthesia level in SA and SA + M was T5 (T3-T8). There was no hypotension or bradycardia and vasopressors were not required.

In experiment M, there was a slight reduction in VT, and minute ventilation was preserved due to a significant increase in breathing frequency (p.01). However, in SA + M there was a significant reduction in VT (p .05) but no change in frequency. As a result, minute ventilation trended downwards in SA + M (p.07). There were no significant changes in VT, breathing frequency or minute ventilation in SA. Mean inspiratory flow rate (MIFR), an index of respiratory drive, was significantly lower in SA + M than SA. Apnea occured occasionally following administration of midazolam but there were no differences among experimental conditions. Mechanics of breathing changed, with a significant increase in rib component of respiration during M (p.03) but not SA or SA + M. The hypercapnic ventilatory response slopes were not significantly different among conditions (Figure 1).




| | Condition | | | |
|---|---|---|---|---|
| | *B* | *M* | *SA* | *SA + M* |
| VT (L) | 0.45 | 0.39 | 0.53 | 0.39 * |
| F | 14.9 | 17.2 ** | 14.6 | 15.5 |
| MV (L/m) | 6.17 | 5.95 | 7.09 | 5.63 |
| MIFR (L/s) | 0.28 | 0.24 | 0.32 | 0.22 * |
| RIB % | 42.6 | 64.5 * | 47.2 | 63.8 |

* $p < 0.05$ ** $p < 0.01$

DISCUSSION. Hypercapnic ventilatory responses were not altered significantly by midazolam alone nor by its combination with spinal anaesthesia. However, there was a trend towards decreased response in SA + M. In addition, the relationship between minute venilation and $ETCO_2$ became more variable after sedation with midazolam. Midazolam altered the mechanics of breathing and resulted in a reduction in minute ventilation in the presence spinal anaesthesia. SA alone did not significantly change the rib component, in spite of paralysis of intercostal muscles. It appears that intercostal muscles were recruited and breathing became less diaphragmatic when midazolam was added to B but not SA.

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# AXILLARY PLEXUS BLOCK USING A PERIPHERAL NERVE STIMULATOR : SINGLE OR MULTIPLE INJECTIONS

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Well before the use of the peripheral nerve stimulator (PNS) became popular, there were two major approaches to axillary blockade: the single perivascular injection and the multiple injection technique[1]. Both approaches have had postulants whom have reported various results[2,3]. However, to our knowledge, no prospective study has been published which compares the success rates of the axillary blockade using a PNS whether one, two, three or all four nerves were stimulated.

The purpose of this prospective, double blind study was to determine if the axillary blockade using a PNS could boast an adequate success rate (90% or more) particularly if using stimulation of less than four nerves.

## MATERIAL AND METHODS

Following Ethics Committee approval and informed consent, 75 patients presenting for upper limb surgery were studied. Each was randomly allocated into one of 5 groups using a randomization block, according to the stimulated nerves: Group I: musculocutaneous (M-C), radial, median and ulnar nerves; Group II: M-C plus one of the other three nerves; Group III: radial nerve; Group IV: median nerve; Group V: ulnar nerve.

A uniform technique of axillary blockade was used: local anesthesia for the skin, use of an isolated 23G needle with constant 0,5 MA current and injection following upper arm movement typical of the stimulated nerve, localized as high in the axilla as possible. The agent used was 1% preservative-free lidocaine with epinephrine 1/200,000 freshly added. Total volume was 30 ml/$m^2$ of body surface. The total volume of anesthetic was divided in equal parts among the nerves stimulated in Group I and in Group II. The total volume was injected on the only nerve stimulated in Groups III, IV, V.

Evaluation of analgesia was done every 5 minutes for a period of 30 min. after completion of the block by a blinded anesthetist, unaware of the group of patient. Analgesia to pinprick using a Wartenberg pinwheel was verified in every dermatome of the upper limb. The motor blockade was evaluated at the end of the 30 minutes. The attending blinded anesthetist decided whether sensitive blockade was sufficient to allow the planned surgery or if completion was necessary (infiltration of one or more major nerves).

Statistical analysis was performed using analysis of variance as well as Scheffe and Fisher's LSD tests for parametric results and Kruskal-Wallis and Mann-Whitney tests for non parametric results. A $p < 0.05$ was considered significant.

## RESULTS

All five groups were similar with regard to demographic variables: age, sex, type and site of planned surgery.

There was a significant difference ($p = 0.0028$) between Groups I and II versus Groups III, IV and V with regard to the number of patients requiring a completion of the blockade (Table 1). In fact, half of the patients in Groups III, IV and V required completion of the blockade compared to only one in each of Groups I and II.

Table 1

Number of patients needing completion of blockade

| | GROUPS | | | | | |
|---|---|---|---|---|---|---|
| COMPLETION | I* | II* | III | IV | V | TOTAL |
| YES | 1 | 1 | 7 | 8 | 8 | 25 |
| NO | 14 | 14 | 8 | 7 | 7 | 50 |
| TOTAL | 15 | 15 | 15 | 15 | 15 | 75 |

* GI or II vs GIII, IV or V: $p = 0.0028$

The motor blockade was found to be more intense in group I than in Group III, IV and V ($p < 0.05$).

## DISCUSSION AND CONCLUSION

When performing axillary blockade using a PNS, better results are obtained when stimulating either the four major nerves or the MC plus a nerve which was selected according to its implication with the surgical site. Injection of one nerve only, high in the axilla, resulted in blocks evaluated sufficient to allow the planned surgery in only 50% of cases. In a previous study[3] the use of a PNS (stimulation of only one nerve) in axillary blockade was found not to be superior to two other non stimulating techniques. Our study explains this poor result: when stimulating only one nerve, the success rates average about fifty percent.

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# THE CLINICAL SIGNIFICANCE OF DIFFUSION HYPOXIA IN CHILDREN

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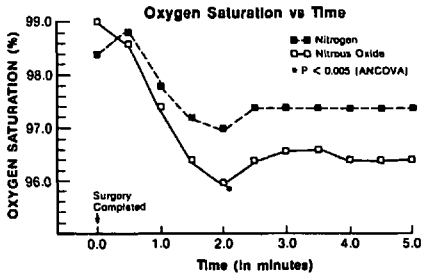
**Introduction:** Hypoxia is a common, potentially-serious occurrence after general anaesthesia in children. A number of factors, including diffusion hypoxia, have been considered to be contributing factors. Recent reports have questioned whether diffusion hypoxia exists and, if so, whether it is clinically significant.[1,2] We hypothesized that diffusion hypoxia exists, but that it is not clinically significant to anaesthetists administering anaesthetics to healthy children undergoing minor surgical procedures.

**Methods:** With parental and Ethics Committee approval, 42, ASA physical status I-II children age 2-12 years were investigated. Patients were excluded from study if they had cardiac disease, respiratory disease or if their tracheas were intubated during the operation. Only patients undergoing inguinal hernia repair, hydrocoelectomy, circumcision and orchidopexy were enrolled in this study. Monitoring included inspired and expired concentrations of oxygen, nitrous oxide and halothane, plus oximetry, ECG, non-invasive blood pressure monitor and end-tidal carbon dioxide. Baseline oxygen saturations were determined with a Nellcor N-1000 monitor while the children breathed room air. Anaesthesia was induced over 2-3 minutes with 70 per cent nitrous oxide, 30 percent oxygen and 2 percent halothane. The children were not intubated. After induction of anaesthesia, an IV and caudal block were established. The dose for the caudal block was 1 ml. $yr.^{-1}$ of 0.25 percent bupivicaine for children undergoing circumcisions and 0.65 $ml.kg^{-1}$ of 0.125 percent bupivicaine with 1/200,000 adrenaline for the other children. The children were randomized to 2 groups. The first group had anaesthesia maintained with 68 percent nitrous oxide, 30 percent oxygen and 2 percent halothane and the second group was identical except the nitrous oxide was replaced by nitrogen and the inspired halothane concentration was 2.5 percent. End-tidal carbon dioxide was determined 5 minutes after the incision and with the fresh gas flows to the coaxial circuit (CPRAM, Dryden Corp.) temporarily (15 seconds) reduced to 300 $ml.min^{-1}$. After the operation was completed, the patients inhaled room air except for an initial 15 second period of 100 percent oxygen delivered at 2150 $ml.min^{-1}$ plus 100 $ml.kg^{-1}.\ min^{-1}$. Airway patency was maintained. The oxygen saturation was recorded every 30 seconds for 5 minutes after completion of surgery. For the purpose of this investigation, we defined clinically-significant hypoxia as an oxygen saturation of 85 percent or less. Demographic data was compared with one-way ANOVA. The difference between baseline oxygen saturation and the lowest oxygen saturation was compared using ANCOVA (covariates were end-tidal CO2 and length of surgery). The average lowest oxygen saturations were compared using ANCOVA. Sample size was based on an alpha of 0.05, a beta of 0.90, a standard deviation of 2 and a predicted oxygen saturation difference of 2 percent.

**Results:** The groups were similar in age, weight, length of surgery, end-tidal carbon dioxide, gender and baseline oxygen saturation. No patients had a clinically-significant hypoxic event, i.e. no patient had an oxygen saturation below 85%. The oxygen saturation decreased by $4.3 \pm 2.0$ and $2.6 \pm 1.5$ for the subjects breathing nitrous oxide and nitrogen, respectively ($P < 0.003$). The nadir or lowest oxygen saturation, was normally observed 2 minutes after the end of the operation (Figure). Patients administered nitrogen during anaesthesia, had a higher oxygen saturation than the nitrous oxide group at the nadir ($P < 0.0001$). The oxygen saturation at the nadir was not affected by length of surgery and end-tidal carbon dioxide, but it was affected by baseline oxygen saturation ($P < 0.001$).




**Discussion:** Hypoxia at the end of an anaesthetic has frequently been attributed to nitrous oxide diffusion and elimination. Although nitrous oxide significantly reduces oxygen saturation at the end of an operation, it does not result in clinically-significant hypoxia in healthy children undergoing minor surgical procedures. We conclude, that clinically-significant hypoxia previously observed in children is not due to diffusion hypoxia. Other causes, such as, partial or complete airway obstruction, irregular breathing associated with shivering or aspiration of blood and saliva are more likely explanations of post-operative hypoxia. Based on our results we administer oxygen to healthy children at the end of an operation for reasons other than the prevention of diffusion hypoxia.

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# THE EFFICACY OF INDOMETHACIN AS A POSTOPERATIVE ANALGESIC FOLLOWING TOTAL HIP ARTHROPLASTY

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## INTRODUCTION:

Indomethacin has been widely used as an anti-arthritic agent for over 25 years, but its efficacy in the treatment of postoperative pain is just beginning to be recognized.[1,2] Pain after total joint arthroplasty is often difficult to control and many modalities have been tried.[3] We designed a prospective, randomized, double-blind trial to evaluate the efficacy of rectal indomethacin as an adjunct to morphine for controlling pain following total hip arthroplasty.

## METHODS:

With institutional approval, fifty patients (ASA I or II) undergoing elective total hip replacement were studied. Patients were excluded if they had a history of peptic ulcer disease, bleeding tendency, hypersensitivity to NSAIDS or to morphine.

After giving informed consent, patients were randomized into one of two groups -- Group I received placebo suppositories, Group 2 received indomethacin suppositories 100 mg q.8h for 5 doses postoperatively, the first one being given after skin closure. Patients in both groups received intravenous morphine via a patient controlled analgesia infusion pump (Bard Harvard PCA) which retains a record of the amount of morphine delivered.

A standardized general anaesthetic protocol was followed with avoidance of narcotic premedication, and limitation of intra-operative fentanyl to less than 7 μg/kg. No narcotic was given within one hour of the conclusion of surgery.

In recovery room, analgesia was initiated with intravenous morphine administered at the nurses' discretion. When the patient was sufficiently awake, patient controlled analgesia was started (bolus of 2 mg, lock-out of 6 minutes).

Subjective pain was measured with 100 mm closed visual analogue scales at 2, 6, 20, 28 and 42 hours postoperatively. Patients were asked to rate their pain at that particular moment. Total morphine consumption to that point was also recorded. Side effects were elicited by direct questioning.

Pain scores between groups were compared using the Mann-Whitney U test. Morphine requirements were analyzed with unpaired t-tests. A p-value of <0.05 was considered significant.

## RESULTS:

Three patients in the placebo group were withdrawn, two for PCA malfunction, one for missed suppositories, leaving 22 in Group 1 and 25 in Group 2 for analysis. The groups did not differ significantly with respect to age, sex, weight, ASA status, type of arthritis or fentanyl administration intra-operatively.

The results of pain scores and morphine use are summarized in Figures 1 and 2. Cumulative morphine dose over the 42 hour study period was 89.6± 43.7 mg in Group 1, and 34.8± 21.8 mg in Group 2 ($p<0.01$). At all time intervals morphine requirements were significantly lower in the indomethacin group than the placebo group. After 20 hours postoperatively, the pain scores in Group 2 were significantly better than those in Group 1.

There was no significant difference between the groups in the incidence of side effects, specifically nausea, heartburn, headache and confusion (Table 1). No patient suffered from excessive postoperative bleeding.

Figure 1.
POST OPERATIVE NARCOTIC REQUIREMENTS

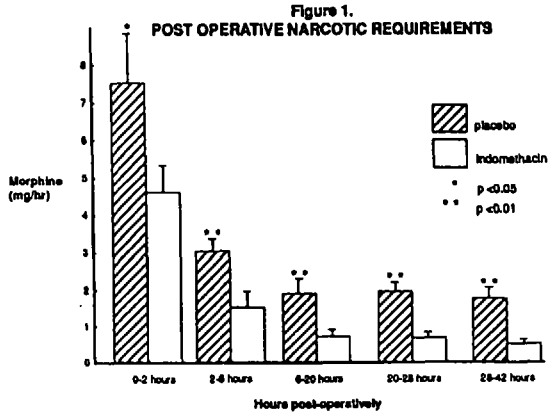


Figure 2.
POST OPERATIVE VISUAL ANALOGUE SCORES

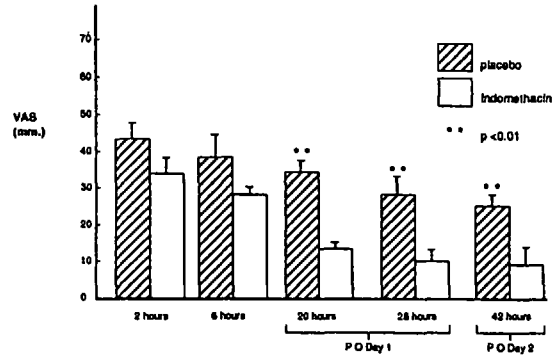


TABLE 1
SIDE EFFECTS

| | Nausea | Heartburn | Headache | Confusion |
|---|---|---|---|---|
| Group 1 (n=22) | 7 | 2 | 2 | 0 |
| Group 2 (n=25) | 6 | 1 | 2 | 2 |

## DISCUSSION:

The use of rectal indomethacin substantially reduced narcotic requirements after total hip replacement without a high incidence of side effects. The combination of indomethacin and morphine provided superior pain relief to morphine alone, even though the patients in the control group had liberal access to morphine via the PCA pump. This synergistic effect would make indomethacin a useful adjunct to intramuscular narcotics.

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# EFFECTS OF ISOFLURANE-INDUCED HYPOTENSION ON RENAL FUNCTION AND HEMODYNAMICS

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INTRODUCTION: Isoflurane-induced hypotension is effective in decreasing operative blood loss and improving surgical conditions. Although this hypotension is often complicated by oliguria, its effects on renal function have not been studied. This study was designed to evaluate the effects of isoflurane-induced hypotension on glomerular filtration rate (GFR) and renal hemodynamics in humans.

METHODS: After informed consent and approval by the Hospital Ethics Committee, 18 patients undergoing an elective orthognathic procedure under hypotensive anaesthesia were studied. Anaesthesia was maintained with fentanyl, $N_2O$, $O_2$ and isoflurane. Hypotension was induced by increasing the inspired isoflurane concentration to maintain a mean arterial pressure (MAP) of 55-65 mmHg. GFR and effective renal plasma flow (ERPF) were measured by inulin and para-aminohippurate clearance respectively. Clearance measurements were made before induction of anaesthesia (PRE), during normotensive anaesthesia (MAP 75-85 mmHg) (ANES), during hypotension (HYPO) and postoperatively (POST). Data are expressed as mean ± SEM, and statistical analysis was done with ANOVA and the Student's t-test for paired data with the Bonferroni correction for multiple comparisons.

RESULTS: Mean duration of controlled hypotension was 236.9 ± 64.1 min. Measurements of GFR and ERPF, and calculated filtration fraction (FF) are presented in Table 1. Calculated effective renal blood flow (ERBF) and renal vascular resistance (RVR) are presented in Table 2. GFR, ERPF and ERBF decreased significantly with induction of anaesthesia ($P<0.005$). However there was no further significant decrease during hypotension. FF increased with induction of anaesthesia ($P<0.001$) and remained at the same level during hypotension. RVR increased with induction of anaesthesia ($P<0.001$) but decreased when hypotension was induced ($P<0.005$).

DISCUSSION: Similar reductions in GFR and ERPF during inhalation anaesthesia have already been reported.[1] However, the absence of further reduction with induced hypotension and the persistance of an increased FF suggest that renal compensatory mechanisms are preserved. Isoflurane produces hypotension by decreasing systemic vascular resistances.[2] In these circumstances, the normal renal response is to decrease renal vascular resistance (RVR), allowing the maintenance of a normal ratio between RVR and systemic vascular resistance.[3] This response seems to be preserved during isoflurane-induced hypotension and it may explain the maintenance of ERPF and ERBF observed in spite of the drop in perfusion pressure. Indeed, the calculated RVR decreased by 18% allowing the ERBF to drop only 16% despite a 29% drop in perfusion pressure. The increased FF during anaesthesia and hypotension represents an increased tonus of the glomerular efferent arteriole. The increased FF combined with the preserved ERPF explain the absence of reduction of GFR during hypotension. Postoperative measurements show that GFR, ERPF and ERBF return to preoperative values suggesting that glomerular function and renal perfusion quickly resume a normal status.

| TABLE 1 | GFR | ERPF | FF |
|---|---|---|---|
| PRE | 113.8 ± 5.7 | 495.7 ± 25.0 | 0.22 ± 0.007 |
| ANES | 97.2 ± 6.0 | 292.5 ± 20.1 | 0.33 ± 0.014 |
| HYPO | 91.4 ± 5.6 | 263.6 ± 15.1 | 0.34 ± 0.014 |
| POST | 144.5 ± 8.9 | 501.9 ± 28.8 | 0.28 ± 0.009 |

Mean ± SEM, GFR: $ml.min^{-1}.1,73m^{2-1}$, ERPF: ml/min.

| TABLE 2 | ERBF | RVR |
|---|---|---|
| PRE | 810.3 ± 48.1 | 9474.0 ± 540.0 |
| ANES | 457.4 ± 32.7 | 15979.2 ± 1069.8 |
| HYPO | 385.2 ± 20.0 | 13112.8 ± 860.7 |
| POST | 769.2 ± 46.4 | 11923.1 ± 664.5 |

Mean ± SEM, ERBF: ml/min, RVR: $dynes.cm^{-5}.sec$.
$ERBF = ERPF/(1-hematocrit)$, $RVR = 80*MAP/(ERBF*10^{-3})$

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## MIDAZOLAM-KETAMINE VS SUFENTANIL FOR RAPID SEQUENCE INDUCTION OF ANAESTHESIA FOR CABG SURGERY

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**Introduction:** Patients with coronary artery disease may present for emergency surgery requiring rapid sequence induction of anaesthesia. Although high dose fentanyl given over 20 sec provides relatively stable hemodynamics during induction and intubation,[1] its use results in delayed awakening and prolonged postoperative ventilation. A midazolam-ketamine infusion given over several minutes has been reported to provide hemodynamic stability similar to high dose narcotics with more rapid emergence from anaesthesia.[2] The present study was designed to compare hemodynamic responses and time to awakening following rapid sequence induction of anaesthesia with midazolam plus ketamine versus sufentanil.

**Methods:** Twenty patients presenting for elective coronary artery bypass (CABG) surgery were randomly assigned in a double blind fashion to receive either midazolam 0.3 mg/kg with ketamine 2mg/kg (M-K) or sufentanil 5 ug/kg (S). All cardiac medications were continued preoperatively and patients were premedicated with lorazepam. A two channel (I1,V5) continuous ECG recorder (Q Med) was applied preoperatively to record myocardial ischemia. Routine monitoring lines were inserted prior to induction. Rapid sequence induction of anaesthesia was performed after preoxygenation for 3 min, as follows: 10% of the muscle relaxant (vecuronium 0.11 mg/kg with pancuronium 0.04 mg/kg) was given followed 60 sec later by the induction agent infused over 60 sec. The remainder of the muscle relaxant was injected over 10 sec and intubation performed 90 sec later. Oxygen saturation ($SaO_2$) and end-tidal CO2 ($ETCO_2$) were recorded during the induction and intubation sequence. Anaesthesia was then maintained with oxygen and enflurane. Ward values (WA) of HR, SBP and DBP were recorded and hemodynamic profiles made at: baseline (BL), 1 min after induction (IND), and 1 and 5 min after intubation (INT-1, INT-5). Patients received fluids, vasopressors, vasodilators, and inotropes as indicated. Diazepam 10 mg was given on bypass and morphine 0.1 mg/kg after bypass. Time from induction of anaesthesia to awakening and readiness for extubation were noted. Patients were questioned 1 day post-operatively about recall, dreams, and hallucinations. Data were analysed using unpaired or paired T-tests for comparisons and Chi-squares for proportions where appropriate. $p < 0.05$ was taken as significant.

**Results:** There was no significant difference between the M-K and S groups with respect to age, sex, LVEF (range 0.15 - 0.55%), use of pre-operative B-blockers or duration of surgery. Aortic cross-clamp time was longer in the S group (60 ± 3 min vs. 48 ± 4 min, $p < 0.05$). There was a significant increase in HR at INT-1 in the M-K group compared to a significant decrease at IND in the S group. MAP was significantly higher at BL in the M-K group, and rose further at INT-1. MPAP followed a similar course to MAP, but the differences did not reach significance. In group S, MAP decreased significantly at INT-1, associated with a significant increase in MPAP. There were no significant changes in PCWP and CI. (Table) One patient in the M-K group had a period of myocardial ischemia at induction (p=N.S). $SaO_2$ was always 95%. The mean $ETCO_2$ were 37.9±1.6 in the M-K group and 37.2±2.1 in the S group at intubation. There were no significant differences in need for intra or post-operative fluids, vasopressors, vasodilators or inotropes between groups. The time from induction of anaesthesia to awakening was significantly shorter in the M-K group (296±7 min vs. 414±36 min, $p < 0.05$). Although patients in the M-K group were extubated earlier compared to the S group (971.9±114.0 min vs. 1237.5±142.3), this did not reach significance. No patient in the M-K group had recall, dreams, or hallucinations. Two patients in the S group reported dreams.

**Discussion:** This study shows that while a rapid sequence induction with sufentanil provides relative hemodynamic stability, use of midazolam plus ketamine is associated with increases in HR and BP that may be unacceptable in patients with coronary artery disease. The latter observation may outweigh any advantage provided by earlier post-operative awakening, especially as time to extubation was not significantly shorter. The hemodynamic changes associated with the use of sufentanil are similar to those reported by Murkin et al[1] using high dose fentanyl for rapid induction of anaesthesia. However, the present study failed to confirm the hemodynamic stability and decreased need for post-operative fluid and vasopressors reported by Tuman et al[2] when using M-K infusions. This may be explained by differences in the dose or rate of administration of these drugs. Thus we can not recommend this drug combination for rapid sequence induction in patients with coronary artery disease.

**Table : HEMODYNAMIC DATA**

| Time | | WD | BL | IND | INT-1 | INT-5 |
|---|---|---|---|---|---|---|
| HR | MK | 66.8±2.8 | 63.5±2.9 | 64.0±4.5 | *81.0±5.3 | 73.0±4.0 |
| (bpm) | S | 65.9±2.8 | 61.9±2.6 | *59.4±3.2 | 62.1±5.1 | 59.9±4.0 |
| MAP | MK | 91.1±3.5 | *104.8±3.2 | 91.8±2.5 | *121.2±5.7 | 93.6±4.4 |
| (mmHg) | S | 94.8±3.1 | 94.3±4.3 | 99.8±6.6 | *83.7±5.1 | 81.6±3.7 |
| MPAP | MK | | 20.2±1.7 | 19.4±1.2 | 26.5±2.7 | 18.0±1.4 |
| (mmHg) | S | | 15.8±0.9 | +20.3±2.0 | +18.4±1.1 | 17.5±1.2 |
| WP | MK | | 12.8±1.2 | 13.7±1.3 | 16.2±2.4 | 10.8±1.1 |
| (mmHg) | S | | 10.3±0.6 | 12.1±1.3 | 10.4±1.0 | 11.3±1.3 |
| CI | MK | | | 2.9±0.3 | 2.9±0.3 | 2.8±0.2 |
| (l/min/M$^2$) | S | | | 2.7±0.1 | 2.8±0.2 | 2.5±0.1 |

* $p < 0.05$ compared to ward + $p < 0.05$ compared to baseline

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# ENDOBRONCHIAL INTUBATION IN DOGS.

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**Introduction:**
Endobronchial intubation occurs frequently in the operating room. Early recognition of this event will allow one to avoid complications [1]. Theoretical arguments based on physiological work in animals and humans, as well as clinical observations, suggests that endobronchial intubation should result in an immediate fall in the end-tidal $CO_2$ and an increase in the arterial to end-tidal $CO_2$ difference [2]. However, recent literature suggests that the end-tidal $CO_2$ may actually rise with endobronchial intubation in mechanically ventilated patients [3]. This study was therefore designed to define the end-tidal $CO_2$ response to endobronchial intubation in mechanically ventilated dogs, as well as to observe the pattern of recovery of end-tidal $CO_2$ following endobronchial intubation.

**Methods:**
The study population consisted of ten mongrel dogs. Induction was carried out with 25mg/kg IV of thiopental and 0.1mg/kg of pancuronium. Each dog was then intubated with an extended Portex #7 cuffed tube. Intubation was checked by auscultation to ensure equal air entry bilaterally. Anaesthesia was maintained using 100% oxygen and 1.5-2.0% Halothane. An arterial line was established. Each dog was then stabilized and ventilated endotracheally for 25 minutes with end-tidal $CO_2$ maintained between 34-42mmHg. At each 5 minute interval, end-tidal $CO_2$, heart rate, blood pressure, airway pressure, arterial blood gas and temperature were recorded. A continuous recording of end-tidal $CO_2$ was also carried out. The arterial blood gas samples were temperature corrected. At the end of the stabilization period the endotracheal tube was directed into one of the mainstem bronchi. The above parameters were then recorded at 2 minute intervals for 20 minutes. The endotracheal tube was then pulled back to the trachea, while all parameters were recorded at 2 minute intervals for 10 minutes. Statistical significance was set at $P<0.05$ by student's two-tailed t-test.

**Results:**
Endobronchial intubation resulted in an immediate fall of end-tidal $CO_2$. The end-tidal $CO_2$ dropped from a mean of 36mmHg to 22mmHg ($P < 0.001$). There was a gradual but incomplete recovery toward baseline after a mean of 5 minutes (Graph 1 - $ETCO_2$). Arterial $CO_2$ increased from a mean of 42mmHg to 47mmHg ($P < 0.001$) (Graph 1 - $PaCO_2$). This small increase in arterial $CO_2$ and large fall of end-tidal $CO_2$ resulted in a change of the arterial to end-tidal $CO_2$ difference from 6mmHg to 22 mmHg (Graph 1 - $PaCO_2$-$ETCO_2$).

**Discussion:**
Accidental insertion of an endotracheal tube into a mainstem bronchus may occur during endotracheal intubation or at any time during the course of anaesthesia. Accidental endobronchial intubation may be detected by bilateral auscultation of breath sounds, observation of chest wall movement, change in airway pressure, bronchoscopy, chest x-ray and knowledge of endotracheal tube size [4]. Early detection of an unintentional endobronchial intubation is required to avoid the consequences of one-lung ventilation. This study shows that end-tidal $CO_2$ measurement may be a useful tool to detect accidental endobronchial intubation during anaesthesia. It should be noted that the sudden decline in end-tidal $CO_2$ occurs immediately upon endobronchial intubation and is transient, climbing to within 3-4mmHg of the baseline within a period of 4 to 8 minutes. This might lend further support to continuous end-tidal $CO_2$ monitoring. In conclusion, endobronchial intubation in dogs results in a consistent fall in end-tidal $CO_2$ which recovers within 5 minutes. This may have clinical implications for the detection of endobronchial intubation in human anaesthesia.

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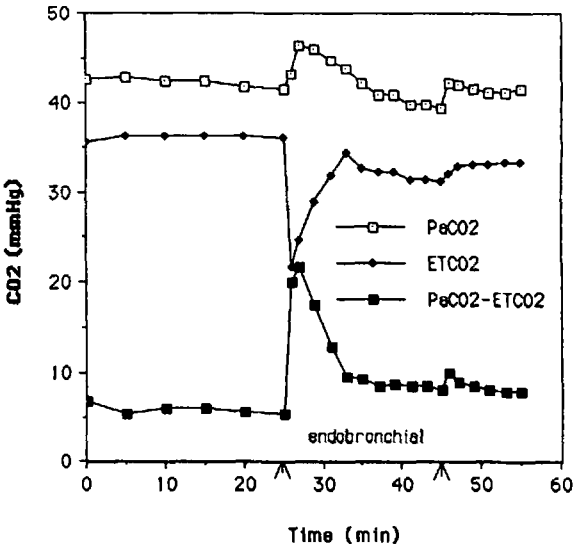
**Graph 1**



## PATIENT CONTROLLED LUMBAR EPIDURAL FENTANYL FOR POST THORACOTOMY PAIN

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### INTRODUCTION

Lumbar epidural fentanyl infusions have been reported to provide good analgesia following thoracotomy.[1,2] There are conflicting reports on the plasma levels of fentanyl which occur following epidural adminstration and it has been suggested that epidural fentanyl analgesia results primarily from vascular absorption.[2,3,4] The present randomized, double blind, placebo controlled study was carried out to compare analgesic effectiveness, dose requirements and respiratory effects of lumbar epidural patient controlled (PCA) fentanyl to IV PCA fentanyl in patients undergoing posterolateral thoracotomy.

### METHODS

Following institutional approval and informed consent thirty-four ASA I-III patients scheduled for elective thoracotomy were familiarized with a dual PCA pump system and a visual analogue pain scale (VAS: 0 = no pain, 10 = severe pain). An epidural catheter was placed at L1,2 or L2,3. Anaesthesia was induced with fentanyl 3-5 ug $kg^{-1}$ and thiopental 2-4 mg $kg^{-1}$ followed by isoflurane, $O_2$, air and metocurine/pancuronium plus further increments of fentanyl to a maximum total of 10 ug $kg^{-1}$. No IV fentanyl was given in the last hour of the procedure.

Patients were randomized to a PCA epidural group (Group 1) or PCA IV group (Group 2). During closure of the chest all patients received both epidural and IV injections; Group 1 received epidural fentanyl 2 ug $kg^{-1}$, concentration of 10 ug $ml^{-1}$, and an IV injection of an equal volume of saline. Group 2 received IV fentanyl 2 ug $kg^{-1}$ and an equal volume of epidural saline. In the recovery room PCA bolus/infusion pumps were connected to both the epidural and a peripheral IV. In Group 1 the epidural pump contained fentanyl 10 ug $ml^{-1}$ and the IV pump contained saline; these were reversed in Group 2. Infusion rates were set to deliver fentanyl 0.75 ug $kg^{-1}$ $h^{-1}$ initially. Patients activated the PCA pumps with two remote control buttons. Each demand delivered 50 ug fentanyl from one pump and an equal volume of saline from the other. Each time a PCA bolus was given the infusion rates were increased by 10 ug $h^{-1}$ to a maximum of 150 ug $h^{-1}$. The objective was to reach a level of analgesia where the patient did not require frequent boluses. VAS was measured at rest and with vigorous coughing every two hours. Whenever the VAS was less than 2.0 at rest the infusion rates were decreased by 10 ug $h^{-1}$. Respiratory rates were recorded hourly, blood gases measured every 3 hours and oxygen saturation monitored continuously. Forced vital capacity and $FEV_1$ were measured the morning after surgery. Data was collected for at least 20 h in all patients. Results are expressed as mean ± SD. Between group comparisons were made with the independent student t-test. $P < 0.05$ was considered significant.

### RESULTS

Twenty-nine patients completed the study. Groups 1 and 2 were demographically similar. Results are summarized in the table and figure. Fentanyl infusion rates in Group 1 (n=14) were significantly less than in Group 2 (n=15) for most of the study. Total fentanyl requirements were significantly less in Group 1 than in Group 2. VAS at rest was less in Group 1 than in Group 2 over the entire study (Table) VAS with coughing was similar in both groups. Averaged over the study period the $PCO_2$ for Group 1 was less than for Group 2. There were no differences in spirometry.

### DISCUSSION/CONCLUSIONS

Both epidural and IV PCA fentanyl produced satisfactory analgesia after thoractomy. Higher infusion rates were required than have been previously reported.[1] Patients receiving epidural PCA fentanyl required significantly less drug, had lower $PCO_2$ levels and overall lower VAS scores at rest than did patients receiving IV PCA fentanyl. Epidural PCA fentanyl is superior to IV PCA fentanyl following thoracotomy.

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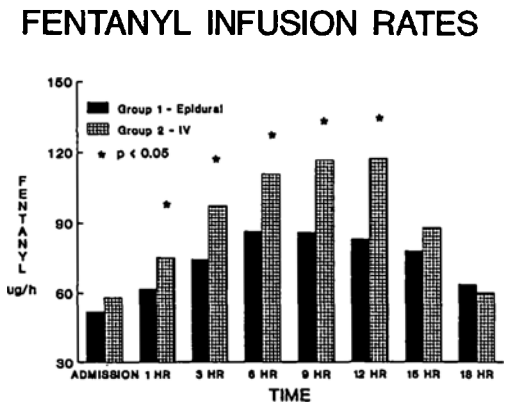
TABLE (Mean ± SD)

| | GROUP 1 | GROUP 2 | P |
|---|---|---|---|
| Total Fentanyl | 1857 ± 693 | 2573 ± 890 | 0.02 |
| VAS resting | 2.5 ± 1.9 | 3.2 ± 2.3 | 0.006 |
| VAS coughing | 5.2 ± 2.1 | 5.7 ± 2.4 | NS |
| $PCO_2$ | 44.7 ± 3.9 | 46.7 ± 5.4 | 0.002 |



# Spinal Anesthesia With Low Dose Meperidine For Knee Arthroscopy In Ambulatory Surgical Patients

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INTRODUCTION:
Recently, arthroscopy of the knee has become a part of ambulatory surgery. At times the Anesthesiologist faces a situation where regional anesthesia is deemed the best choice for these patients. Meperidine has been reported to have local anesthetic properties and can be used as a sole anesthetic agent for spinal anesthesia. Therefore, we designed a prospective study to evaluate the efficacy of spinal meperidine as the sole anesthetic agent for ambulatory knee arthroscopy.

METHODS:
Following institutional approval and informed consent, 16 patients (10 males, 6 females) ASA I or II were included in this study. The mean age of these patients was 41.2 yrs (22-64 yrs). None of the patients received premedication. Intra-operative monitoring included EKG, BP, HR, $O_2$ Sat, Temp, Resp. Rate and $ETCO_2$. After establishing IV access, spinal anesthesia was performed in the sitting position with a 25G spinal needle through L3-4 or L4-5 interspace. Preservative-free 5% meperidine (0.5mg/kg body weight) was used as the anesthetic agent and patients were kept in sitting position for 10 minutes. Vital signs were recorded every minute for the first 10 minutes and thereafter every three minutes for the duration of the case. The onset and extent of sensory blockade was tested with pin prick and ice cubes. The Motor blockade was determined according to modified Bromage score. Intra-operatively, sedation was achieved with Midazolam I.V. in increments of 1 mg. Patients were monitored for any possible complications. Post-operative analgesia was considered to be from the end of surgery to the first time patient asked for pain medication or until the time of discharge from hospital.

RESULTS:
The onset of sensory blockade was 4-8 minutes (mean 5.8±1.6) and the duration extended up to 100-130 minutes (mean 110±5). The degree of motor blockade at 10 minutes, Grade 0 (n=3), Grade 1 (n=3), Grade II (n=7) and Grade III (n=3). The mean duration of surgery was 58 minutes (range 50-70 mins). The mean midazolam requirement for intra-operative sedation was 3.2 mg(2-4 mg). The operative conditions were excellent in all patients. The patients had no evidence of drowsiness or respiratory depression. BP, HR, EKG, $O_2$ Sat and $ETCO_2$ were well maintained intra-operatively as well as post-operatively. Only one patient developed itching and one patient had nausea intra-operatively which were managed symptomatically. None of the patients developed spinal headache. The mean post-operative analgesia was 3.8 hours (2-6 hrs).

DISCUSSION:
5% Meperidine (a phenylpiperidine derivative) in aqueous solution acts like a hyperbaric local anesthetic agent. It's action on spinal nerve roots produces axonal blockade which explains the production of sensory analgesia with minimal motor blockade. The prolonged analgesic effects may be due to its action at the nociceptive synaptic junction in the dorsal horn of the spinal cord. The half life of intrathecal meperidine is short and the rostral spread is minimal probably due to its high lipid solubility. So when respiratory depression occurs, it will usually occur in the first hour after the administration of spinal anesthesia.

In this study, by using low dose meperidine (0.5mg/kg) we were able to achieve good painfree operative conditions with good hemodynamic stability. There were minimal adverse effects attributed to the lower dose of meperidine. Thus, low dose spinal meperidine appears to be a good anesthetic for ambulatory knee arthroscopy.

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## SELECTION OF VEHICLE FOR EPIDURAL MEPERIDINE INFLUENCES NOCICEPTIVE LATENCY IN RABBITS

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Introduction: Manipulation of the physico-chemical characteristics or components of local anesthetics (LA) is known to modify the performance of epidural (Epi) and spinal anesthesia. This includes addition of dextrose,[1] change of baricity,[2] temperature or pH of the solution[3] and addition of vasoconstrictors; etc. Whether or not this also applies to epidural opiates has not been well documented. This study was undertaken to evaluate the effect of changing the vehicle of Epi meperidine (M) on its nociceptive latency (L).

Methods: This study was approved by the institutional animal care and study committee. One week after lumbar laminectomy and implantation of a Epi catheter, 12 New Zealand albino rabbits weighing 3-4 kg were studied in 2 groups (G): G1. (n=6) received M (0.75mg/kg dissolved in normal saline (NS) epidurally. The pH of the injectate was 5.5. G2 (n=6) received M 0.75 mg/kg dissolved in artificial CSF (rabbit),[4] containing water 99.0%, glucose 750 mg/l, sodium 149 mEq/l, potassium 3 mEq/l, calcium 54 mg/l, magnesium 2.2 mEq/l, phosphate 23 mg/l, chloride 127 mEq/l, gluconate 2.8 mEq/l. The pH of M dissolved in artificial CSF was 7.7.

Analgesic testing was performed with electric stimulation (1 hz, 3 msec and 50-70 volts, via skin electrodes on the lower back) using a S6 Grass Stimulator. L, the interval between time zero of stimulation to withdrawal of hind limbs was recorded.

The results were analyzed using analysis of covariance. The response of the vehicles (CSF and NS) versus time were compared. The time adjusted difference between the 2 vehicles was tested. $p < 0.05$ was considered statistically significant.

Results: Fig 1 depicts L for NS and CSF. The slopes of the 2 regression lines were found to be parallel. The time adjusted difference between NS and artificial CSF as vehicle was statistically significant. $t = 3.17$ ($p = 0.0024$, 2 tailed).

Discussion: The results of the present study suggest that substituting artificial CSF for NS in Epi M shortened L. This is contrary to the fact that within certain limit, alkalinization enhances the effect of LA. Briefly, the blocking effect of LA depends on their penetration of the nerve membrane which is only permeable to LA in the nonionized form. This nonionized fraction is increased by raising pH of the solution thus facilitating membrane penetration. The differences between LA and opiates here, could be due to differences in the site of action. LA works on the axonal membrane while opiates act on spinal opioid receptors.

Recently, studies with morphine and a number of structural-related analogues revealed that the important structural features of the morphine allergenic (that is, IgE binding) determinant comprises the cyclohexenyl ring with a hydroxyl group at C-6 and, most importantly, a methyl substituent attached to the N atom.[5] Change of vehicle may have altered the analgesic effect of M but may not act through structural chemical changes. However, it is conceivable that change of vehicles could influence binding at the opioid receptors[6] or affect receptor sensitivity.

Precipitation of LA in CSF has been reported.[7] It may be possible that increase of pH could cause precipitation of meperidine from solution thus decreasing its effect. We did not observe any gross precipitation, but microscopic precipitation could not be ruled out.

In any event, unfolding this mystery requires further investigation.

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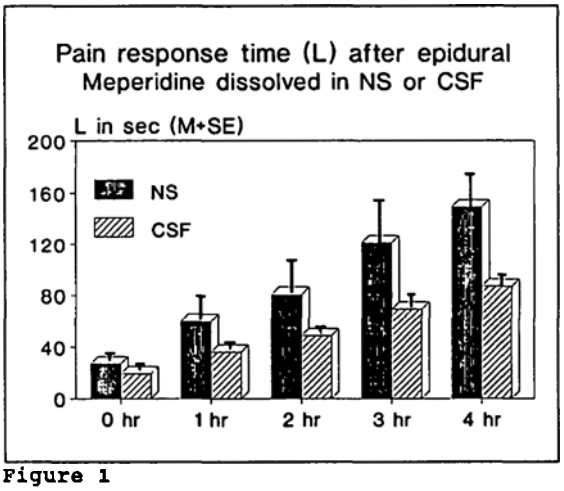


Figure 1

# THE ANALGESIC INTERACTION BETWEEN INTRATHECAL MORPHINE, LIDOCAINE AND BUPIVACAINE IN THE RAT

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**Introduction**: The purpose of these experiments was to systematically evaluate the analgesic interaction between intrathecal morphine, bupivacaine and lidocaine in the rat.

**Methods**: All experimental procedures received prior approval from our institution's Animal Research Ethics Committee. Male Sprague-Dawley rats weighing 300-400g were implanted with chronic intrathecal (i.t.) catheters as previously described(1). All experiments used the Paw Pressure Test, and the Hot Plate Test(52.5 °C). In the absence of a response the test was terminated at 400g and 60 sec. respectively. Baseline test latencies were determined. Drugs were then administered by single bolus i.t. injection and the rat's analgesic state was followed for a maximum of 3 hrs. Motor function was assessed by examination of the Righting, Placing and Stepping Reflexes and hindlimb tone at 5, 10, and 15 minutes after drug administration. Data was converted to the % of Maximum Possible Effect (%MPE= (Post Drug Value-Baseline Value)/(Cutoff value-Baseline value)X100%). The following drug combinations were evaluated: 1) Morphine(1ug) + Lidocaine(100ug) 2) Morphine(1ug)+ Bupivacaine(25ug) 3) Morphine(0.3ug)+ Bupivacaine(25, 8 and 2.5ug) 4) Morphine(0.1ug)+ Bupivacaine(25ug). All drug administrations were in a volume of 10 uL followed by a 10 uL flush of normal saline. In all experiments the morphine plus local anesthetic groups were matched with morphine plus saline and saline plus local anesthetic controls. For each dose group 7-11 rats were examined. Rats were used for a maximum of 3 experiments with a minimum of 3 days between studies and no more than 21 days after implantation.

**Results**: The intrathecal injection of morphine produced a dose dependent increase in the nociceptive threshold as measured by the PP and HP tests with no effect on motor function. The i.t. administration of bupivacaine and lidocaine at doses up to 25 and 100ug respectively had no effect upon motor function or PP/HP responses. Bupivacaine(75ug) or lidocaine(500ug) resulted in mild levels of analgesia but was accompanied by moderate hindlimb dysfunction (onset 30 sec., duration 5-10 min.). The ED50 for maximum %MPE with morphine was 1.0ug in both the PP and HP tests. Co-administered with bupivacaine(25ug) morphine's ED50 for the maximum %MPE was 0.30ug in the PP and 0.22ug in the HP test. Fig.1 presents the time course of the effects on the PP threshold of a low dose of morphine (1ug), an ineffective dose of bupivacaine and a combination of the two. Mean maximum %MPE increased from 46%±13 to 82%±9, $p<0.05$. The area under the curve (AUC) of the %MPE vs. time was calculated by the trapezoidal integration method to express the overall magnitude and duration of anti-nociceptive effect for each test. Fig.2 shows a dose response curve for these AUCs for morphine and morphine together with an analgesically inactive dose of bupivacaine(25ug) in the PP test. A similar left-ward shift in morphine's dose response was seen in the HP test (data not shown).Lower doses of bupivacaine (8 and 2.5ug) with 0.3ug morphine showed a progressive decrease in analgesia but still greater than 0.3ug morphine alone in both tests. Similar potentiative effects with regard to peak effect and duration of action of morphine were observed with addition of an otherwise ineffective dose of lidocaine (100ug) on these same tests (data not shown).Bupivacaine(25ug) combined with 0.1ug morphine did result in some increase of analgesia but the difference was not statistically significant. Naloxone 1.0mg/kg s.c. given 30 min. after i.t. morphine(1ug) with bupivacaine(75ug) resulted in immediate return to baseline in all analgesic tests.

**Discussion**: Our data demonstrates that very low doses of i.t. bupivacaine and lidocaine that alone do not have any analgesic effect, are able to significantly augment i.t. morphine analgesia in the PP and HP tests as manifest by increase in peak effect and duration of action. The mechanism for this interaction is uncertain but appears not to depend on a local anesthetic induced conduction blockade. There appears to be an enhancement of opiate receptor mediated analgesia. This synergistic analgesic interaction does not appear to be accompanied by any motor dysfunction.

**Ref**: (1) Yaksh TL, Rudy TA. Physiol Behav. Vol.17, pp1031-36.

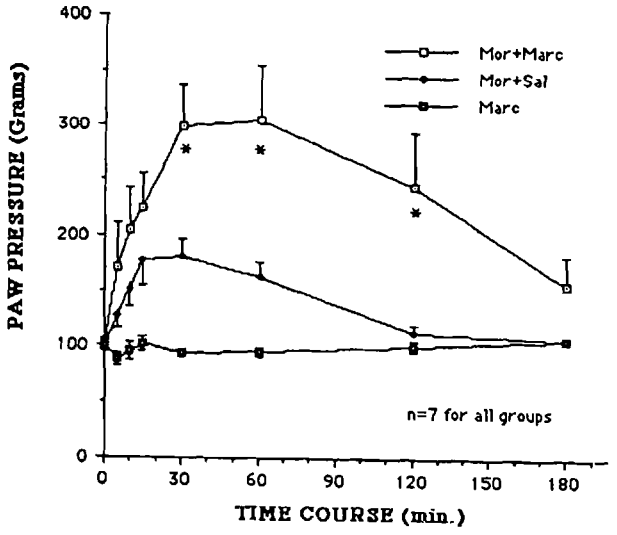


Fig 1. Data are presented as mean ± SEM * denotes time points when Mor 1ug + Marc 25ug significantly greater than morphine 1ug + sal. ($p<.05$ : one way ANOVA and Newman-Keuls test)

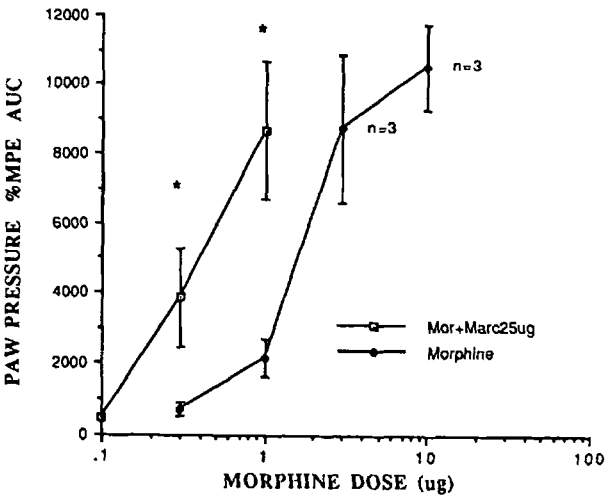


Fig. 2 Data presented as mean ± SEM, n=7-11 unless otherwise stated. * $p<.05$ (unpaired student's t-test)

# INTRATHECAL MORPHINE AND BUPIVACAINE IN THE RAT; ANALGESIC SYNERGY WITHOUT AUGMENTATION OF MOTOR DYSFUNCTION OR HYPOTENSION.

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**Introduction**: It has recently been demonstrated in the rat that low doses of intrathecal (i.t.) bupivacaine(25ug), that alone do not have any analgesic effect, are able to augment i.t. morphine analgesia in the Hot Plate and Paw Pressure tests (Penning and Yaksh, unpublished data) It is not known if this synergistic interaction is unique to the antinociceptive actions of these drugs. Therefore the purpose of these experiments was to evaluate systematically the interaction of i.t. morphine and bupivacaine on motor function, blood pressure(BP) and heart rate(HR) and to compare this to the effect on a nociceptive endpoint.

**Methods**: All experimental procedures received prior approval from our institution's Animal Research Ethics Committee. Male Sprague-Dawley rats weighing 300-400g were implanted with chronic intrathecal catheters as previously described(1). Phase 1 of this study focused on motor dysfunction. A baseline motor function score was assigned to each rat prior to drug injection. Both left and right sided Placing/Stepping Reflex and Righting Reflex was graded as 0,1 or 2, (0 being absent and 2 normal). Motor power of each limb was assessed as follows: normal=2, weak=1 and flaccid=0. A normal aggregate score of 16/16 was required for animals to enter the study. Rats received either morphine(1ug) + bupivacaine(75ug), bupivacaine(75ug) alone or morphine(1ug) alone, (n=10, 8, 3 respectively), by i.t. injection in a volume of 20uL followed by a 10uL flush of normal saline. The motor function score was followed for 30 minutes. Phase 2 of the study assessed BP, HR, and analgesia in the Hot Water Tail Dip Test (53°C). Under halothane anesthesia, neurologically normal rats with chronic i.t. catheters were prepared with tail artery catheters(PE-50). BP and HR were then continuously recorded with a Grass Model 79D Polygraph. The rats were awakened and a baseline Hot Water Tail Dip Withdrawal Latency(TWL) was performed. Rats received either morphine(30ug), morphine(1ug), or saline by i.t. injection in a volume of 10uL followed by a repeat TWL test in 15 minutes. Each rat then sequentially received i.t. bupivacaine(25ug, 75ug and 150ug) at times 20, 30 and 40 minutes after the morphine/saline injection. Bupivacaine was 5ug/ul. A TWL was determined 5 minutes after each i.t. bupivacaine injection. In the absence of a response the test was terminated at 15 seconds. Data was converted to percent of maximum possible effect(%MPE).

**Results**: Fig.1 shows the time dependent loss of motor function for both groups, with maximum motor block at 2 min. and all animals back to baseline by 30 min. A cumulative motor function score was calculated (t=2.5,10 and 15) and found not to differ in the presence of morphine(1ug). The group means ±SEM were (46.6 ±1.7 vs. 44.6 ±1.54, p=0.42 by 2-tailed unpaired t-test). Rats injected with morphine(1ug) alone showed no motor dysfunction at any time. (Phase 2) Fig.2 shows the mean arterial BP(MBP) at 15 min.after the initial i.t. injection(saline,

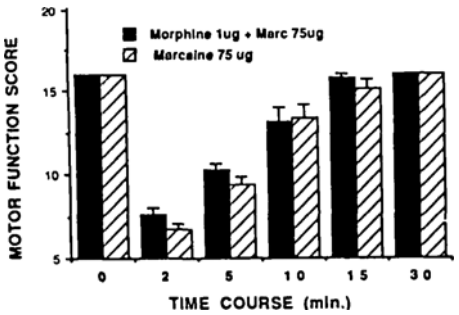


Fig 1. Data presented as mean ± SEM Mor 1ug + Marc 75ug n=10, Marc 75ug n=8.

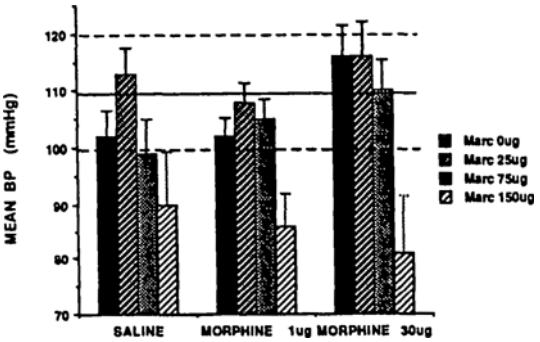


Fig 2. Bar data presented as mean ± SEM. Horizontal lines represent MBP±SD for all 16 rats. n=5,7,4 for saline, morphine (1ug) and morphine 30ug respectively. No statistical difference between groups at any time (ANOVA).

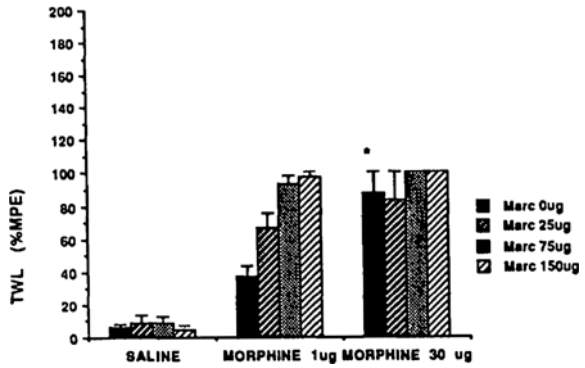


Fig 3. Data presented is mean ± SEM. All points in saline group statistically significant p<.05 (ANOVA). * greater than morphine 1ug (p<.01)

morphine(1ug) or morphine(30ug)) and also at the time of minimum MBP after each sequential bupivacaine injection. This uniformly occurred 2-3 min after injection. The high dose morphine had no sympatholytic action and more importantly did not augment the effect of bupivacaine. No significant trend in HR response was detected in any group. Fig.3 shows the relative lack of effect of bupivicaine on the TWL at these doses and the powerful synergistic analgesic interaction between spinal morphine(1ug) and bupivacaine.

**Discussion**: These data suggests that the augmented somatomotor inhibition of local anesthetics by morphine does not extend to the sympathetic or motor block produced at the spinal level by local anesthetics. Though the mechanism of the augmentative interaction between local anesthetics and morphine is not clear, the selective inhibition argues for an action on the processing of afferent evoked activity in the dorsal horn and not directly on the motor or autonomic outflow.

**Ref**: (1)Yaksh TL, Rudy TA, Physiol Behav. Vol.17, pp1031-36.

# OXYGEN DESATURATION IN ELDERLY PATIENTS DURING CATARACT SURGERY

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Introduction: Cataract surgery is commonly performed using retrobulbar block with neuroleptanalgesia. However the use of short-acting narcotics such as alfentanil or fentanyl in combination with a benzodiazepine has not been adequately assessed in elderly patients. Alfentanil has a faster onset, shorter duration of action and is less potent than fentanyl but may cause centrally mediated apnoea and bradycardia in high doses.[1] The purpose of this study was to compare the cardio-respiratory effects of diazepam plus alfentanil or diazepam plus fentanyl for cataract surgery.

Methods: After Institutional Approval, 70 consenting patients over 50 years and scheduled for unilateral cataract surgery were randomly assigned to have diazepam (0.1 mg/kg) plus alfentanil (5 µg/kg) or diazepam (0.1 mg/kg) plus fentanyl (1 µg/kg). Each narcotic was diluted with a water soluble emulsion of diazepam to 10 ml in normal saline and administered as 0.1 ml/kg by intravenous injection at a rate of 0.03 ml/kg/min. Retrobulbar block was performed with 10 ml 0.25% bupivacaine. Pulse oximetry, respiratory rate, blood pressure and ECG were continuously monitored before injection and throughout surgery. All patients had oxygen administered by mask.

Results: The patient demography (age, weight, ASA, sex, co-existing disease profile and drug therapy) was similar in both groups. There was no change in heart rate or blood pressure following administration of either study drug. Pre-injection and post-injection oxygen saturation was inversely related to age in both groups (pre-injection $r = -0.77$, $p < 6.0^{-6}$, post-injection $r = -0.54$, $p = 0.003$) but there was a significant change in slope (0.10 vs 0.25) such that the magnitude of oxygen desaturation post-injection increased with age. Thus oxygen saturation 5 min after injection averaged 96% in patients less than 60 years and 89% in patients over 80 years compared to pre-injection values of 99% and 97% respectively. The weighted average oxygen saturations (corrected for age) were similar for both narcotics before and 5 minutes after injection. Recovery of oxygen desaturation was significantly faster with alfentanil/diazepam than fentanyl/diazepam.

TABLE Oxygen Saturation Corrected for Age

| | Pre-inj | 5min | 10min | 15min | 20min | 25min | 30min |
|---|---|---|---|---|---|---|---|
| ALFENTANIL | 97.5 | 91.9 | 95.2 | 96.2 | 96.7 | 97.2 | 96.8 |
| FENTANYL | 96.8 | 91.3 | 92.4 | 93.2 | 94.3 | 95.8 | 96.2 |
| P | 0.09 | 0.52 | $3.5^{-1}$ | $8.8^{-1}$ | $4.0^{-4}$ | $8.6^{-1}$ | 0.71 |

There were 10 patients (28.6%) in each group who had oxygen saturations less than 90% and 3 in each group with less than 85% 5 min after injection. In all cases this coincided with depression of respiratory rate during sleep and was quickly reversed by vocal command. For alfentanyl/diazepam the reduction in weighted average oxygen saturation was significant up to 15 min after injection whereas this was significant up to 25 min after injection with fentanyl/diazepam. Logistic regression analysis of all demographic factors confirmed that age and both study drugs were the only significant risk factors for oxygen desaturation.

Discussion: Oxygen saturation is decreased to the same degree after alfentanyl/diazepam and fentanyl/diazepam but recovery is faster with alfentanil/diazepam. Oxygen saturation decreases with age but after narcotic/diazepam injection is significantly further decreased due to centrally mediated respiratory depression. We conclude that the combination of low-dose alfentanil/diazepam is suitable for cataract surgery providing good analgesia and sedation with rapid recovery. However careful monitoring of oxygen is mandatory to avoid the potential hazards of periodic bradypnoea in elderly patients.

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## INTRA-ARTICULAR BUPIVACAINE DOES NOT DECREASE NARCOTIC REQUIREMENTS AFTER ARTHROSCOPIC SURGERY IN ADOLESCENTS

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It has been a common practice of many orthopaedic surgeons to instill bupivacaine into the knee joint prior to completion of arthroscopic surgery in order to provide postoperative pain relief. This prospective, double-blind study investigates the efficacy of that technique in providing adequate analgesia and decreasing postoperative narcotic requirements in teenage children following diagnostic arthroscopy and arthroscopic knee surgery.

Methods: Institutional approval and patient as well as parental consent were obtained for this randomized double blind study. Forty-three unpremedicated healthy (ASA PS 1 or 2) patients, ages 13 to 18 years, scheduled for arthroscopic knee surgery by the same surgeon were entered sequentially into the study. Prior to arrival into the operating room suite all patients were instructed in the use of the Linear Analogue Pain Scale.[1] Following intravenous induction (thiamylal 5-7 mg/kg) anaesthesia was maintained with $N_2O/O_2$/halothane or isoflurane. The trachea was intubated without the use of succinylcholine (to avoid the possibility of postoperative muscle pain). Ventilation was assisted or controlled as deemed appropriate by the anaesthetist. No intraoperative narcotics were administered. All patients received intravenous fluid volume equal to 4 times their calculated hourly maintenance rate during the first hour of surgery.

Just prior to the completion of the arthoscopic procedure, the surgeon injected the contents of a sequentially numbered vial into the knee joint through the arthoscope. All vials were prepared and assigned by the pharmacy using a computer generated random number program. Each vial contained either placebo (saline) or 0.25% bupivacaine (maximum dose 2 $mg.kg^{-1}$). Following emergence from anaesthesia, the patients were transported to the Post Anaesthesia Care Unit (PACU) where their pain was evaluated by a trained observer at predetermined intervals with an Objective Pain Scale.[2] Simultaneously, patients rated the intensity of their pain with a 0-10 Linear Analogue Pain Scale.[1] A pain evaluation (score) $\geq$ 6 on either scale on two sequential evaluations separated by five minutes was an indication that severe pain was present and that treatment with intravenous fentanyl (1-2 $mcg.kg^{-1}$) was required. Patients were discharged home when they met previously established standard discharge criteria. A follow-up interview was conducted by telephone 24 hours later. The number of patients who received intravenous fentanyl (pain score $\geq$ 6) in the bupivacaine group was compared to those in the placebo group using chi-square analysis. $P<.05$ was considered significant.

Results: Twenty-one patients received intra-articular bupivacaine and 22 patients received saline. The number of patients in each group who scored $\geq$ 6 on either pain scale and therefore received intravenous fentanyl was not significantly different among the two groups (table).

| Pain Score | Bupivacaine (n = 21) | Placebo (n = 22) |
|---|---|---|
| $\geq$ 6 (fentanyl administered) | 4(19%) | 9(41%) |
| < 6 (no fentanyl) | 17(81%) | 13(59%) |
| $X^2 = 2.43$ | | P = .12 |

Discussion: Arthroscopy of the knee is a common procedure in the practice of sports medicine. Most of the patients are otherwise healthy and are frequently discharged home on the day of surgery. Since one of the goals of ambulatory anaesthesia and surgery is to provide prompt and pain free recovery, there is a tendency to use local and regional anaesthetic techniques rather than narcotic analgesics in as many patients as possible. Intra-wound irrigation with local anesthetics has been found to be effective following herniorrhaphy in children.[3] Unfortunately intra-articular bupivacaine irrigation of the knee, although very simple to perform, was not effective in reducing the requirement for narcotic analgesics following arthroscopic knee surgery in adolescents. This finding is in agreement with previous reports in adults.[4] These results may be due to the fact that there is only minimal pain following most arthroscopic surgery, that bupivacaine fails to penetrate intact synovium and joint capsules, or that pain following arthroscopy originates outside the capsule of the knee joint.

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# EXTENSIVE APPLICATION OF EPIDURAL ANAESTHESIA AND ANALGESIA IN A TEACHING UNIVERSITY HOSPITAL.

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Introduction. Epidural anaesthesia and analgesia (EAA) has many adnvantages over general inhalational anaesthesia. EAA blocks afferent pain pathways from the surgical site and thereby markedly attenuates release of various stress hormones. Perioperative pain after abdominal procedures can be abolished almost completely by EAA with local anaesthetics and opioids realizing virtually stress-free surgery and recovery. EAA induced sympathetic block without hypotension reduces left ventricular work load and improves myocardial oxygen supply and consumption relationship(1).

Other salutary effects of EAA include, attenuated hypertensive response to endotracheal intubation, decreased intraoperative blood loss, improved postoperative nitrogen balance and pulmonary function, no organ toxicity and markedly improved overall outcome in high-risk surgical patients(2).

However, unacceptably high incidence of complications related to epidural puncture(3) intimidated many anaesthesiologists into staying away from it.

We have been persuing EAA as a major anaesthetic technique at a teaching university hospital with excellent results. Applicability and actual incidence of complications of EAA at our department are surveyed and reported here.

Method. All the anaesthesia residents were encouraged to get expertise in performing mid and high thoracic epidural block as soon as they acquire fundamental techniques of general anaesthesia and lumbar epidural block.

Epidural puncture was made at proximity to the mid-point of the operative area, with blunt Tuohy needle and normal saline filled glass syringe for detecting loss of resistance. Local anaestheic was injectied through epidural catheter.

Lower abdominal and extremity procedures were performed under lumbar epidural block with supplemental intravenous sedatives and analgesics. Upper abdominal procedures were performed under mid thoracic epidural block without endotracheal intubation. Patients for total and proximal gastrectomy were intubated but no long acting muscle relaxants or potent inhaled anaesthetics were added.

Intrathoracic, chest wall and some cervical procedures were done under high thoracic epidural block, mostly with endotracheal intubation. Many intrathoracic cases received epidural catheter insertion for postoperative analgesia, and these patients were not included in epidural anaesthesia.

Results.

1. Applicability of EAA and the site of operation.

There were 40010 anaesthetics in total during the study period, and EAA was the major anaesthetic technique in 15902 patients (39.7%).

79.5% and 71.1% of upper and lower abdominal procedures were done under EAA. Some neck, chest wall and intrathoracic procedures were also done under EAA.

2. Incidence of epidural puncture related complications.

There were 17500 patients who received epidural puncture in this series, and EAA was the major technique in 15902 patients. Epidural block was unsuccessful in 741 patients (4.2%). Of these, succesful epidural block was attained in 471 patients (2.7%) after re-puncture. Anaesthetic method was changed to subarachnoid block or general anaesthesia in 270 patients (1.5%).

Bleeding and intravascular cannulation were seen in 79 patients (0.5%). Inadvertent dural puncture occurred in 64 patients (0.4%). Frank local anaesthetic toxicity was seen in 4 patients (0.02%).

Inadvertent dural puncture, bleeding, intravascula cannulation and inadequate block occurred more frequently in lumbar epidural than in thoracic epidural puncture. There were no dire complications such as epidural hematoma, permanent neural or brain damage due to epidural puncture.

Discussion. EAA has aforementaioned numerous advantages over general inhalational anaesthesia and can be utilized as a major technique at a teaching university hospital. As much as 40% of all the surgical procedures at a typical general hospital could be managed under EAA, which contrasts markedly with the reported statistics of a typical Canadian hospital(4).

Allowing qualified trainees to perform mid and high thoracic epidural puncture at an early stage of training did not increase the incidence of epidural puncture related complications. Occasional unsuccessful blocks with the incidence of less than 5% are not completely avoidable, and re-puncture often results in successful block.

Bleeding and intravascular cannulations are most common potentially dangerous complications of epidural puncture. Inadvertent dural puncture occurred in 0.4%, which is well below the suggested 1% threshold of wrong puncture technique(5), or early report of unacceptable incidence of 2.5%(3).

It is significant to note that none of these small numbers of complications developed into incapacitating states such as intractable headache, epidural hematoma, permanent neural or brain damage.

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## ANALGESIA AND POSTOPERATIVE HYPOXAEMIA AFTER GASTRIC PARTITION WITH AND WITHOUT BUPIVACAINE WOUND INFILTRATION

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Introduction. Wound infiltration with local anaesthetics to reduce postoperative pain and narcotic consumption has yielded conflicting results (1-3). The present study was designed to examine the effect of intraoperative bupivacaine wound infiltration on postoperative pain control, morphine consumption, and oxygen saturation ($SaO_2$) in morbidly obese patients after vertical banded gastric partition.

Methods. The study was approved by the institutional review board and written, informed consent was obtained from all patients who participated in the study. Patients (n = 58) were randomized to receive either 50 ml of normal saline or bupivacaine, 0.5% with 1:200,000 epinephrine, infiltrated into the abdominal incision just before wound closure. Postoperative analgesia consisted of patient-controlled morphine for all patients. For the first 24 hr after operation, the following data were recorded: total amount of morphine administered, patients' assessments of pain as determined from a questionnaire every 4 hr, and $SaO_2$ determined by pulse oximetry every 2 hr while patients breathed room air.

Results. In over 40% of patients, $SaO_2$ was < 90% at least one time. $SaO_2$ decreased over time in both groups and differed between them only at 20 hr when $SaO_2$ was lower with bupivacaine ($P < 0.05$; Fig.). Morphine usage did not differ between the two groups--69.5 + 5.8 mg with saline and 76.7 + 5.8 mg with bupivacaine (mean ± SEM), nor did pain assessment.

Discussion. Gastric partition patients are at a high risk of suffering postoperative hypoxaemia, and the data from our study show that the risk is highest 20-24 hr after operation. Bupivacaine may have been ineffective because of infiltration technique, a large volume of distribution of bupivacaine in these obese patients, or both. This study demonstrates that postoperative respiratory status in this patient population should be monitored closely.

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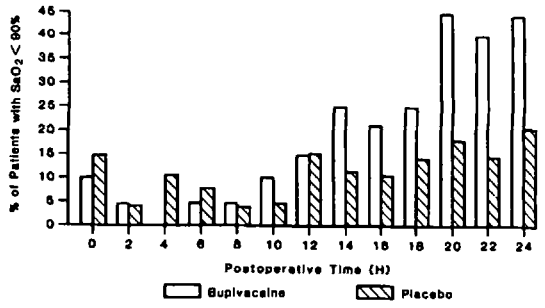


Figure. Postoperative oxygen saturation ($SaO_2$) after wound infiltration with bupivacaine (n = 29) (open columns) or saline (n = 29) (lined columns). *$P < 0.05$ compared with saline.

# BUPIVACAINE ADDED TO EPIDURAL FENTANYL DOES NOT IMPROVE POSTOPERATIVE ANALGESIA

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## Introduction:

Epidural infusions of fentanyl combined with bupivacaine have been shown to be effective for postoperative analgesia.[1] Compared to epidural fentanyl this combination claims to offer both improved analgesia and reduced side effects. To our knowledge a random double-blind comparison has not been performed. The purpose of this study was to compare the combination of fentanyl and bupivacaine to fentanyl alone in terms of both analgesia and side effects.

## Methods:

Following institutional approval and written informed consent, twenty one patients scheduled for elective total knee joint replacement were assigned in a random, double-blind fashion, to receive a continuous epidural infusion of either fentanyl or a mixture of fentanyl and bupivacaine for postoperative analgesia. Infusion concentrations were fentanyl 10 μg/ml with or without bupivacaine 1 mg/ml. Patients with significant cardiovascular disease, coagulopathy, previous spinal surgery, or age over 75 were excluded. Prior to surgery an epidural catheter was inserted at the $L_{2-3}$ or $L_{3-4}$ interspace. Epidural anaesthesia was induced with 2% $CO_2$ lidocaine and 0.5% bupivacaine. Intravenous sedation was administered as necessary. Postoperatively, upon return of motor function, the epidural infusion was started at 6 ml/hr. Analgesia was assessed using a visual analogue scale, (0 = no pain and 100 = worse pain ever). The presence of side effects were noted including; sensory loss to both pinprick and temperature, motor blockade, and postural hypotension. Assessments were made at discharge from recovery room, the afternoon of the operative day, the morning and afternoon of the first postoperative day, and the morning of the second postoperative day. Inadequate analgesia was treated with a 3 ml bolus and increasing the infusion rate by 2 ml/hr. Demographic data was analyzed using unpaired t-tests or $\chi$-square for parametric and nonparametric data respectively. Pain score and infusion rate results were compared using two factor ANOVA for repeated measures.

## Results:

The demographic data is presented in the table. The groups were similar with respect to age and weight. There was however a difference in sex and height distribution. Four patients, (two from each group), were removed from the study due to catheter dislodgement. One patient in the fentanyl and bupivacaine group developed significant hypotension and respiratory depression requiring treatment with fluids and naloxone. There were no detectable differences in pain scores or infusion rates for the two groups (Figures 1&2 respectively). There were also no detectable differences in the incidence of side effects between the two groups. A single patient in the fentanyl-bupivacaine group had unilateral motor and sensory loss ($L_{3-4}$).

| | Fentanyl | Mixture |
|---|---|---|
| Number of Patients | 10 | 11 |
| Sex (male/female) | 8/2 | 2/9* |
| Age (yr) | 69±4 | 65±5 |
| Height (cm) | 174±9 | 164±9* |
| Weight (kg) | 82±14 | 89±18 |

* different from fentanyl $p<0.05$

**Figure 1.**

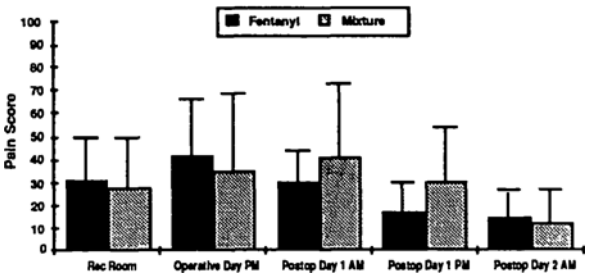
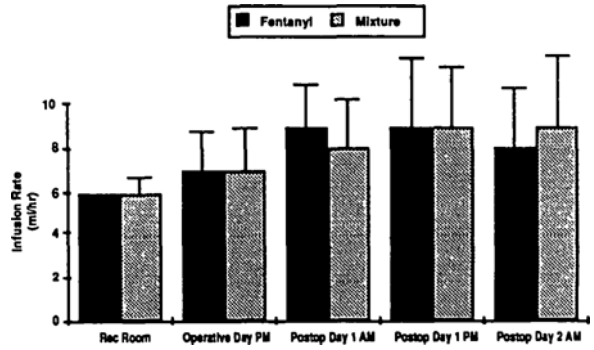



**Figure 2.**




## Discussion:

We found no clinically or statistically significant difference between the two groups with respect to pain scores, amount of narcotic required or the presence of side effects. We conclude that the addition of bupivacaine to an epidural fentanyl infusion does **not** improve postoperative analgesia and potentially **increases** morbidity.

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## COMPARISON OF TWO METHODS OF LIMB EXSANGUINATION

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The success of intravenous regional anaesthesia (IVRA) is dependant to a great extent on the degree of exsanguination of the limb involved. In order to compare the efficacy of two commonly used methods of exsanguination: elevation of the limb to 45 degrees for 3 minutes (EOL) and wrapping the limb with an Esmarch bandage (EB), a series of experiments were carried out using fluid displacement from a water bath to measure the volumes involved.

**Method**

A closed water bath, into which a subject's limb could be inserted via a side port opening into a plastic bag, was linked by means of a narrow tube to a measuring cylinder.

(1) A tourniquet was applied to the subject's limb and inflated to occlude blood flow. After inserting the limb into the bath the latter was filled with water. The tourniquet was released and the tank refilled to capacity. The volume required to refill the bath represented the degree of exsanguination due to the hydrostatic pressure of the water in the bath and this volume was recorded (EH).

(2) The limb was next exsanguinated by EOL after which the tourniquet was inflated to occlude arterial inflow. The arm was positioned in the bath, the bath filled and the tourniquet deflated. The volume of water displaced was measured and added to the EH. The sum represented the volume of blood exsanguinated from the limb (EV1).

(3) Step (2) was repeated exsanguinating the limb by EB and EV calculated (EV2). Consistency of exsanguination was achieved by having all EB applied by the same investigator who also applied all the tourniquets.

(4) The limb was removed from the bath and the volume of water required to refill the bath was measured. This, added to EH, represented the total limb volume (LV). $EV_1$ and $EV_2$ were compared for each limb.

**Results**

Measurements were made on 21 upper limbs of 13 subjects. The mean and standard deviation for EV1 and EV2 were calculated, Table 1.

| | |
|---|---|
| EV1 | 27.0±14.1 |
| EV2 | 59.9±19.2 |

Comparison with two-tailed paired student t Á=0.001 gave a value for p of $< 0.01$.

**Conclusions**

The results suggest that exsanguination by EB is significantly more effective than by EOL. During IVRA in which efficient diffusion of local anaesthetic agent is required, exsanguination with EB would increase the reliability of the technique. This experimental method also allows for evaluation of other methods of limb exsanguination.

# Hypobaric Spinal Anesthesia in Percutaneous Nephrostomy

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INTRODUCTION:
Percutaneous nephrostomy, originally described 30 years ago has virtually replaced the need for surgical nephrostomy. The transcutaneous placement of a catheter into the renal pelvis is a safe, simple and effective method for the relief of supravesical obstruction. Additionally, it serves as access for such interventional procedures as stricture dilatation, biopsies of the renal pelvis and stone removal(1). The procedure involves the percutaneous placement of a needle through the posterior flank into the renal pelvis with subsequent dilatation to permit the placement of a large bore catheter. Infiltration of the tract with lidocaine has traditionally been the most commonly utilized anesthetic method. Unfortunately, this method does not provide adequate pain relief during tract dilatation or intervention manipulation of the genitourinary tract. In this study hypobaric spinal anesthesia in the prone patient was evaluated for its ability to provide adequate regional anesthesia during percutaneous nephrostomy.

PERCUTANEOUS NEPHROSTOMY
Percutaneous nephrostomy (PCN) is performed with the patient in the prone position. Under floroscopic guidance a needle is inserted through the posterior flank, below the 12th rib, into the posterior calix of the kidney. A guide wire is inserted through the needle into the renal pelvis. Over the guide wire the tract is dialated to 11 fr. A 10 fr. catheter is placed in the renal pelvis and secured to permit drainage. Alternatively, through an established tract interventional manipulation of the genitourinary tract, such as stone, extraction may be accomplished.

METHODS:
Five patients received hypobaric spinal anesthesia prior to undergoing percutaneous nephrostomy. The patients were placed prone on the radiographic examination table. The use of floroscopy greatly simplified the placement of a 25 gauge needle into the subarachnoid space at the $L_3$-$L_4$ interspace. 0.5ml of 0.5% bupivicaine mixed with 1.5ml of sterile $H_2O$ was injected slowly and the spinal needle was removed. The segmental spread of analgesia was studied by pinprick and a sensory level was established. Motor nerve block was evaluated using a modified Bromage scale (2) every 30 min. Hemodynamic monitoring was performed throughout the procedure with BP and pulse rate recorded every 15 mins. Sensitivity to pinprick was evaluated every 30 mins until the anesthetic effect dissapated.

RESULTS:
After hypobaric spinal anesthesia the sensory level in 3 patients extended from $T_8$-$S_1$ and in 2 patients from $T_{10}$-$L_5$. None of the patients had any significant loss of motor function and all had a score of zero on the modified bromage scale. All five patients denied experiencing any discomfort during the procedure. Two patients had an episode of mild hypotension which was easily reversed with rapid hydration. The length of the analgesic effect ranged from 90 to 180 minutes.

DISCUSSION
Hypobaric spinal anesthesia is particularly effective in percutaneous nephrostomy for several reasons:
1: In the prone patient hypobaric bupivicaine produced a sensory block with minimal impairment of motor function. This effect is presumably due to the dorsal distribution of hypobaric solution in the subarchnoid space of the prone patient. This assymetric distribution will predominately effect the dorsal nerve roots with relative sparing of the central nerve roots.
2: Since hypobaric solutions remain localized to the area of the injection, minimal side effects due to sympathetic blockage occur. (3)
3: The presence of floroscopy permits rapid cannulation of the subarachnoid space. Even in patients with severe degenetive changes in the lumbar spine, spinal anesthesia was easily and rapidly accomplished.

The use of hypobaric spinal anesthesia for percutaneous nephrostomy has not been previously described. This study demonstrates that this anesthetic technique is both safe and effective for intraventional urologic technique.

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## THE USE OF REGULARLY SCHEDULED ORAL MORPHINE IN THE TREATMENT OF POST SURGICAL PAIN SECONDARY TO TOTAL HIP ARTHROPLASTY

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INTRODUCTION. Post surgical pain (PSP) is a common form of acute pain. Effective treatment of PSP is important for recovery from surgical procedures. However, many reports have shown that treatment of PSP is often inadequate despite the availability of many effective narcotic analgesic agents. One reason for this inappropriate pain management, is the continued use of intermittent or on demand intramuscular narcotic administration (1). The oral route of narcotic administration for the treatment of PSP has not been extensively investigated (2). This pilot study was designed to examine the efficacy and patient tolerance of regularly scheduled oral morphine in the treatment of PSP.

METHODS. After institutional ethics committee approval patients who were scheduled to undergo total hip arthroplasty were enrolled in the study after informed consent was obtained. All patients had their PSP controlled initially with 1-4mg of morphine I.V. as needed every 10-15 minutes while in the post-anaesthetic room. Upon arrival on the ward, all patients received 20mg of oral morphine. This was repeated q4h at regularly scheduled times as designated by the pharmacy. If breakthrough pain occurred during the study, the patients were instructed to request medication and were given a 10mg dose of oral morphine. When this additional morphine was requested, the next regularly scheduled oral solution was increased by 10 mg. Pain intensity was evaluated prior to each oral dose using a 10 cm visual analog scale (VAS). Level of sedation was assessed before each dose using a 4 point scale where 1 stands for awake, 2 - easily arousable, 3 - difficult to arouse, and 4 - unarousable. Respiratory rate was also recorded prior to each dose. If the patient scored either a 3 or 4 on the sedation scale, or their respiratory rate was less than 10, the dose was omitted. The incidence of nausea and vomiting was also recorded during the study period. The patients were removed from the study when the investigators felt that any subsequent pain could be controlled effectively with PRN acetaminophen with codeine. Antinauseants were used at the discretion of the investigators.

RESULTS. Thirteen patients were enrolled in the study ranging in age from 31 to 83 years. Of these 13 patients, 11 completed the study. One patient was withdrawn from the study after just 2 doses of oral morphine due to inadequate pain relief. This patient had a history of extreme pain following a previous total hip arthroplasty and required high levels of intramuscular narcotics and a psychiatric intervention. The second patient was withdrawn after 24 hours due to epigastric pain unrelieved by antacids. It was difficult to determine if oral morphine was the cause of this discomfort, but the patient was withdrawn from the study despite excellent PSP control. All of the patients completing the study appeared to have good PSP control (see graph) and only 3 patients requested a PRN oral morphine dose at anytime during the study. No parenteral narcotics were required. Patients remained on regularly scheduled oral morphine for approximately 48 hours. Five patients had one episode of vomiting, while one patient had two episodes of emesis. Vomiting occurred only when the patients were moved, were being ambulated, or drank excessive amounts of fluid. These patients did not report significant nausea before or after the vomiting episodes. Sedation scores were (1) or (2) in all study patients for the duration of the study with the exception of one patient who had a single sedation score of (3). This occurred following a dosage increase (20 to 30mg) 36 hours after surgery and as per study protocol the subsequent dose was withheld and the patient exhibited no further problems.

DISCUSSION. The use of 20mg of oral morphine every four hours for the treatment of PSP secondary to total hip arthroplasty appeared to be effective and well tolerated by this patient population. This method of PSP treatment has many potential advantages over the use of intermittent intramuscular morphine injections and other forms of PSP treatment as it is easier to administer, titrate, has high patient acceptability and is inexpensive. A double-blind controlled study is presently underway to further evaluate this method of PSP treatment.

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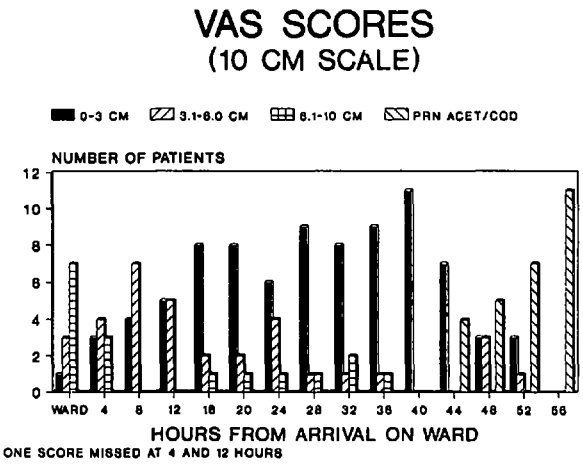

# POST SPINAL HEADACHE: A COMPARISON OF MIDLINE AND LAMINAR APPROACHES

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## INTRODUCTION

It is generally accepted that post spinal headache (P.S.H.) results from a continuing loss of cerebrospinal fluid (C.S.F.) through the dural opening left by the spinal needle. The size of needle used to create the dural hole has proven to be an important determinant of P.S.H. Clinical studies demonstrate an increased frequency of headache following dural punctures made with larger needles and a reduced number when thinner needles are used. The relationship between needle size and the subsequent shape and dimensions of the hole created has been studied only in laboratory models using human dural samples.[1,2] Midline punctures made with larger needles directed perpendicular to the dura produce correspondingly larger holes and leak fluid at a significantly higher rate than those made by smaller needles. This observation would account for the difference in frequency of headaches noted with needles of varying size. However, another factor which significantly affects leakage is the "angle of approach"[1] made by the needle with the longitudinal fibres of the dura. Altering the angle from 90° to 30° significantly lessens fluid loss through the puncture site. It has been postulated that the oblique angle of entry produces a flap valve mechanism which more effectively seals the hole left by the withdrawn needle.

In clinical practice, angles of entry similar to those used in laboratory studies are recreated when the midline and laminar approaches to dural puncture are employed (Figure 268,269).[3] The purpose of the current study is to determine whether use of the laminar technique is significant in reducing the occurrence of P.S.H. when compared to the midline approach.

## METHODS

Patients age 50 years and under who agreed to spinal anaesthesia following discussion of potential complications were randomized to receive dural puncture performed by either a midline or laminar approach. The anaesthetic technique was standardized for all patients and varied only in the method of needle insertion. It incorporated the following: performance of dural puncture in the sitting position by a single anaesthetist, use of a 22-gauge Becton-Dickson needle with the bevel oriented in the long axis of the dura, and infusion of two litres of crystalloid solution. Anaesthetic agents consisted of lidocaine (5%) or hyperbaric pontocaine (0.5%) with or without adrenaline.

Midline punctures were carried out at the $L_3$ $L_4$ interspace in the usual manner. Needle placements for the laminar approach began 1-2 cm lateral to the centre of the $L_4$ $L_5$ interspace. The spinal needle was directed towards the midline in an antero-cephelad direction to penetrate the dura at the higher $L_3$ $L_4$ interspace.

All patients were questioned 3 to 21 days following surgery for any anaesthetic related problems. Posturally induced headaches were classified as minimal, mild, moderate, or severe.[4] Statistical comparisons were made using Chi-square analysis. $P < 0.05$ was considered significant.

## RESULTS

Table I indicates the range of angles and distances encountered while performing dural puncture.

Interviews with 81 patients receiving single dural punctures indicated that one of 36 patients (2.8%) in the midline group and three of 45 (6.7%) in the laminar group developed moderate P.S.H.'s. Minimal headaches were observed in one patient of each group. No significant difference was present between groups.

## DISCUSSION/CONCLUSIONS

It was concluded that a 22-gauge, Quincke point spinal needle piercing the dura at an acute angle does not reduce the incidence of P.S.H. The discrepancy between predicted and actual outcome could be due to several hypothetical causes. In vitro dural thicknesses of 0.5-2.0 mm likely represent some post mortem shrinkage and thickening of the tissue. Estimates made during laminar surgery place the in vivo thickness to be 0.2-0.3 mm, which would not be sufficient to permit creation of an effective self-sealing flap. Also, the dural opening may be enlarged or changed in shape if movement of the dura across the sharp bevel occurs when the bevel is engaged within the dura. Furthermore, flexion of the needle's shaft from uneven pressure on the hub exerted by the thumb and index finger may be transmitted to the needle tip, producing a cutting movement in the tip at a time when it passes into or is pulled out of the dura.

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| TABLE I | MIDLINE | LAMINAR |
|---|---|---|
| Angle in sagittal plane | 80°-90° | 20°-55° |
| Angle in transverse plane | 0°-3° | 7°-20° |
| Distance from midline | 0 cm | 1-2 cm |

Figure 268. The three approaches for performing subarachnoid block. *A*, Midline approach. *B*, Lateral approach. *C*, Laminar approach. Also see Figure 269.

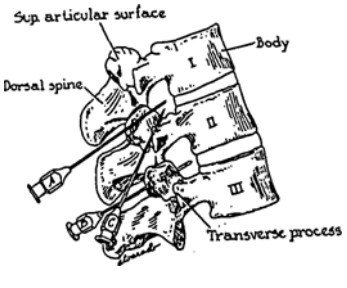
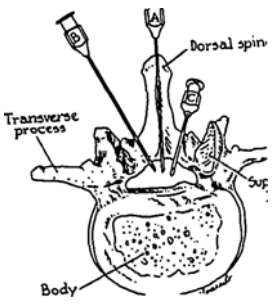



Figure 269. The three approaches in performing lumbar puncture. *A*, Conventional approach. *B*, Lateral approach. *C*, Laminar approach.



## THE EFFECTS OF THREE KINDS OF ANESTHESIA ON LOWER ESOPHAGEAL SPHINCTER PRESSURE

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Introduction: By using esophageal manometric technique, the changes of lower esophageal sphincter pressure (LESP)were observed after epidural block, sodium oxybutyrate (r-OH)-ketamine intravenous anesthesia and intravenous procaine balanced anesthesia to provide reference basis for clinical anesthesia.

Methods: Thirty patients (15 each male and female) of ASA Grade I, aged 19-56 years, undergoing selective surgery were divided into three groups of 10 each according to different anesthetic methods.All of them had no history of gastrointestinal disease or of receiving drug therapy. Group I,the patients underwent epidural block, with about 12ml of a mixture of 1.33%lidocaine and 0.16%dicaine, injected at $T_{8-9}$. The analgesia levels reached $T_{5-12}$ in 30 min. Group II, patients were given r-OH (80 mg/kg) and ketamine (1.5mg/kg)intravenously. Group III,the infusion of 1%procaine containing 0.06%succinylcholine was adopted at a rate of 1mg/kg/min on average. The controlled ventilation was performed with a face mask to supply sufficient oxygen when respiration depressed. The trachea was intubated and connected with an anesthetic machine about 20 min after the begining of infusion.

The esophageal manometry was performed with a constantly perfused catheter. All the patients were instructed to fast and not given premedication prior to every study. An open-tipped polyvinyl chloride catheter(1mm, i.d.) passed via the nose into the stomach. The lumen was continuously perfused with normal saline at a rate of 0.6ml/min by means of a infusion pump, and was connected to a external transducer, the output from which was transmitted through the preamplifier to a recorder. In group I, II, III, the gastric pressure(GP), LESP, barrier pressure (BrP), pressure of esophageal body were measured by stationary pull-through technique 5 min before and 30, 20, 30min after the beginning of inducement. All of those steps were finished before incision.

Results: In group I, there was no difference in LESP compared to the value measured before anesthesia. No differences were noted in LESP, GP and BrP after r-OH plus ketamine intravenous anesthesia. In group III, LESP decreased from 20.15 to 11.15mmHg on average ($P < 0.01$),which made BrP decrease from 13.75 to 6.15 mmHg on average ($P < 0.01$) (Table).

Discussion: It is now generally believed that the major barrier preventing reflux is LESP. The presence of reflux is usually associated with low LESP (0 - 5 mmHg). High LESP values($> 15$ mmHg) are usually not associated with reflux (1,2,3). In the present study, we observed that the mixture of procaine plus succinylcholine depressed markedly LESP, BrP (45%, 55%).These changes relate to procaine seeing that succinylcholine does not affect smooth muscle directly.Therefore, there is the potential risk of reflux and aspiration.The effective measures to prevent reflux should be taken. There was no change in LESP although sympathetic innervation of lower esophageal sphincter and stomach was block because of this epidural anesthesia. A slight increase of BrP resulted from a significant decrease of GP ($P < 0.01$). The decrease of GP is probably due to the relaxation of abdominal muscles. The results suggest that the epidural block itself would not increase a risk of reflux.

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TABLE (Mean±SD)

| | | GP (mmHg) | LESP (mmHg) | BrP (mmHg) |
|---|---|---|---|---|
| I (n=10) | BA* | 6.15±3.69 | 19.75±4.76 | 13.60±3.92 |
| | AA* | 4.30±3.43 | 19.95±4.18 | 15.65±4.40 |
| | P | $< 0.01$ | $> 0.05$ | $> 0.05$ |
| II (n=10) | BA* | 5.80±2.29 | 19.65±3.95 | 13.85±4.61 |
| | AA* | 5.50±2.77 | 18.15±5.14 | 12.65±6.08 |
| | P | $> 0.05$ | $> 0.05$ | $> 0.05$ |
| III (n=10) | BA* | 6.40±2.60 | 20.15±4.55 | 13.75±4.48 |
| | AA* | 5.00±1.67 | 11.15±3.69 | 6.15±3.89 |
| | P | $> 0.05$ | $< 0.01$ | $< 0.01$ |

BA* = Before Anesthesia
AA* = After Anesthesia

# INTRATHECAL HYPOBARIC FENTANYL WITH LIDOCAINE FOR HIP SURGERY

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INTRODUCTION:
When opioids are injected in the intrathecal and epidural spaces they produce selective block of pain conduction.(1) Opioids act on receptors located in the substantia gelatinosa of dorsal horn of the spinal cord to produce sensory, but not motor or sympathetic blockade.(2) We have found that fentanyl and xylocaine 1% are hypobaric. We wanted to evaluate the efficacy of the combination of these drugs to provide a good operative analgesia and hemodynamic stability.

METHODS:
After Research Committee approval five elderly ASA III and IV class of patient undergoing orthopedic surgery (hemiarthroplasty, bipolar hip replacement) were studied. Patients who had evidence of coagulopathy or known allergy to opioids were excluded. Intravenous line placement was achieved. The patients were monitored with EKG, automatic blood pressure monitor, pulse oximeter and nasopharyngeal temperature probe.
A spinal puncture was performed at L3-4 or L2-3 interspace aseptically with the patient either in the right or left lateral decubitus position. When free flow of clear CSF was established, fentanyl 25 mcg (0.5 ml) and xylocaine 25 mg (1% - 2.5 ml) (total 3 ml) was injected. Onset of analgesia was tested with pin prick and motor block by Bromage score and these were recorded. Arterial BP, heart rate (HR) and $SaO_2$ were monitored every 2 minutes for the first 10 minutes and then every 5 minutes throughout the procedure. Midazolam in incremental doses was used for sedation as needed. Visual analog score was used for assessment of pain in the postoperative period by the nursing staff, and the time when analgesics were first administered was recorded.

RESULTS:
We studied five patients undergoing orthopedic procedures. Good surgical anesthesia was obtained with sensory levels from T8-9 to S1-2 in all patients. Motor blockade was incomplete in all 5 patients. Before spinal anesthesia mean arterial pressure (MAP) ranged from 78-113 mm Hg and HR ranged from 64-84 beats/min.
Post-spinal anesthesia MAP ranged from 81-112 mm Hg at 5 min., 80-114 mm Hg at 10 min. and 80-109 mm Hg at 15 min. HR remained unchanged and SaO2 was maintained in all patients.(Table I)

DISCUSSION:
Administration of intrathecal opioids produces analgesia by binding to opioid receptors located in the substantia gelatinosa of the dorsal horn of the spinal cord. Fentanyl is highly lipid soluble and has a rapid onset of action and only small amounts of free drug is present in the CSF for rostral spread, thereby causing very little respiratory depression. In all five patients we studied had rapid onset of analgesia and no respiratory depression. Hemodynamic stability was maintained all throughout. All patients had postoperative analgesia lasting from 5.75 to 7 hrs. One patient had more then 10 hrs of postoperative analgesia.
From this study we conclude that selective spinal anesthesia can be achieved by a combination of intrathecal fentanyl and low dose lidocaine. This technique is good for elderly patients in whom hemodynamic stability is very important. An added benefit is good postoperative analgesia and early ambulation.(3)
We recommend the use of this technique in elderly patients who are undergoing surgery and are candidates for regional anesthesia.

TABLE I HEMODYNAMICS N=5

| | Pre Spinal | Post Spinal | | |
|---|---|---|---|---|
| | | 5min | 10 min | 15min |
| MAP mm Hg | 95±15 | 93±14.5* | 92.6±14.7* | 90.6±14.6* |
| BPM | 73.6±7.9 | 74.4±7.9* | 74.8±7.8* | 74.8±7.8* |
| SaO2% | 96±1.87 | 96.4±1.5* | 97.4±2* | 97.4±2* |

Values are Mean ± SD
* Statistically not significant
Paired t-test performed

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## SPINAL ANESTHESIA WITH PLAIN BUPIVICAINE FOR LUMBAR SPINE SURGERY.

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Introduction: Plain bupivicaine as an agent for isobaric spinal anesthesia has been reported to be unreliable (1) or unpredictable (2) despite less hemodynamic instability (3). Our experience has been a uniformly predictable level of anesthesia with minimal alteration in heart rate or blood pressure, even in sick or elderly patients. We report our results with isobaric bupivicaine with epinephrine for lumbar spinal surgery.

Method: Charts of twenty-three consecutive patients for lumbar spinal surgery (laminectomy, discectomy, fusion) between March and November of 1989 were reviewed. All patients received spinal anesthesia in the sitting position with 0.5% plain bupivicaine with 0.2 mg epinephrine via 22 guage, sharp spinal needle at either $L_{2-3}$ $L_{3-4}$ or $L_{4-5}$. Age, ASA status, maximum level achieved, dose and hemodynamic treatment was identified. Statistical analysis was made with student's T-Test. Results are presented in Table 1.

Results: There were no failures of spinal anesthesia in the series. None of the patients required treatment for changes in heart rate or blood pressure There is no statistically significant effect of age, ASA status or dose on level. Three patients required infiltration of the upper border of the incision to either begin the surgery or complete skin closure. There were no complications and no evidence of post lumbar puncture cephalgia.

Discussion: Retrospective review of this series suggests plain bupivicaine with epinephrine to be a reliable, safe agent for spinal anesthesia for lumbar laminectomy in an older (60.6 yr), sick (ASA 2.6) population. Minimal hemodynamic alteration with a predictable, adequate level of appropriate duration is the result, as was reported by Moller (3). We observed neither the failures (4/40) or hypotension (8/40) reported by Logan (1). It may be that addition of epinephrine to bupivicaine, or epinephrine itself improves lower extremity spinal anesthesia (4). The benign effects of the prone position with spinal anesthesia is also suggested by this report. Addition of glucose (2) appears to increase level of anesthesia achieved; the prone position might not be as benign with high thoracic level. The minimal inconvenience of superficial skin infiltration is certainly preferable.

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Table 1. Bupivicaine Dose (S.E.M.)

| DOSE | 12.5 MG | 15.0 MG | >15.0 | Overall |
|---|---|---|---|---|
| AGE | 70.4(2.7) | 56.8(4.6) | 38(0.4) | 60.6(3.2) |
| ASA | 3.06 | 2.59 | 2.0 | 2.60(0.21) |
| LEVEL (thoracic) | 8.5(0.51) | 8.0(0.92) | 10 | 8.21(0.91) |
| N | 15 | 6 | 2 | 23 |

# THE EFFECT OF HYALURONIDASE ON THE SPEED OF ONSET OF RETROBULBAR ANAESTHESIA

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INTRODUCTION Hyaluronidase has been used in retrobulbar anaesthesia to improve the quality of the block. Hyaluronidase depolymerizes hyaluronic acid which is the ground substance of connective tissue. Disruption of hyaluronic acid is thought to facilitate spread of the local anaesthetic solution. A recent study demonstrated that hyaluronidase does improve the efficacy of retrobulbar anaesthesia when measured at ten, twenty, and thirty minutes after injection (1). The purpose of our study was to compare the speed on onset of retrobulbar anaesthesia with and without hyaluronidase, by evaluating the quality of the block in the first five minutes.

METHODS Hospital Ethics Committee approval was obtained for the study. Retrobulbar blocks were performed on thirty-two patients undergoing cataract surgery. The patients were randomized into two groups, one which received hyaluronidase in the local anaesthetic solution and one group which did not. Each patient was given 5 ml of local anaesthetic consisting of a 50:50 mix of 2 percent carbonated lidocaine and 0.5 percent bupivicaine. The hyaluronidase group received 15 units of hyaluronidase in the 5 ml of local anaesthetic. The ophthalmologist and the investigator were both blinded as to the content of the syringes. At one, two, and five minutes after injection the ophthalmologist made an assessment of the quality of the block. A scoring system of 0-2 was used to assess movement of the globe in each of the superior, inferior, lateral, and medial directions as well as to evaluate the movement of the upper lid. A score of 0 was given for no block, 1 for partial block, and 2 for complete akinesia. At each time interval the added scores could range from 0 to 10, 10 being complete akinesia of all five measured movements. Surgical anaesthesia was present when the upper lid was completely blocked and when the total score was greater than 8. The Mann-Whitney U Test was used to assess the results and a level of significance of P 0.01 was selected.

RESULTS Of the thirty-two patients, fifteen received hyaluronidase and seventeen did not receive hyaluronidase. At all three time intervals the quality of the block was significantly greater in the hyaluronidase group. All fifteen patients who received hyaluronidase had a sufficient block at five minutes to permit the start of surgery. Only eleven of the seventeen patients not receiving hyaluronidase had surgical anaesthesia at five minutes. None of the hyaluronidase group required reblocking while six of the non-hyaluronidase group needed an additional injection of local anaesthetic prior to surgery. Indications for supplemental injection included a score of 8 or less at 5 minutes or isolated failure to block the upper lid.

DISCUSSION This study demonstrates that the addition of hyaluronidase to the local anaesthetic solution used in a retrobulbar block will speed the onset of surgical anaesthesia. It has also been shown to reduce the requirements for supplemental injections prior to surgery.

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# POSTOPERATIVE PAIN MANAGEMENT IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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## Introduction:

Chronic pain is a common problem in patients with inflammatory bowel disease. It has recently been shown that these patients have increased intraoperative narcotic requirements.[1] It is our clinical impression that these patients also have increased postoperative narcotic requirements. We have used continuous epidural analgesia in these patients with poor results. The purpose of this study was to describe our clinical experience in patients with inflammatory bowel disease and compare postoperative narcotic requirements for patients receiving intramuscular narcotics (IM), patient controlled analgesia (PCA), and continuous epidural analgesia (CEA).

## Methods:

We retrospectively reviewed the charts of patients with ulcerative colitis and Crohn's disease who underwent laparotomy. Patients were divided into three groups. The IM group received morphine or meperidine at 3–4 hour intervals. The PCA group received intravenous morphine 1 or 2 mg with a lockout time of either 6 or 10 minutes. The CEA group received a continuous infusion of epidural fentanyl 10 μg/ml with bupivacaine 1 mg/ml at a rate of 3–10 ml/hour. To compare the groups morphine equivalents were calculated for the first three postoperative days assuming that; meperidine 75 mg = fentanyl 100 μg = morphine 10 mg.[2] Intramuscular and intravenous morphine were considered equipotent, as were intravenous and epidural fentanyl.[3] Demographic data was collected including, duration of illness, preoperative narcotic use, preoperative steroid therapy and prior surgical experience. Statistical assessment of the data was performed using ANOVA and $\chi$-square for parametric and nonparametric data respectively. A value of $p<0.05$ was considered statistically significant.

## Results:

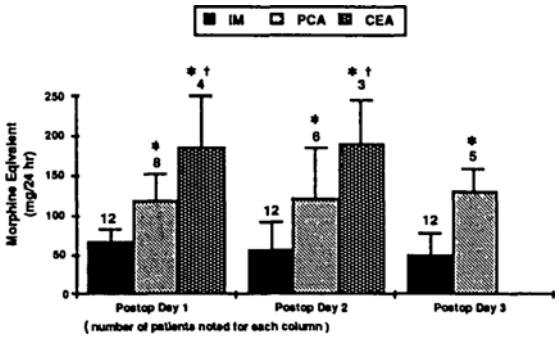
Results are shown in the table. Demographic data for the groups was similar with three exceptions. Patients in the CEA group were shorter. Patients in the PCA group were all males and only one patient in this group used narcotics preoperatively. Narcotic requirements (mean ± SD) for the first three postoperative days are shown in the figure. The IM group received the least amount of narcotics. The PCA group received almost twice this amount and the CEA group almost three times as much as the IM group. The patients in the IM group frequently received the maximum prescribed dose of narcotic. The majority of the PCA group (6/8), required morphine 2 mg/ml/injection with a 6 minute lock-out. All patients in the CEA group had evidence of motor and/or sensory block, indicating correct placement of the epidural catheter. During the first postoperative day, despite repeated boluses and rate increases, five of the nine epidural patients were discontinued because of inadequate analgesia. Complications associated with epidural analgesia included one inadvertent dural tap and eight episodes of hypotension which required treatment. Reports of excessive motor and sensory block were frequent. On the second postoperative day, two of the four remaining epidural patients had clinically significant motor and sensory loss and bupivacaine was deleted from their infusion.

## Discussion:

Patients with inflammatory bowel disease have large postoperative narcotic requirements. Although CEA has been accepted as being a superior form of postoperative analgesia, it is technically more difficult, time consuming, and expensive. Epidural analgesia is also associated with an increased morbidity. This study suggests that the benefits of continuous epidural analgesia, in this particular patient population, do ***not*** outweigh the risks.

| | IM | PCA | CEA |
|---|---|---|---|
| Total Patients (#) | 12 | 8 | 9 |
| Crohn's (#) | 5 | 2 | 5 |
| Ulcerative Colitis(#) | 7 | 6 | 4 |
| Duration of Illness (yrs) | 11±8 | 5±3 | 14±10 |
| Preop Narcotics (#) | 8 | 1* | 3 |
| Preop steroids (#) | 8 | 7 | 6 |
| Prior Surgery (#) | 5 | 3 | 6 |
| Age (yr) | 38±18 | 31±18 | 41±11 |
| Height (cm) | 173±9 | 177±5 | 165±11*† |
| Weight (kg) | 67±11 | 71±9 | 65±9 |
| Sex (m/f) | 8/4 | 8/0* | 4/5 |
| Postop Day One Morphine Equivalents (mg/24 hr) | *69±25* | *119±34** | *188±61*†* |

* different from IM $p<0.05$
† different from PCA $p<0.05$

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# TOPICAL LIPOSOMAL TETRACAINE FOR IV CANNULATION

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## Introduction:

Topical anaesthesia for IV insertion and phlebotomy is very desirable to decrease unnecessary pain. Liposomal tetracaine has been shown to decrease the pain of pinprick [1]. This study was designed to assess the efficacy of liposomal tetracaine in decreasing pain during IV cannulation.

## Methods:

150 patients presenting for elective operations were studied. Exclusion criteria were: allergy to local anaesthetics, active eczema, sensory deficits at the IV sites or history of major psychiatric disorder.

Patients served as their own controls. Subjects were radomized to receive either placebo (empty liposomes) or liposomal tetracaine (0.5% base) in a double-blind fashion. This was applied 1 - 2 1/2 hours prior to IV insertion on one of the upper limbs (test site). After application the sites were covered with a parafilm wax square to provide occlusion. Two 18 gauge IVs were started; one at the test site and one at a comparable area on the other upper limb (pain control site). This control site was untreated prior to cannulation, thus providing a baseline for pain perception. The order that the IVs were started was alternated between treated site and control site. Immediately after placing each IV, a pain score for each was obtained using a 10 point visual analogue scale. All IVs were placed prior to premedication. If the IV had a flashback of blood on insertion but could not be advanced, the scores were obtained and the IV was removed. Nine subjects were eliminated from the study: 4 because of premedication, 1 sample was washed off prematurely, 3 went early to the OR and 1 patient's operation was cancelled. Follow-up of erythema, edema, induration and blistering occurred on days 1, 2 and 7 either in person or by phone. All IVs, scores and follow-up were done by one person. Level of statistical significance was set at $p < 0.05$.

## Results:

There were 70 patients in the liposomal tetracaine (LT) group and 71 in the placebo (P) group. There was no significant difference in age, weight, or sex between the two groups. No significant difference was found between the placebo pain scores and control site scores. There was a significant difference between the LT site pain scores and its control (LT < control, $Z = -5.2$, $P < 0.001$) by the Wilcoxon matched pair signed rank test. Also, a significant difference was found between the tetracaine group scores and the placebo group scores (LT < P, $Z = -3.9$, $P < 0.001$) by the Wilcoxon rank sum test. No significant difference was found between the LT control and the P control pain scores.

Few complications occurred, with no difference in the incidence of erythema, edema or blistering in the two test groups. One person in the LT group developed transient induration at the test site.

**COMPLICATIONS:**

| SITE | ERYTHEMA | EDEMA | WHEAL | INDURATION |
|---|---|---|---|---|
| LT (n=70) | 17 | 3 | 0 | 1 |
| P (n=71) | 9 | 2 | 0 | 0 |
| CONTROL (n=141) | 27 | 4 | 0 | 0 |
| | LT vs P - ns | | | LT vs P - s |
| | LT vs C - ns | | | LT vs C - s |
| | P vs C - ns | | | P vs C - ns |

ns=non-significant, s=significant $p<0.05 (\chi^2)$

**STATISTICS:**

| | Z | P |
|---|---|---|
| LT (n=70) vs C (n=70) | -5.200 | <0.001 |
| P (n=71) vs C (n=71) | -1.400 | >0.05 |
| LT (n=70) vs P (n=71) | -3.900 | <0.001 |
| C (n=70) vs C (n=71) | -0.500 | >0.05 |

## Discussion:

To minimize the effect of variation in pain perception by different people, each patient was used as their own control.

There was a significant difference between the pain score of the LT site compared to the control site, indicating lesser pain on the LT site. No such difference was found with placebo compared to its control. Although the LT vs control was statistically significant, the magnitude of the actual difference was small, indicating that clinically the difference may not be significant.

Most other studies utilized pinprick detection for determining anaesthetic efficacy. It could be that IV cannulation is a more discriminating test of anaesthetic effect.

Liposomal tetracaine is safe, with few adverse effects and no serious side effects were demonstrated in this study. No wheal formation was seen and only one person had any induration.

Recently, McCafferty et al [2] showed superior anaesthesia to pinprick using 5% tetracaine cream compared to EMLA (eutectic mixture of local anaesthetics). Incorporation of tetracaine into liposomes should decrease systemic absorption and decrease toxicity [3]. A 2% LT is being developed for testing and may show a more clinically significant result. In conclusion, the pain reduction with 0.5% liposomal tetracaine was not clinically useful.

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## Ischiorectal Space Block for Anorectal Surgery

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General, regional and local anaesthesia have been used for anorectal surgery [1,2,3]. Advantages of local anaesthesia techniques are reduced incidence of urinary retention, post-operative analgesia, absence of spinal headache and less low back pain compared with general and spinal anaesthesia[1,4]. Unfortunately the local anesthesia techniques previously described involve painful submucosal or intrasphincteric injections and are often heavily supplemented by intravenous sedation[2,3,4,5]. We will describe a technique of local anaesthetic injection into the potential ischiorectal space which has proved to be simple, safe and efficacious.

METHODS

Local anaesthetic (lidocaine 0.6%, bupivicaine 0.18% with epinephrine 1:300,000) was placed in the ischiorectal space (20-25 cc per side) supplemented by subcutaneous wheals (10cc)(Fig 1). Ten patients were initially provided with post-operative analgesia as a pilot study which suggested that the block promoted early ambulation and added to patient comfort. Therefore twenty consecutive ASA I/II patients were approached to have the ischiorectal space block (ISB) for anorectal surgery (hemmorhoidectomy 61%, lateral subcutaneous sphincterotomy 22%, fistulotomy 11% and polypectomy 6%). The patients were guaranteed that general anaesthesia would be provided upon request. Presented are the preliminary data for the first eighteen of these surgical anaesthesisa patients (72% inpatients and 28% outpatients).

The surgeons assessed the block for adequacy of surgical anaesthesia and sphincter relaxation (Fig 2), preservation of the anatomy of the operative field and effect on hemostasis. The amount of local anaesthetic supplementation by the surgeon and the incidence of conversion to general aneaesthesia was recorded. The anaesthetist (authors) assessed the anatomy and relative ease of administering the block and all sedatives given before and after placement of the block were noted. Post-operative analgesic requirements (24 hours) including the time to first narcotic analgesic and hourly visual analogue pain scores (6 hrs) were recorded. Twenty-four hours after surgery the nurses (observers) assessed the patient's experience (excellent, good, fair or poor) prior to eliciting the patient's opinion (in person or in a telephone interview) on the same nonparametric scale (Fig 2).

RESULTS

The female to male ratio was 3:2 and the average age of each sex group was 43 yrs. Oral premedication was given to three patients (lorazepam 1.7±0.6 mg) and intravenous sedation prior to placement of the block consisted of fentanyl or morphine or alfentanil and midazolam or diazepam and/or *thiopental (*at injection of the local anaesthetic in 5 patients-Tab 1). A single patient received alfentanil 1500 ug (combined bolus and infusion) prior to the block and 1250 ug during the surgery. The duration of surgery was 27±18 minutes and the time to start of surgery from beginning the placement of the local anaesthetic was 12±2 minutes. Seven patients were given additional sedation as fentanyl 50±29 ug and midazolam 1 mg (n=3) or diazepam 2±0.4 mg (n=2) during surgery. No patient requested or required conversion to general anesthesia. The time to first narcotic analgesic was 4±2 hours (n=13) and five patients needed no analgesia.

Post-operative pain control is to be compared with a group of consecutive 'control' patients presenting for similar surgery under general anaesthesia (on completion of the local anaesthesia study). Plasma bupivicaine levels are also pending. Six blocks required supplementation with local anaesthesia by the surgeon with an average of 6±5 cc of 1% lidocaine with 1:200,000 epinephrine. Four of these patients were among the 33% of the blocks deemed difficult to administer due to anatomical variation[5]. The most frequent site of inadequate anaesthesia was in the posterior midline often associated with a fissure. Placement of the block was felt not to have had a discernable effect on anatomy or hemostasis.

DISCUSSION

Overall the ISB for surgical anaesthesia was well accepted (good or excellent) by the patients (78%) and two (11%) rated the experience as fair due to vasovagal episodes experienced post-operatively due to return of pain on the ward. Surgical conditions were adequate in all but one patient, who had inadequate relaxation of the sphincter, likely due to insufficient volumes of local aneasthetic in a large, muscular patient of 90 kg. There were no failed blocks necessitating conversion to general anaesthesia and no patient requested general anesthesia during any of the procedures. We consider the ISB a safe and effective alternative anaesthetic technique particularly when a general anaesthetic is undesirable and other regional anaesthesia techniques are either refused, relatively contraindicated or felt to be technically difficult.

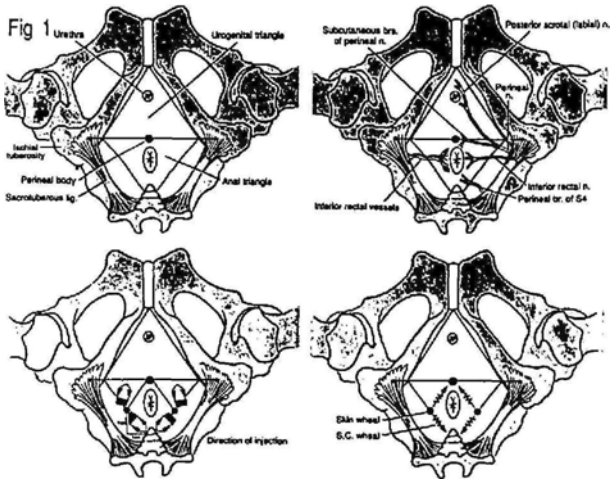
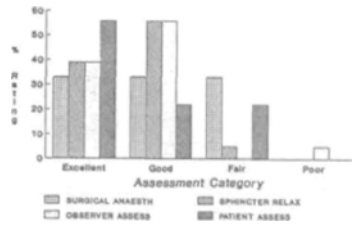



FIG 2 Ischiorectal Space Block Assessment

Tab 1 Intravenous Sedation Prior to administering ISB (n=18)

| Drug | | Dose (SD) |
|---|---|---|
| Fentanyl or Morphine or Alfenta | (n=14) | 83 ug (23) |
| | (n=1) | 10 mg |
| | (n=1) | 1.5 mg |
| PLUS | | |
| Diazepam or Midazolam and/or Thiopent | (n=9) | 4 mg (2) |
| | (n=7) | 3 mg (2) |
| | (n=5) | 65 mg (22) |

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# CONTINUOUS INFUSIONS OF LUMBAR EPIDURAL FENTANYL AND INTRAVENOUS FENTANYL FOR POST-THORACOTOMY PAIN RELIEF. I: ANALGESIC AND PHARMACOKINETIC EFFECTS

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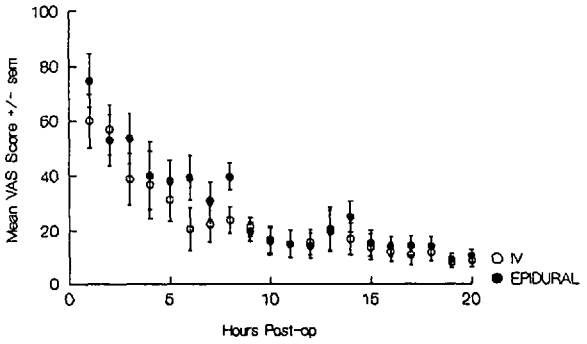
Intravenous and epidural infusions of fentanyl are effective for postoperative pain relief. However the mechanism of action of epidural fentanyl (i.e. spinal uptake vs systemic absorption) is unclear. This study compared the dose requirements, analgesic effects and systemic uptake of continuous lumbar epidural and intravenous fentanyl infusions in post-thoracotomy patients.

**Methods:** With institutional approval and informed consent, fourteen patients undergoing thoracotomy were studied. Immediately prior to surgery a lumbar epidural catheter was inserted. No premedication was given and after a thiopental/succinlycholine induction the patients were maintained with $N_2O$, isoflurane and pancuronium. The patients were randomly allocated to one of two groups: Group Epi=lumbar epidural infusion of fentanyl and i.v.infusion of normal saline. Group IV=lumbar epidural infusion of normal saline and i.v. infusion of fentanyl. The study was double blinded. One hour after induction a bolus of 1.5 ug/kg of fentanyl was administered via the allocated route and an infusion of 1.0 ug/kg/hr fentanyl was begun. This was continued through the first postop day. Postoperative pain was assessed using a visual analogue pain score (100=severe pain, 0=no pain). If the pain score was > 33 a further bolus of 0.5 ug/kg fentanyl was given and the infusion was increased by 0.25 ug/kg/hr. This was repeated at intervals of not less than 30 minutes. Following infusion rate changes plasma fentanyl concentration was measured at 15 min intervals for one hour, hourly for 4 hours, and then at 2 hour intervals. Results were analyzed using t-tests, Mann Whitney U, and repeated measures analysis of variance. $p < 0.05$ was considered significant.

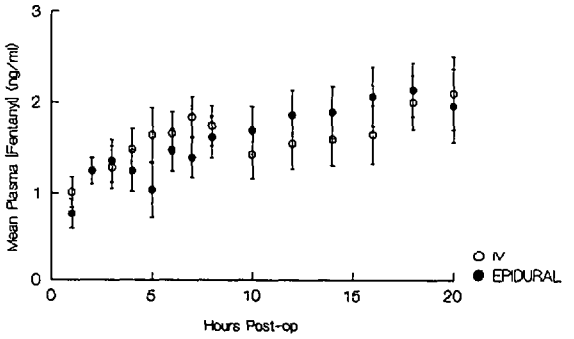
**Results:** There were no statistical differences between groups for age, weight, height, sex or duration of surgery. Pain scores (fig.1), and plasma fentanyl concentrations (fig.2) were not significantly different between the two groups. Although the mean infusion rate was higher for the epidural group (fig.3), the between group difference was not statistically significant.

**Discussion:** Lumbar epidural and intravenous infusions of fentanyl can provide good post-thoracotomy pain relief. However the lack of significant differences in dose requirement and plasma concentration between the epidural and intravenous groups supports systemic absorption as a major mechanism of action for lumbar epidural fentanyl.

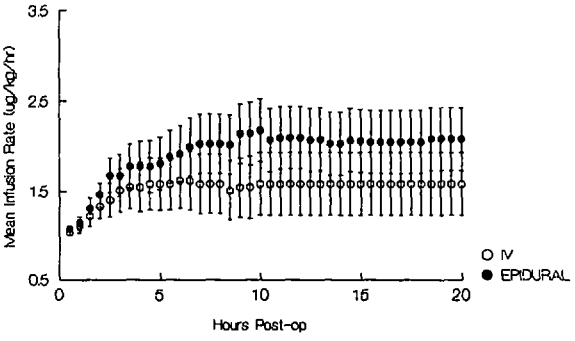
VISUAL ANALOGUE PAIN SCORE fig.1




PLASMA FENTANYL CONCENTRATION fig.2




FENTANYL INFUSION RATE fig.3



## AN IN VITRO MODEL FOR EVALUATING THE ACCURACY OF PULSE OXIMETERS

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### INTRODUCTION

The pulse oximeter is undoubtedly a major advance in non-invasive patient monitoring. Unfortunately it is also the only clinical monitor which can not be easily calibrated by the user. An in vitro calibration method was recently described by Mendelson,[1] but the method is technically complicated, requires expensive equipment, and large quantities of blood.

We have developed and evaluated a simple finger model for calibrating pulse oximeters which is inexpensive, requires very little fabrication, and uses only 0.5-1 ml of blood for each calibration point.

### METHODS AND MATERIALS

The model finger calibration device was assembled from a disposable plastic test tube (12.5 x 75 mm), a 7 cm length of silastic tubing (ID = 4.4mm, OD = 8 mm), and a rubber squeeze bulb (from a Welsh Self-Retaining ECG sensor, Burdick Product No. 007364) as shown in Figure 1). Blood was obtained from one of the authors or blood bank. A portion of the blood was fully oxygenated in a tonometer (IL237), and was used to calibrate a Hemoximeter (Radiometer OSM2b). A second portion of blood was deoxygenated in the tonometer and a range of saturations was obtained by mixing the saturated and desaturated blood. Approximately 1 ml of blood was placed in the bottom of the test tube and the space above the blood was filled with $N_2O$ before the model finger was assembled as shown in Figure 1. The unit was then inserted all the way into a Nellcor adult digit oxygen transducer (model DS-100A). Pulsations within the tube were produced by squeezing the bulb approximately 150 times per minute. The amplitude of the pulsations was observed on the bar-graph display of a Nellcor pulse oximeter (Model N100). A constant amplitude was maintained until a stable oxygen saturation reading was obtained for at least 20 seconds. After the saturation measurement was recorded, the blood was transferred anaerobically into a 3ml syringe and its oxygen saturation determined using the Hemoximeter.

The Hemoximeter ($SaO_2$) and pulse oximeter ($SpO_2$) measurements were plotted and the linear relationship between the two measurements was determined using the method of least squares.

### RESULTS AND DISCUSSION

The linear regression analysis showed an excellent correlation (r = 0.99) between the Nellcor pulse oximeter and the Hemoximeter (Figure 2) in the range of clinical interest. The three lowest saturation values were excluded from the analysis. The scatter of points may have been due partly to variations in haemoglobin concentration.

In addition to its use as a calibration device, this model may also facilitate the exploration of the physiological limits of pulse oximetry.

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Figure 1

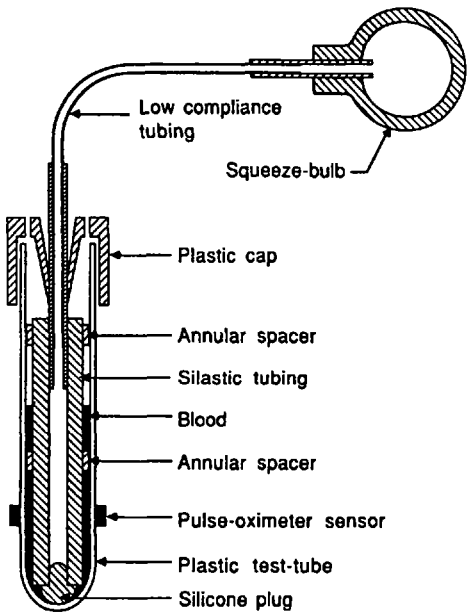
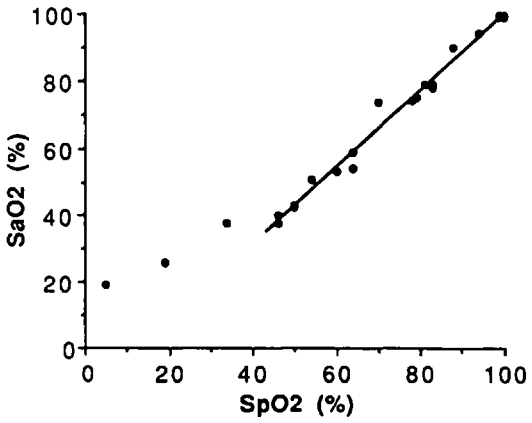



Figure 2



# BLOWTORCH ENDOTRACHEAL TUBE FLAME

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Introduction. The flame observed during airway surgery following laser ignition of an endotracheal tube (ETT) in an oxygen enriched atmosphere has been variously described as "blowtorch", "explosion", and "rocket". The chemical and physical processes of combustion are here applied to the analysis of a model of such flame propagation in order to more fully understand this phenomenon and develop a method to avoid its catastrophic consequences during anesthesia.

Method. Counterflow intraluminal flame spread (i.e., flame advancing over the surface of a fuel opposite the direction of the oxidizer flow[1]) was created in polyvinylchloride (PVC) ETT's by introducing various concentrations of oxygen, either undiluted, or diluted by nitrogen or helium, at various flow rates into the proximalend of the tube and igniting the distal end with a butene pilot flame. The PVC ETT's tubes were horizontally positioned, 4 cm sections, of 5.5 mm I.D. The experiment was performed under a gas evacuation hood. Effluent gas was collected into previously evacuated pyrex collecting chambers for gas chromatographic and chemical analysis. Gas analysis was performed by flowing the effluent gas through $Ca(OH)_2$ solution with back titration to a colorimetric end point. A video camera was used to record the image resulting from midpoint laser ignition and the videotape was played at slow speed.

Results. Ignition of the distal end of the ETT resulted in counterflow intraluminal flame spread. Gas chromatographic analysis revealed organic products of pyrolysis and combustion to be CO, $CO_2$, $CH_4$, hydrocarbon alkane and alkene chains, benzene, and other aromatics. $Ca(OH)_2$ back titration of effluent gas revealed abundant acid production, interpreted to be hydrogen chloride.

Observation of the videotape clearly confirmed a counterflow flame spreading toward the oxidant, and a coflow flame travelling to and exiting out of the distal end of the tube. Upon exiting the tube, the flame was maintained in air.

Discussion. Laser ignition at the midpoint of an ETT through which oxygen is flowing results in counterflow intraluminal flame spread, which consumes virtually all of the incoming oxygen and produces incompletely oxidized products of consumption (i.e., gaseous fuel). These products flow through the tube in the direction of oxidant flow, preceded by the gas slug of oxidant that was in the distal end of the tube prior to ignition. We postulate that the coflow flame observed at that interface of fuel and oxidant which exited at the distal end of the tube and was then maintained as a diffusion flame supported by air is the previously observed "blowtorch", "explosion", or "rocket" flame. During general anesthesia the direction of this "blowtorch" flame during inhalation would be toward the lung, and the flame would be supported by alveolar oxygen.

We conclude that the driving force for the coflow flame is the gaseous fuel produced by the counterflow flame spread phenomenon. Our efforts are currently directed toward development of an ETT with an intraluminal surface that will not support the spread of the counterflow flame.

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# POTASSIUM CORRECTION OF HYPOTHERMIC HYPOKALEMIA INDUCES HYPERKALEMIA AFTER REWARMING

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**Introduction**. Hypokalemia observed during hypothermia[1,2] was believed to result from intracellular $K^+$ redistribution[3]. Correction of this redistribution hypokalemia was described to induce severe hyperkalemia after rewarming was accomplished[1]. Interaction of endogenous $K^+$ shifts due to body temperature change, and exogenous supplementation may have significant clinical relevance. This study, conducted on rats, was designed to determine how full correction of hypokalemia during hypothermia influences serum $K^+$ concentration after rewarming. Compared are the results from animals in which the body temperature was changed without serum $K^+$ correction.

**Methods**. Approval for the study was obtained from the Animal Investigational Committee. Four groups of Wistar rats (each N=6) were anesthetized with thiopental, ureters were bilaterally ligated, and hypothermia was achieved by ice water immersion. Animals were breathing spontaneously. ECG was monitored during the cooling and rewarming period. The first set of experiments was performed on 12 rats, divided into two groups, to study spontaneous shifts of serum $K^+$ during the induction of hypothermia and rewarming. Half of the rats were cooled to 30±0.5°C and half to 32±0.5°C. Serum $K^+$ concentration was determined prior to cooling, after achieving desired hypothermia, and after rewarming with the heating lamp. The second set of experiments was performed on the same size group, and on the similar body temperatures (31±0.5 and 29±0.5°C). In these two groups, hypothermic hypokalemia was slowly supplemented with potassium chloride (7.45% KCl) via the internal jugular vein, until normal (pre-cooling) $K^+$ concentrations were achieved. Following serum $K^+$ normalization in hypothermia rats were rewarmed. Blood gases were drawn during hypothermia.

**Results.** Lowering of the body temperature spontaneously decreased serum $K^+$ concentration. Fig. 1 represents this observation showing statistically significant onset of hypokalemia with cooling in both groups (N vs. H, $P<0.001$), as well as spontaneous normalization of serum $K^+$ during rewarming to normothermia (N*). Serum $K^+$, after rewarming, was not different from the precooling concentrations (N vs. N*, P=NS). Fig. 2 shows serum $K^+$ concentrations from two groups of animals cooled from normothermia (N=37°C) to 31°C and 29°C (H) (N vs. H, $P<0.001$), followed by $K^+$ supplementation to normalize kalemia (H*), and consequent changes in serum $K^+$ after acute rewarming was accomplished (from H* to N, $P<0.001$). For the period of cooling, arrhythmias were not recorded. In the $K^+$ corrected group, ventricular ectopic beats and AV-blocks were present during the period of rewarming. During hypothermia blood gases uniformly showed respiratory alkalosis (pHa=7.54±0.03. $PaCO_2$=23±4 mmHg).

**Discussion**. Hypokalemia induced by hypothermia normalized during rewarming strongly suggested that the pathogenesis of hypokalemia was due to temporary $K^+$ redistribution into different body compartments, and not due to the actual electrolyte loss. That was clearly demonstrated in animals with ligated urethers. The exact site of $K^+$ redistribution is most probably the liver[4]. A spontaneous decrease in serum $K^+$ concentration may be explained by two mechanisms: 1) increased sympathetic tone, that characterizes mild hypothermia,[5] stimulates intracellular $K^+$ transport via $\beta_2$-adrenergic receptors.[6] 2) spontaneously breathing rats, lightly anesthetized and stimulated by cold environment, developed respiratory alkalosis which might also promote intracellular $K^+$ distribution.[7] We have shown that rewarming acts such as endogenous $K^+$ load by redistribution of $K^+$ into the extracellular compartment, fully correcting hypothermic hypokalemia. Additional $K^+$ administration during the hypokalemic stage may result in "overshoot" hyperkalemia after the emergence from hypothermia (Fig. 2 between H*-N*). The rats supplemented with $K^+$ were normokalemic during hypothermia (Fig. 2 H*) but developed hyperkalemia after rewarming (Fig. 2 N*). During emergence from hypothermia, the mechanism that physiologically counteracts hyperkalemia (energy dependent ionic pump) may lag in recovery behind the actual rise in body temperature. It may be easy to overburden this slowed transport mechanism by endogenous shifts or exogenous $K^+$ load.

**Conclusion**. Redistribution hypokalemia in hypothermia has transient nature and needs not be corrected, unless ECG reveals cardiac dysrhythmias. If there is a need for $K^+$, it should be given in a rather slow and conservative manner.

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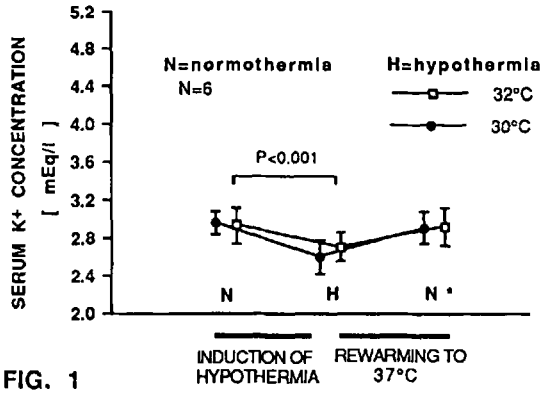


FIG. 1

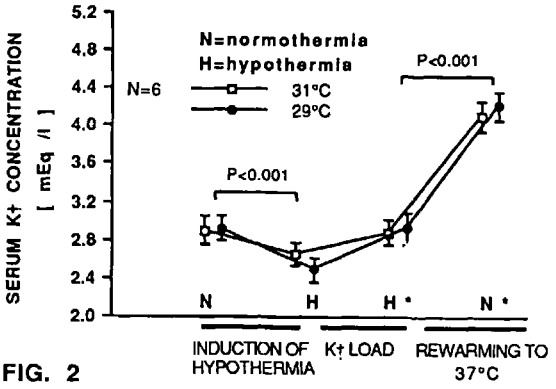


FIG. 2

# TIME CONSTANT RELATED DISTORTION IN SIDE-STREAM CAPNOGRAPHY

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**INTRODUCTION** Side-stream capnographs aspirate gas at the sample site and transport it through a sampling tube to an analyzer located inside the unit. This transport process causes signal distortion due to capnograph response time limitations, the result of which is to low-pass filter (smooth) the "true" capnograph signal. An important clinical consequence of this distortion is that one may obtain capnographic recordings which fail to go to zero at end-inspiration under conditions where no rebreathing is present (factituous rebreathing). Similarly, it may also result in underestimation of the CO2 concentration at end-expiration. This report presents an analysis of these problems.

**ANALYSIS** As stated, side-stream capnographs distort the "true" capnograph signal by low-pass filtering. The degree of low-pass filtering depends on the nature of the true capnograph signal and the capnograph time constant. In mathematical terms, the distorted capnograph signal is the true signal convolved with the capnograph impulse response. If T is the capnograph time constant for a first-order system, then the impulse response is $h(t)=1-\exp(-t/T)$, and the distorted signal may be viewed as the convolution of this with the true capnograph signal. Here we consider two signal models (square wave and sinusoid) to examine distortion effects for various time constants and respiratory frequencies.

**SQUARE-WAVE MODEL** In the first model considered, the "true" capnogram is a square wave of amplitude A, minimum value zero and respiratory frequency f breaths/min (solid portion of Fig. 1A). It can be shown that with a capnograph time constant of T seconds, the resulting capnogram is in error from the true minimum and maximum by an amount given by

$$A[1-\exp(-Z)]/[\exp(Z)-\exp(-Z)], \quad \text{where } Z=30/fT.$$

Table 1 tabulates the error for various values of f and T. As a graphic example, the dotted portion of Fig. 1A shows the resulting distorted signal when T=0.6 seconds and f=36 breaths/min.

**SINUSOIDAL MODEL** In the second model the "true" capnograph is sinusoidal with peak-to-peak amplitude A and minimum value zero . It can be shown that here the error from the true minimum or maximum is given by

$$(A/2)\sqrt{(1 - 1/ (1+(\pi fT/30)^4 ))}.$$

Table 1 tabulates the error for various values of f and T. As an example, the dotted portion of Fig. 2B shows the resulting signal when T=0.6 second and f=36 breaths/min.

**DISCUSSION** Although capnography is in common clinical use, its technical limitations are not always fully appreciated. In this report we illustrate two problems in side-stream capnography: underestimation of end-tidal CO2 concentration and overestimation of end-inspiratory CO2 concentration (factious rebreathing). Both these problems stem from smoothing (low-pass filtering) of the capnograph signal. The degree of distortion depends on the time-constant of the capnograph, the respiratory frequency and the nature of the respiratory waveform. In this study it is shown that capnograph signal distortion increases with both capnograph time constant and respiratory frequency. The degree of distortion will also vary with the form of the respiratory waveform: in this study the errors associated with a sinusoidal waveform were larger than for square-wave waveforms. Actual clinical respiratory waveforms will have intermediate properties, so that these results can be used to establish upper and lower error bounds for actual clinical tracings.

An examination of Table 1 shows that the errors that would be expected under ordinary clinical circumstances are not always insignificant, especially in the pediatric setting where respiratory frequencies tend to be higher. For example, the time constant for the original Puritan-Bennett capnograph may vary from 0.091 to 0.273 seconds. In the worst case (T=0.273) with respiratory frequencies of 20 and 40 breaths per minute the end-tidal CO2 is underestimated by about 7 and 17 percent respectively when the respiratory signal is sinusoidal. Under these circumstances an identical error in the end-inspiratory CO2 level exists.

| | Square Wave Model | | | Sinusoidal Model | | |
|---|---|---|---|---|---|---|
| | f (breaths/min) | | | | | |
| T(sec) | 20 | 40 | 60 | 20 | 40 | 60 |
| 0.1 | 0.000 | 0.055 | 0.66 | 1.061 | 3.879 | 7.657 |
| 0.2 | 0.055 | 2.298 | 7.586 | 3.879 | 11.66 | 18.86 |
| 0.3 | 0.669 | 7.586 | 15.88 | 7.657 | 18.86 | 26.56 |
| 0.4 | 2.298 | 13.30 | 22.27 | 11.66 | 24.37 | 31.51 |
| 0.5 | 4.743 | 18.24 | 26.89 | 15.46 | 28.45 | 34.83 |

**Table 1.** Percent errors in capnograph minima and maxima for various respiratory frequencies and capnograph time constants according to the two models studied. T is the capnograph time constant. Note that significant errors may occur, especially at respiratory frequencies in the pediatric range.

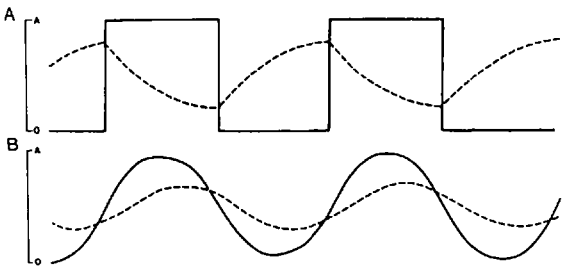


**Figure 1.** Examples of capnograph distortion for square-wave (top) and sinusoidal (bottom) respiratory waveforms. Solid curves denote the true waveforms while dotted curves show the result of capnograph distortion. Here the capnograph time constant is 0.6 seconds and the respiratory frequency is 36 breaths per minute. (These values were deliberately chosen to graphically illustrate capnograph distortion effects; smaller time constants and respiratory frequencies are the norm in ordinary clinical practice.)

## TEMPERATURE MONITORING DURING MAJOR ABDOMINAL AND THORACIC SURGERY

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**Introduction:** When a body cavity is widely opened during major surgery, a single thermometer may not always reflect body temperature. Therefore, we evaluated changes in rectal and esophageal temperatures during major lower abdominal or thoracic surgery, using the tympanic membrane temperature as a standard for core temperature.

**Methods:** After obtaining informed consent, fifty-five patients undergoing major lower abdominal or thoracic surgery were studied. Patients undergoing lower abdominal surgery were divided into two groups: Group 1 (n=15) was ventilated with passive heated and humidified anesthetic gases using Humid-Vent 1$^{TM}$, and Group 2 (n=15) was ventilated with active heated and humidified gases at about 35°C, using Cascade 1$^{TM}$. Patients undergoing thoracic surgery were similary divided into those (Group 3, n=13) ventilated using Humid-Vent 1$^{TM}$, and those (Group 4, n=12) ventilated using Cascade 1$^{TM}$. There were no differences in age, body weight, and body height among the four groups.

Anesthesia was maintained by fentanyl and nitrous oxide, and artificial ventilation with a non-rebreathing system was used. Tympanic membrane, esophageal, and rectal temperatures were monitored using disposable thermistor probes and thermometers (Model 6500, Mon-a-Therm). Temperatures were recorded every 20 min during the first 180 min of the surgery, and 20 min after the end of the surgical procedure. Differences between rectal and tympanic membrane temperatures (DRT) and differences between esophageal and tympanic membrane temperatures (DET) were calculated, and the values during and after the surgery were compared with those immediately before the surgery, using Wilcoxon test. Differences among the four groups were assessed using Kruskal-Wallis test. Data were presented as mean ± SD and a $P<0.05$ was regarded as significant.

**Results:** DRT was decreased significantly in all groups 20 min after the beginning of the surgery (Fig. 1). It reached a plateau within 80 min in groups 3 and 4, but continued to decrease below 0 until 160 min in groups 1 and 2. DRT returned to the preoperative level 20 min after the surgery in groups 2, 3, and 4. In contrast, DET tended to increase in all four groups, and postoperative values were significantly higher than preoperative values in groups 1 and 2 (Fig. 2).

**Discussion:** Our finding of decreased DRT during lower abdominal surgery is compatible with a previous study (1). However, that study did not differentiated abdominal, thoracic, and peripheral surgeries. Our results showed that the decrease of DRT was a result of opening the abdominal cavity.

Bissonnette B, et al found that to heat and moist inspired gases increases esophageal temperature above tympanic membrane temperature in children during peripheral surgery (2). They also showed there was no difference in the effect between passive and active heating combined with humidifying. However, we found that DET was significantly lower in Group 3 than in the other groups. This suggests that Humid-Vent 1$^{TM}$ does not adequately warm and humidify inspired gases in adult patients undergoing thoracic surgery.

In conclusion, monitoring rectal temperature may lead to overestimation of hypothermia during major lower abdominal surgery. On the other hand, influence of thoracic surgery on esophageal temperature can be minimized by using a heated humidifier to warm anesthetic gases, but not by using a heat and moisture exchanger.

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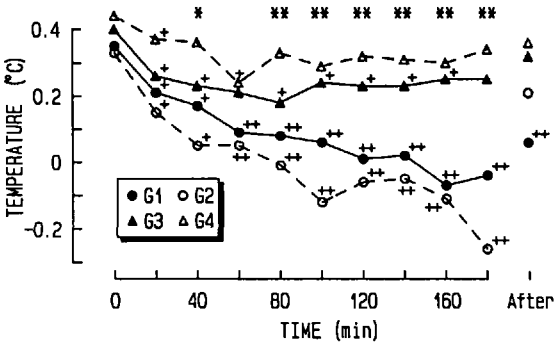


Fig. 1. The mean DRT during and after the surgery. +P<0.05, ++P<0.01 compared with the value at 0 time. *P<0.05, **P<0.01 among four groups.

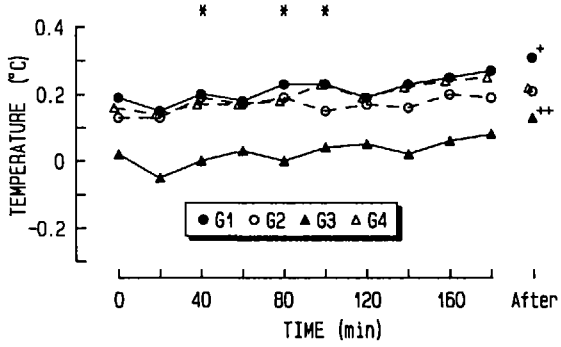


Fig. 2. The mean DET during and after the surgery. +P<0.05, ++P<0.01 compared with the value at 0 time. *P<0.05 among four groups.

# SALINE SOAKED PLEDGETS PREVENT $CO_2$ LASER INDUCED TRACHEAL TUBE CUFF IGNITION

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Introduction: The laser is proving an important tool in surgery. However, its high power and proximity to combustible tracheal tubes has led to frequent airway fires which have caused severe burns to patients. The shafts of these tracheal tubes may be adequately protected from the laser by techniques such as wrapping them with the appropriate type of foil tape.[1] However, the cuffs of these tubes cannot be protected by foil wrapping and remain vulnerable. We performed a controlled evaluation of the recommendation[2] that saline soaked pledgets be used to prevent laser induced tracheal tube cuff ignition.

Methods: Twelve Mallinckrodt (Glens Falls, NY, USA) polyvinylchloride size 7.0 mm ID Hi-Lo tracheal tubes were studied. The tracheal tubes were each inserted into 100 cc Pyrex graduated cylinders with a 2.5 cm internal diameter which served as a "mock trachea." The tubes were connected to a circle anaesthesia system and were flushed with 5 L/min of oxygen for 5 min. The cuffs were then inflated with 20 cc of air and the system pressure was adjusted to 20 cm $H_2O$ by adjusting the pop off valve on the anaesthesia machine. Six tracheal tubes (group 1) were inserted into graduates and had 3 saline soaked Merocel (Amercal Corp., Mystic, CT, USA) 1x3 inch pledgets placed above their cuffs so that the cuffs were completely covered. The remaining 6 tracheal tube (group 2) cuffs were similarly inserted into graduates but were unprotected. A Cooper (Santa CLara, CA, USA) 500 % $CO_2$ laser was set to 40 W in the continuous mode of operation with a beam diameter of 0.66 mm and it was directed at the tracheal tube cuffs for 1 min or until tracheal tube ignition occurred.

Results: There was no ignition of any of the tracheal tube cuffs protected by the saline soaked pledgets after 1 min of 40 watt $CO_2$ laser fire. Steam was produced by laser application to the pledgets and in some cases a small area of brown thermal decomposition of the pledgets was noted however no flames occurred. All six tracheal tube cuffs which were not protected by saline soaked pledgets were ignited in < 1 sec of laser fire and the graduated cylinder was filled with flames and smoke. The incidence of tracheal tube fires was significantly greater in group 2 than group 1 as determined by the Mann Whitney U-test ($P<0.01$).

Discussion: The laser has enjoyed increasing use in surgery due to its power, precision, hemostatic effects and decreased incidence postoperative pain and edema. More surgical applications continue to be described. However, the use of the laser for airway surgery has been associated with catastrophic airway fires. An endotracheal tube can be converted to a veritable blow torch by the laser and serious burns to patients have occurred. In a survey of the complications of laser airway surgery conducted by Fried,[3] a group of otolaryngologists active in this type of surgery noted that airway fires and explosions were the most common serious complication occurring during these cases. The incidence of these fires has been stated to be 0.57% making them one of the most common significant adverse events in clinical anaesthesia.

To protect the shafts of combustible red rubber and polyvinylchloride tracheal tubes from the effects of the laser, the use of foil tape has been recommended. Sosis[1] has shown that self adhesive 3M no. 425 aluminum and Venture copper foil tapes provide excellent protection of polyvinylchloride and red rubber tracheal tube shafts from the $CO_2$ and Nd-YAG lasers after it is carefully applied in an overlapping manner.

Smaller diameter endotracheal tubes are usually selected for airway surgery than those used for non-airway surgery so that the surgeon's field will be less obscured by the tracheal tube. These smaller tracheal tubes require a large cuff to make an adequate seal with the trachea and hence the cuff presents an easy target for the laser. The alignment of the laser along the axis of an operating laryngoscope during laser airway surgery predisposes to its direction at the cuff. Furthermore, the cuffs of combustible tracheal tubes cannot be protected from the laser with metallic tapes. They are fabricated from very thin materials and are therefore more prone to combustion than are the shafts of these tracheal tubes.

The present study shows that saline soaked pledgets provide excellent protection of polyvinylchloride tracheal tube cuffs when 40 watts of continuous laser energy was directed at the cuffs. The pledgets can be placed above the tracheal tube cuff by the surgeon before the laser is actuated. They must be kept moist for if they dry they will become combustible. The pledgets must be carefully retrieved after surgery. Radio-opaque coloured strings are attached to the pledgets used in this study which will facilitate their retrieval, however the strings are easily cut by the laser. Thin metal (jewelry) chains or wires which can be attached to the pledgets have been suggested as a laser resistant means of retrieving the pledgets.[2] It is also recommended[4] that saline be used to fill the tracheal tube cuffs during laser airway surgery. The saline will act as a "built in fire extinguisher" if laser perforation of the cuff occurs. It also acts as a heat sink. A small amount of methylene blue should be placed in the cuff so that the surgeon can stop the laser if the blue colour is seen.[2]

Nitrous oxide should not be employed during laser airway surgery since it supports combustion due to its exothermic decomposition into nitrogen and oxygen. The minimum acceptable inspired fraction of oxygen which will give a satisfactory arterial oxygen saturation as determined with a pulse oximeter should be used. The remainder of the gas mixture should consist of helium or nitrogen.

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# EFFECTS OF PORTAL CLAMPING ON MYOCARDIAL CONTRACTILITY

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## Introduction

During liver resection, portal clamping maneuver is often performed to decrease the amount of bleeding. It is well known that in many species portal clamping for more than 30 minutes leads to serious shock state. However it was not known whether the shock might be caused by either the reduction of preload or the decrease in cardiac contractility. Therefore we assessed left ventricular inotropic state during and after portal clamping by measuring the slope of the end-systolic pressure diameter relationship (ESPDR) that is independent of preload or afterload and relatively insensitive to altered heart rate but sensitive to large changes in contractility [1].

## MATERIALS AND METHODS

We anesthetized 16 mongreal adult dogs with pentobarbital and intubated.Anesthesia was mainteined with continuous infusion of pentobarbital.

(EXPERIMENT I) A catheter was placed in a femoral artery for measurement of mean arterial pressure (MAP). A pulmonary artery catheter was inserted from a femoral vein. Using this catheter, pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP),and cardiac output were measured. Cardiac index (CI), systemic and pulmonary vascular resistance index (SVRI&PVRI) were calculated. A midline laparotomy was performed and the portal vein was isolated. After cardiovascular control data had been obtained, the portal vein was clamped for 15 minutes. At 5, 10, and 15 minutes after portal clamping, hemodynamic recordings were taken. After portal reperfusion, hemodynamic measurements were obtained at 5, 10, 15, and 30 minutes and then every 30 minutes up to 120 minutes postrelease.

(EXPERIMENT 2) 11 dogs were anesthetized in the same way as that of the first study. A pair of ultrasonic crystals were implanted on the endocardial surface to determine the internal diameter of left ventricular minor axis (LVD). A catheter-tip micromanometer was placed for measurement of left ventricular pressure (LVP). A balloon-tipped aortic occlusion catheter was positioned in the descending aorta. After obtaining control data, portal vein was clamped for 15 minutes. This was done in 6 dogs. In the other 5 dogs portal vein was not clamped and these dogs were reported as shams. End diastolic (ED) point was defined at the R-wave of ECG. End systolic (ES) point was defined at LVP/LVD was maximal [2]. With these data, %shortening was calculated. ESPDR was calculated from data obtained during a transient occlusion of aorta. As afterload was increased in successive beats, a wide range of LVESPs and LVESDs were obtained. Linear regression was performed on these data pairs to determine the slope and the intercept values.

## RESULTS

Table 1 and 2 present the data from the experiments. MAP,LVSP and CI decreased markedly during portal clamping and increased after release but were not returned to the control values. SVRI increased during portal clamping and returned to control value after release. PCWP,LVEDP, and LVEDD tended to decrease during portal clamping. %shortening and ESPDR were unchanged during portal clamping and after release.

Table 1. Hemodynamic data in experiment 1

| | control | portal clamp | | | after release | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 5mn | 10min | 15mn | 5min | 10min | 15min | 30min | 60min | 90mn | 120min |
| HR | 160 | 183* | 157 | 153 | 146 | 150 | 153 | 159 | 164 | 165 | 166 |
| (beats/min) | ±15 | ±15 | ±8 | ±10 | ±11 | ±12 | ±12 | ±14 | ±15 | ±13 | ±14 |
| MAP | 136 | 80* | 59* | 54* | 93* | 96* | 99* | 101* | 111* | 111* | 116* |
| (mmHg) | ±11 | ±6 | ±10 | ±6 | ±6 | ±6 | ±5 | ±6 | ±5 | ±7 | ±6 |
| MPAP | 12 8 | 5.8* | 5.5* | 5.4* | 11.4 | 11.3 | 11.6 | 11.8 | 13.0 | 13.5 | 13.9 |
| (mmHg) | ±4.1 | ±2.2 | ±2.3 | ±2.4 | ±3.8 | ±3.8 | ±3.9 | ±4.9 | ±5.1 | ±5.5 | ±5.4 |
| PCWP | 8.2 | 1.8 | 2.6 | 1.6 | 4.1 | 4.2 | 5.3 | 7.9 | 7.4 | 9.1 | 8.4 |
| (mmHg) | ±4.6 | ±1.6 | ±1.6 | ±1.5 | ±2.5 | ±2.5 | ±3.3 | ±4.9 | ±5.2 | ±5.0 | ±5.0 |
| CI | 2.9 | 1.0* | 0.9* | 0.9* | 1.8* | 1.9* | 2.0* | 2.3* | 2.4* | 2.3* | 2.4* |
| (ℓ/min/m²) | ±0.3 | ±0.1 | ±0.1 | ±0.1 | ±0.4 | ±0.4 | ±0.3 | ±0.4 | ±0.4 | ±0.4 | ±0.5 |
| SVR | 3894 | 6908* | 5311* | 4731 | 4447 | 4359 | 4174 | 4062. | 4123 | 4143 | 4325 |
| (dynes sec/cm⁵/m²) | ±451 | ±858 | ±941 | ±678 | ±613 | ±559 | ±441 | ±581 | ±671 | ±563 | ±747 |
| PVR | 170 | 333 | 320 | 352 | 312 | 271 | 274 | 237 | 283 | 239 | 279 |
| (dynes sec/cm⁵/m²) | ±66 | ±80 | ±115 | ±78 | ±33 | ±30 | ±43 | ±14 | ±16 | ±28 | ±17 |

Values are means± SE; n=5dogs; * P<0.05 compaired with the control

Table 2. Left ventricular pressures and dimensions data in portal clamp group of experiment 2

| | Control | Portal clamp | | | after release | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 5 min | 10 min | 115mn | 5 min | 10min | 15min | 30min | 60min | 90mn | 120min |
| LVSP | 141 | 95* | 96* | 94* | 128 | 131 | 130 | 135 | 140 | 140 | 139 |
| (mmHg) | ±11 | ±14 | ±15 | ±16 | ±16 | ±12 | ±13 | ±13 | ±14 | ±14 | ±15 |
| LVEDP | 5.2 | 4.0 | 2.6 | 2.3 | 6.0 | 5.2 | 4.5 | 4.3 | 5.3 | 6.2 | 6.4 |
| (mmHg) | ±1.9 | ±2.6 | ±2.1 | ±2.3 | ±1.7 | ±1.8 | ±1.9 | ±1.6 | ±1.7 | ±2.4 | ±2.2 |
| LVEDD | 37.4 | 35.1* | 35.0* | 34.8* | 37.9 | 37.3 | 37.1 | 36.8 | 37.0 | 37.5 | 37.6 |
| (mm) | ±7.0 | ±6.7 | ±6.9 | ±6.5 | ±7.5 | ±7.1 | ±7.0 | ±6.8 | ±6.8 | ±7.3 | ±7.2 |
| % Shortening | 10.8 | 10.2 | 10.3 | 11.0 | 10.2 | 12.7 | 10.8 | 10.9 | 10.8 | 10.1 | 10.6 |
| (%) | ±2.2 | ±2.0 | ±2.1 | ±2.4 | ±2.5 | ±2.9 | ±2.7 | ±2.3 | ±2.2 | ±2.5 | ±2.4 |
| % Changes of slope | 100 | 106.0 | 113.3 | 119.0 | 115.1 | 109.7 | 107.7 | 148.0 | 144.2 | 153.2 | 118.3 |
| (%) | ±0 | ±10.9 | ±16.7 | ±16.6 | ±24.7 | ±18.0 | ±20.4 | ±28.8 | ±15.7 | ±30.9 | ±9.6 |
| Do | 30.2 | 31.5 | 31.6 | 31.5 | 31.6 | 31.2 | 30.4 | 31.0 | 32.0 | 32.4 | 31.8 |
| (mm) | ±5.7 | ±5.0 | ±4.7 | ±4.8 | ±5.3 | ±4.8 | ±5.9 | ±5.7 | ±5.8 | ±5.8 | ±5.1 |

Values are means ± SE; n=6 dogs: LVSP, left ventricular peak systolic pressure; LVEDP, left ventricular end-diastolic pressure, LVEDD, left ventricular end-diastolic diameter; % Shortening, (LVEDD−left ventricular end-systolic diameter)/ LVEDD×100; % Changes of slope, % changes of slope of ESPDR (% control); Do diameter intercept of the ESPDR slope line: * P<0.05 Compaired with the control.

## DISCUSSION

These results suggested that marked decrease in blood pressure during portal occlusion is not due to the reduction of myocardial contractility but to the reduction of preload. We assume that the decrease in preload results from massive pooling of blood in the splanchnic bed because of the smoll amount of portosystemic anastomosis in dogs [3].

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## SOFTWARE TO ANALYZE REGIONAL LEFT VENTRICULAR FUNCTION

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### Introduction

Regional left ventricular function (LVF) is frequently assessed experimentally by measuring changes in wall segment length using piezoelectric crystals. Although analysis of dimension signals can be and frequently is performed manually, it is time consuming, observer dependent and subject to inaccuracies. Computer software to analyze a specialised application like this is not available commercially. However, using ASYST (Asyst Software Technologies), a software program that can be customised by the user, we have developed an application program that will analyze pressure and dimension signals from the left ventricle (LV). The program recognises R wave peaks and performs beat-by-beat analysis. We have used this program to analyze pressure length loops and have compared manual and computer analysis of segment lengths from a stunned myocardium model.

### Methods

Five anaesthetized and mechanically ventilated mongrel dogs were studied. LV pressure was measured with a Millar MPC-500 catheter tip transducer, and dP/dt was obtained by differentiating this signal using an analog circuit. To measure changes in segment length, pairs of piezoelectric crystals were implanted in an area of the myocardium supplied by the left anterior descending artery (LAD), and an area supplied by the circumflex artery. To produce an area of stunned myocardium the LAD was occluded for 15 minutes and then reperfused. Aortic pressure was controlled by a snare placed around the aorta. Haemodynamic variables, segment length and ECG signals were recorded continuously on a Gould ES1000 recorder. Data was collected at intervals prior to and after LAD occlusion. Analog signals from the recorder were digitised using a Data Translation DT2801 A/D conversion board plugged into an IBM AT personal computer. Using ASYST to control the operation of the board, signals were digitised at a sampling frequency of 200 Hz in each channel, then sorted into beats. End-diastolic length was determined as the length at the beginning of the upslope of the positive left ventricular dP/dt. End-systolic length was determined as the length 20 msec before peak negative left ventricular dP/dt. The program was used to automatically plot pressure length loops, the LV end-systolic pressure length and LV pressure percent systolic shortening relationships.

### Results

Fig 1 shows a comparison of segment length at end-systole and end-diastole measured manually and by computer n=330. The correlation coefficient (r) was 0.99. The mean difference was 0.0095 mm with 95% confidence interval 0.0242 to -0.005 and the limits of agreement were 0.28 and -0.26 mm. Fig 2 is an example of computer generated pressure length loops.

### Discussion

The advantage of ASYST is that it can be customised to analyze complex physiological signals.

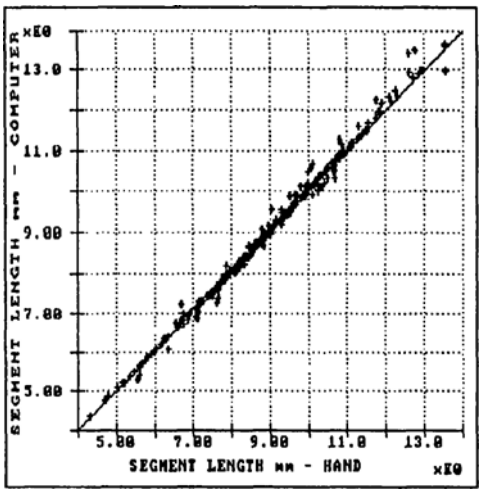


Figure 1 Segment length measured manually and by computer, with line of identity.

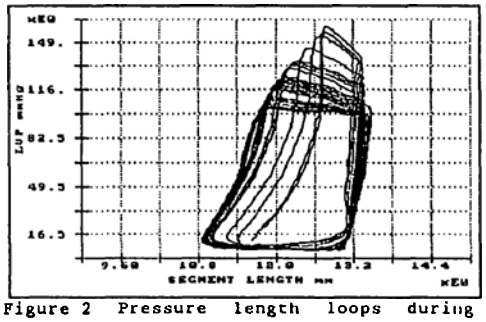


Figure 2 Pressure length loops during aortic occlusion.

The application program we developed has four basic options that allow the user to display and examine the ECG, sort the data into individual beats, analyze each beat, and graph various parameters in a customised format. The options are chosen from a main menu with pop up sub menus. For analysis this program can quickly take the average of a series of beats leading to greater accuracy in the calculation of segment length and percent systolic shortening. The graph menu allows the user to plot all the pressure length loops or specify individual loops. Graphs of the LV end-systolic pressure length and LV pressure percent systolic shortening relationships can be plotted automatically.

There was good agreement between the manual and computer analysis of segment length. Manual analysis is time consuming. Our program enables faster analysis so that more beats can be analyzed and complex pressure length relationships can be studied, leading to greater accuracy in the assessment of regional left ventricular function.

# CHANGES OF ANTITHROMBIN III AND ANTITHROMBIN III-HEPARIN COMPLEX LEVELS, AND ACT IN CARDIAC SURGERY

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INTRODUCTION:

For anticoagulation during cardiopulmonary bypass (CPB), heparin is used. Although a fixed heparin regimen is commonly used, there may be as much as a 12-fold variation in individual patient response to a given dose of heparin in terms of prolongation of activated clotting time (ACT) (1). There also exists a wide variation in the response to heparin within a single patient during cardiac surgery (2). Heparin enables antithrombin III to rapidly inhibit activated coagulation factors. Anticoagulation effect of heparin is reversed with protamine after CPB. Although coagulation profile is most commonly determined by ACT, ACT is affected by many other factors such as hypothermia (3). We, therefore, designed a study to determine 1) plasma levels of heparin, antithrombin III, and antithrombin III-heparin complex, and 2) the relationship among the above factors, ACT, and activated partial thromboplastin time(aPTT) in patients undergoing hypothermic CPB.

METHODS:

We studied nine adult patients (age 48±6 years, height 161±7cm, and body weight 59±11kg, mean±SD) undergoing CPB without blood transfusion. Preoperative coagulation studies (prothrombin time, aPTT, bleeding time, and platelet count) were all within normal limits. Informed consent and institutional approval were obtained. All patients were premedicated with morphine 0.1mg/kg, hydroxyzine 50-75mg and scopolamine 0.5mg intramuscularly one hour prior to induction. All patients were anesthetized with diazepam, fentanyl, morhpine and enflurane as required. CPB using a membrane oxygenator was instituted and maintained with a perfusin index of 2.4l/$m^2$/min. Moderate hypothermia with rectal temperatures between 26 and 28°C was utilized. We measured the following parameters at each measuring point (A-G): blood temperature, ACT, aPTT, plasma levels of heparin, antithrombin III, and antithrombin III-heparin complex, and complete blood count. Blood samples were drawn through an arterial catheter after 10ml of blood were removed to clear heparin flush solution in the cathter and pressure tubing. ACT was measured using 2.5ml of blood. ACT was determined by an automated method using Hemochron (International Technidyne, Edison, NJ). Complete blood count, aPTT, electrolytes and blood gases were also measured.The rest of the blood sample was put into ice and centrifuged to obtain plasma for measuring antithrombin III, heparin, and antithrombin III-heparin complex activities. The biological activity of plasma antithrombin III-heparin complex was determined by photometory using a chromogenic substrate(Behringer Mannheim, Tutzing, Germany).

A:after induction of anesthesia
B:three minutes after intravenous administration of heparin 250U/kg through a central line before CPB
C:thirty minutes after initiation of CPB
Heparin 125U/kg was added to 1700ml of priming solution.
D:one hour after initiation of CPB
E:two hours after initiation of CPB
F:after returning the residual perfusate in the cardiopulmonary bypass circuit to the patient
G:five minutes after reversal of heparin with protamine sulfate
Protamine 1.5mg was administered for 100U of heparin given.

Data were analyzed by Student t-test and ANOVA. A p value of less than 0.05 was considered significant.

RESULTS:

| | AT III (%) | heparin (U/ml) | AT-H (U/ml) | aPTT (sec) | ACT (sec) |
|---|---|---|---|---|---|
| A | 83 ±8 | <0.1 | <0.1 | 30.7 ±4.0 | 130 ±14 |
| B | 82 ±6 | 3.58 ±0.60 | 1.33 ±0.38 | >300 | 458# ±67 |
| C | 41# ±4 | 2.66* ±0.42 | 0.70* ±0.23 | >300 | 721# ±130 |
| D | 46# ±6 | 2.73* ±0.43 | 0.78* ±0.21 | >300 | 682# ±213 |
| E | 50# ±8 | 2.83* ±0.57 | 0.92* ±0.34 | >300 | 480 ±73 |
| F | 52# ±8 | 2.73* ±0.41 | 0.85* ±15 | >300 | 465# ±72 |
| G | 60# ±8 | <0.1 | <0.1 | 39.2 ±8.4 | 136 ±13 |

mean ±SD *p<0.05 compared with B
#p<0.005 compared with A
AT III:antithrombin III
AT-H :antithrombin III-heparin complex

DISCUSSION:

Although antithrombin III level was decreased to almost a half of the initial value after initiation of CPB, ACT was adequately prolonged. aPTT was always longer than 300s after heparinization. Prolongation of ACT during CPB was related not only to antithrombin-III heparin complex levels but also to other factors such as hypothermia because the plasma levels of antithrombin III-heparin complex were unchanged during CPB. Stable levels of heparin and antithrombin III-heparin complex during CPB were probably due to decreased metabolism of heparin and to diuresis-induced hemoconcentration. Adequete neutralization of heparin effect by protamine sulfate was suggested by normalization of ACT and unmeasurable level of heparin activity.

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# A RANDOMIZED STUDY OF CHANGES IN SERUM CHOLESTEROL, TRIGLYCERIDES, HIGH DENSITY LIPOPROTEINS, AND CORTISOL DURING CARDIAC SURGERY IN PATIENTS ANAESTHETISED WITH PROPOFOL-SUFENTANIL VS ENFLURANE-SUFENTANIL.

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**Introduction:** Propofol, a substituted phenol, is currently undergoing Phase IV clinical trials in Canada. The drug is formulated soyabean glycerol, egg-phosphatide emulsion.[1] Patients presenting for cardiac surgery frequently have abnormalities of serum triglycerides (TRI), cholesterol (CHOL), and high density lipoproteins (HDL). Prolonged administration of propofol in its current formulation could lead to abnormalities in TRI, CHOL, HDL metabolism as has been observed during administration of lipid emulsions for total parenteral nutrition.[2] In addition, complete depression of steroidogenesis following prolonged administration of propofol, as has been demonstrated for etomidate,[3] would be undesirable. As a preliminary study of the effects of prolonged administration of propofol, this study sought to determine whether administration of propofol for periods of 3-6 hours during cardiac surgery was associated with an increased incidence of abnormalities of TRI, CHOL, and HDL when compared to a standard anaesthetic regimen. In addition, we sought to determine whether, in a subgroup of these patients, there was significant depression of steroidogenesis when measured 18-24 hrs following cardiac surgery.

**Methods:** Following institutional approval and after informed consent, 39 patients agreed to participate in the study. Patients with preserved ventricular function (EF>40% with LVEDP<16) and scheduled for elective coronary artery bypass graft surgery (CABG) were eligible. All cardiac medications were continued into the perioperative period. On the morning of surgery and the first postoperative day, blood was collected for serum TRI, CHOL, HDL, and cortisol levels. Premedication consisted of morphine 0.1-0.2 mg/kg, promethazine 0.25-0.5 mg/kg, and diazepam 0.1-0.2 mg/kg 60-90 min prior to surgery. Following placement of intravenous, intra-arterial, pulmonary artery, and coronary sinus catheters, patients were randomly assigned to one of two groups. Group 1 received sufentanil 0.2 µg/kg over 1 min followed by propofol 1-2 mg/kg over 1-3 min for induction of anaesthesia. Maintenance anaesthesia consisted of a propofol infusion of 50-200 $\mu g.kg^{-1}.min^{-1}$ supplemented by sufentanil up to 5 $\mu g.kg^{-1}$ for hemodynamic abberations not controlled by propofol. Group 2 received sufentanil 5 ug.kg-1 over 1-3 min for induction of anaesthesia. Maintenance anaesthesia consisted of enflurane 0.25-3.0% as required for hemodynamic stability supplemented by sufentanil to a total dose of 7 $\mu g.kg^{-1}$. Both groups received diazepam 0.15 $mg.kg^{-1}$ prior to initiation of cardiopulmonary bypass (CPB) and 0.05 $mg.kg^{-1}$ at skin closure. Patients were then admitted to the CVICU where the nursing staff were blinded to the treatment group. Sedation, analgesia, and the use of vasopressors and vasodilators was unrestricted. Statistical differences ($p<0.05$) were determined by paired t-tests, chi square or t-tests with Bonferroni correction as appropriate.

**Results:** The groups were similar with respect to age, sex, number of grafts received, total cross-clamp time, and total duration of CPB and anaesthesia (Table 1). Mean sufentanil dose was 2.1±1.2 $\mu g.kg^{-1}$ in Group 1 vs 6.6±1.4 $\mu g.kg^{-1}$ in Group 2 ($p<0.05$). There were 32 patients with a complete set of data for TRI and CHOL. Group 2 (ENF/SUF;n=13) had a significantly higher CHOL prior to surgery (7±2 vs 6±1 mmol/l; $p<0.05$) than Group 1 (PROP/SUF;n=19) (Table). No other significant differences were seen between the groups with respect to TRI, HDL, or Cortisol levels either pre- or postoperatively. However, for both groups there were significant decreases in TRI, CHOL, and HDL following surgery and elevation in Cortisol levels (Table).

**TABLE:** COMPARISON OF DEMOGRAPHICS AND BIOCHEMISTRY VARIABLES IN TWO GROUPS OF CARDIAC SURGICAL PATIENTS. GROUP 1 RECEIVED PROPOFOL + SUFENTANIL WHILE GROUP 2 RECEIVED SUFENTANIL + ENFLURANE (ALL RESULTS MEAN±SD).

| PARAMETER | GROUP 1 | n | GROUP 2 | n |
|---|---|---|---|---|
| AGE(yr) | 57±10 | 20 | 59±6 | 19 |
| No. GRAFTS | 3.1±1.0 | 20 | 3.2±0.6 | 18 |
| X-CLAMP TIME (min) | 50±22 | 20 | 56±21 | 18 |
| CPB TIME (min) | 99±55 | 20 | 102±38 | 18 |
| ANESTHESIA TIME (min) | 278±96 | 20 | 286±59 | 18 |
| SUF(µg/kg) | 2.1±1.2 | 20 | 6.6±1.4* | 18 |

| | PRE-CPB | POST-CPB | n | PRE-CPB | POST-CPB | n |
|---|---|---|---|---|---|---|
| CHOLESTEROL (mmol/l) | 6±1 | 3±1** | 19 | 7±2* | 3±1** | 13 |
| TRIGLYCERIDE (mmol/l) | 3±1 | 2±1** | 19 | 3±3 | 1±1** | 13 |
| HDL(mmol/l) | 1±0 | 1±0** | 19 | 1±0 | 1±0** | 10 |
| CORTISOL (mmol/l) | 374±49 | 613±212** | 7 | 425±167 | 727±483** | 5 |

*p<0.05 vs Prop/Suf
**p<0.05 vs Pre-CPB

**Conclusions:** Failure to demonstrate a significant difference in levels of TRI, CHOL, HDL, and cortisol between the two groups following cardiac surgery suggests that propofol is unlikely to produce deleterious changes in these parameters following prolonged surgery. Studies employing its use for prolonged sedation e.g. in the ICU are warranted.

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## PREOPERATIVE ANXIETY AND MYOCARDIAL ISCHAEMIA: IS THERE A RELATIONSHIP?

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### INTRODUCTION

Over 75% of ischaemic episodes in patients with coronary artery disease are not associated with angina.[1] In patients with unstable angina, a subgroup with a pattern of predominantly silent ischaemia (SI) has a very unfavorable prognosis.[2] SI has been noted to occur during normal daily activities and is not necessarily associated with physical exertion. Mental stress may be an important precipitant of SI[3]. There is some evidence that perioperative myocardial ischaemia may be associated with an increased incidence of postoperative myocardial infarction in patients undergoing coronary artery bypass surgery[4]. Our objective was to determine the incidence of ischaemia, both overt and silent, preoperatively in patients presenting for coronary bypass surgery and to determine if a relationship exists between ischaemia and the degree of psychological stress experienced by patients awaiting surgery.

### METHODS

A total of 30 patients scheduled for elective coronary artery bypass surgery were studied. Patients were excluded from the study if there was evidence of atrial fibrillation, conduction defects or left ventricular hypertrophy on ECG. Anti-anginal medications were continued up to the time of surgery. A real time Holter monitor (Series 8000 Marquette Electronics) was used to record leads II and CS5 of the ECG. Recording commenced within 3 hours of admission to hospital and continued until induction of anaesthesia. Significant ST segment depression was defined as a planer or down-slopping shift of the ST segment of at least 1 mm, measured 80ms after the J point and persisting for at least 60 seconds. Significant ST segment elevation was defined as an upward shift of the ST segment of at least 1 mm, 80ms after the J point compared to the resting recording. Patients were requested to note the time, onset and severity of chest pain and to record any associated subjective sensations of emotional upset. The Spielberger State-Trait Anxiety Inventory was administered on the evening before surgery during the period of monitoring. Results were subjected to statistical analysis utilizing the nonparametric Wilcoxan matched pairs sine ranks test.

### RESULTS

Twenty-six patients (mean age 62) completed the study protocol. Four patients were excluded due to data loss. The mean duration of Holter recording was 13.9 hours and three patients had one or more episodes of ischaemic ST segment depression during the recording period. The mean duration of these episodes was 13.3 minutes (range 8-26 min.). No patient had angina during the study.
Assessment of Spielberger State-Trait Anxiety Inventory revealed two patients with scores two standard deviations above the mean for a comparable group of in-hospital medical/surgical patients. There was no relationship between the anxiety scores and ischaemia.

### DISCUSSION

We established no relation between preoperative anxiety and SI. Indeed this group of patients displayed a remarkable lack of anxiety at the prospect of open heart surgery. This may be related to the extensive preoperative patient education program in place at our institution. Alternatively, admission to hospital may have terminated their anxiety rather than exacerbated it given the imminent prospect of definitive surgical treatment.
The low incidence of SI in this group was also surprising but may reflect the population studied that is, elective surgical patients on maximal medical treatment. Further investigation of the relationship between psychological stress and SI in patients out of hospital awaiting cardiac surgery may identify a subgroup at risk due to their anxiety state.

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# COMPARISON OF BIOIMPEDANCE AND THERMODILUTION MEASUREMENTS OF CARDIAC OUTPUT DURING AORTIC SURGERY

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**INTRODUCTION:** Recent technological advances enable non-invasive, continuous measurements of cardiac output (CO) to be performed using the transthoracic electrical bioimpedance (TEB) technique. The TEB method of CO determination utilizes a new equation defined by Sramek, which relates changes in thoracic electrical conductivity to changes in thoracic blood volume and blood flow in the descending thoracic aorta[1]. The purpose of this study was to compare the accuracy and trending capability of TEB with the thermodilution (TD) method of measuring cardiac output during abdominal aortic surgery.

**METHODS:** Ten patients undergoing elective abdominal aortic surgery (AAS) were studied after approval of the protocol by the Human Experimental Procedures Committee. Patients were excluded if there was a history of congestive heart failure or myocardial infarction in the previous 6 months, or if a left bundle branch block was present on the preoperative ECG. Patients were premedicated and managed intraoperatively according to the discretion of the attending anaesthetist. In addition to routine monitors, a 7F Swan-Ganz catheter was inserted prior to induction using local anaesthesia. Each thermodilution estimate of CO ($CO_{TD}$) was determined from the average of three values correlating within 10% at end-expiration, using the Marquette Electronics 8000 monitor and 10 ml boluses of D5W at room temperature. A TEB cardiac monitor (Bomed NCCOM3™, Irving, Calif.) was also attached using 8 surface ECG electrodes in a configuration previously described[2]. The TEB cardiac output measurements ($CO_{TEB}$) were recorded from the values displayed on the monitor using the slow mode, which automatically averages each value from 16 successive artifact-free beats. Simultaneous measurements were performed at the following times: awake (A), post-induction (B), post-intubation (C), before skin incision (D), one and twenty minutes after skin incision (E and F respectively), before aortic cross-clamping (G), one and twenty minutes after aortic cross-clamping (H and I respectively), before declamping (J), one and twenty minutes after declamping (K and L respectively), and at the end of surgery (M). Data were analyzed by linear regression analysis, with statistical significance assumed when $p<0.05$.

**RESULTS:** One hundred simultaneous measurements were obtained, and are presented in the scattergram of Figure 1. There appears to be generally good correlation overall, with a product-moment correlation of $r = 0.71$, $y = 0.88x + 0.57$, and $p<0.001$. A comparison of $CO_{TEB}$ and $CO_{TD}$ with the line of identity ($y = x$) also shows that neither method of measurement consistently over or underestimates CO. Cardiac output measurements by TEB and TD were averaged at critical events during surgery in order to compare trends over time, as presented in Figure 2. $CO_{TEB}$ correlated well with $CO_{TD}$ throughout the surgical course.

Fig. 1

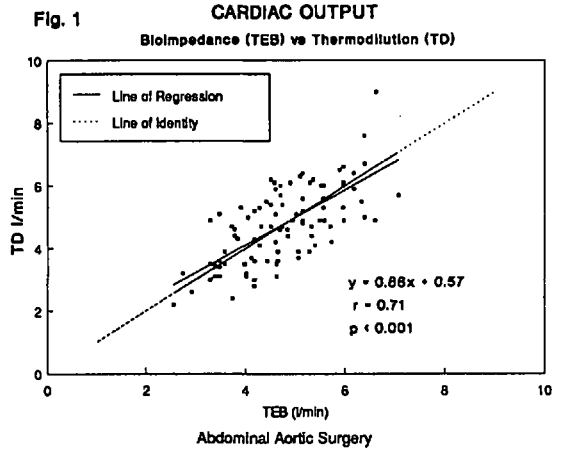
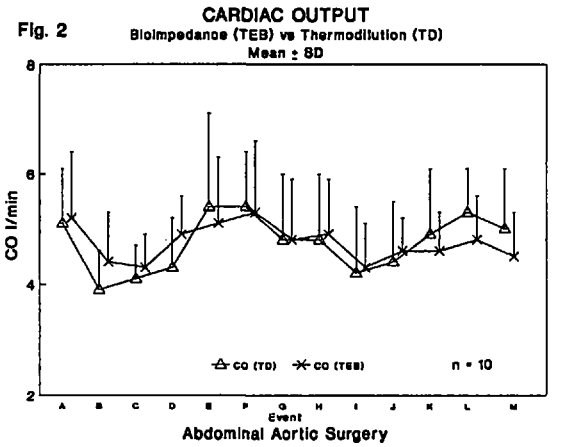



Fig. 2




**DISCUSSION:** Despite the fact that the thermodilution technique provides only an estimate of cardiac output, it remains the most practical reference for determining the potential clinical utility of non-invasive methods of cardiac output measurement. In this study, $CO_{TEB}$ provides reasonable correlation and good trending capability compared to $CO_{TD}$ during AAS. The bioimpedance technique for measuring cardiac output may potentially be very useful in the perioperative setting.

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# OPERATING ROOM NOISE

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**Introduction**
Environmental noise has been shown to affect the psychological and physiological wellbeing of the individual.[1] Concern has been expressed about noise levels in the operating room.[2] Although testing has established a quantitative base of information from which to address these concerns,[3] the operating room environment has not been studied extensively with regard to noise.

**Methods**
We used a Metrosonics dB308 Noise Dosimeter/Analyzer to measure noise levels in six operating rooms. Rooms are designated for differing surgical procedures: Rooms 1 and 2 - orthopaedic surgery; Room 3 - ophthalmic surgery; Room 4 - plastic, orthopaedic or general surgery; Room 5 - otolaryngological surgery; and Room 6 - neurosurgery. We analysed noise levels for a minimum of three test periods over an average time range spanning 3-8 hours total, for each room. A ceramic microphone was used with an operating range of 45-140.6 decibels [dB(A)]. For each study, the microphone was positioned on the anaesthetic machine, within 1 metre of the patient's head.

**Results**
A summary of data obtained is shown in Table I.

**TABLE I**

| | L10 | L50 | L90 |
|---|---|---|---|
| Room # 1 | 69 | 60 | 54 |
| Room # 2 | 68 | 61 | 56 |
| Room # 3 | 64 | 56 | 51 |
| Room # 4 | 65 | 58 | 51 |
| Room # 5 | 69 | 62 | 57 |
| Room # 6 | 69 | 62 | 54 |

L10, L50, L90 in dB(A)

L10 denotes the level in average decibels above which 10% of the data lie. L50 and L90 are defined in a similar fashion, with L90 commonly used to indicate the ambient or background noise level. These values represent weighted averages of multiple tests performed in each room.

In addition, the Dosimeter calculated a range of averaged or 'equivalent' (Losha) sound levels for each test. These values are derived by taking into account the logarithmic nature of the sound level and are shown in Table II.

**TABLE II**

| | Losha Range in dB(A) |
|---|---|
| Room # 1 | 63.0 - 67.9 |
| Room # 2 | 59.7 - 67.9 |
| Room # 3 | 57.3 - 61.2 |
| Room # 4 | 60.2 - 63.6 |
| Room # 5 | 64.4 - 66.1 |
| Room # 6 | 63.4 - 65.8 |

**Discussion**
The results show that the ophthalmic operating room was the quietest. This may reflect the nature of the work and lack of multiple staff and heavy instruments. The United States Occupational Safety and Health Association standard for noise exposure suggests that there is risk of hearing loss at sustained values of 85 dB(A) in a continuous 8 hour period.[4] Our data suggest that there is no occupational hazard for hearing loss associated with these operating rooms. However, noise levels are such that, at times, speech discrimination could be impaired. This may be significant in an environment where a misunderstanding could have disasterous consequences.

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# RECOVERY ROOM EVENTS IN EYE PATIENTS: SHOULD IT INFLUENCE YOUR ANAESTHETIC TECHNIQUE?

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## INTRODUCTION

Currently few hospitals in Canada have a systematic method of recording recovery room complications. We have developed a data base to record post-operative recovery room (RR) events (defined as undesirable or less than ideal occurrences in the recovery period). As a pilot study for this project, we studied patients undergoing eye surgery since they tend to be at risk for peri-operative complications because of their advanced age and co-existing disease.[1] It is still controversial as to whether general anaesthesia (GA) is as safe as neuroleptanalgesia (NL) for this group of patients.[2] Using the database, we compared the rate of recovery room events in patients receiving GA versus NL.

## METHODS

Over a one month period, the RR nurses documented all undesirable events as they occurred in 103 consecutive eye patients on a revised recovery room form. Events were divided by systems and included cardiac (eg. hypo/hypertension, dysrhythmias etc.), respiratory (eg.desaturation, bronchospasm etc.), neurological, fluid-renal-metabolic and miscellaneous. These events were specifically pre-defined by the authors. Pre-operative data, (ASA status, current illnesses), all peri-operative medications, duration of surgery and RR time was then entered into a database. Differences between the GA and NL groups were analyzed by the Chi-squared test (Fisher's exact test where necessary) and Student's t-test where appropriate and a p value $< 0.05$ was considered significant.

## RESULTS

Thirty patients out of 103 had events in the RR for an overall incidence of 29%. Of these patients, 83% of them had GA's. Patients over the age of 70 who had a GA had significantly more events than those who had a NL. ($p=0.001$) There were no life-threatening events in either group which required the immediate attention of an anaesthetist. The most frequent events were desaturation (SaO2<90%), hyperglycemia (BS>15) and bradycardia (HR<50 X >15 min). Patients in the GA group were younger ($p<0.001$), but there was no difference between their ASA status.
There was no difference in the room air SaO2 done before discharge between the two groups. Patients whose surgery was greater than 2 hours had significantly more events (13/17) than those whose surgery was less than 2 hours 17/56). ($p=0.04$)

There was no difference in the room air SaO2 done before discharge between the two groups. Patients whose surgery was greater than 2 hours had significantly more events (13/17) than those whose surgery was less than 2 hours 17/56). ($p=0.04$)

Results are summarized in this table:

| | GA | NL |
|---|---|---|
| number of patients | 57 | 46 |
| mean age (years) | 55±20* | 72±9* |
| number of >70 yrs | 19 | 27 |
| avg # illnesses | 1.05 | 1.56 |
| avg # current meds | 48 | 57 |
| ASA status I-II | 41 | 33 |
| ASA status III-IV | 15 | 12 |
| # pts. with events | 25* | 5* |
| # RR events | 34* | 6* |
| # pts>70 yrs who had events | 12* | 2* |
| mean SaO2 on R/A on D/C | 94 | 93 |
| # pts with SaO2<90 | 7 | 2 |
| # pts nausea/vomiting | 4 | 0 |

* denotes statistical significance $p<0.05$

## DISCUSSION

In our study, patients undergoing a GA had significantly more undesirable events in the RR ($p<0.001$) than the NL group despite comparable pre-operative status. Elderly people were more likely to have an event if they had a GA. The incidence of desaturation, nausea and vomiting, was also higher in the GA group, though not statistically significant. Duration of surgery correlated with the incidence of events, as previous studies have shown.[3]

This data suggests that NL is preferable when feasible for this group of patients because of a lower incidence of RR events. None of these events were life-threatening, but were deemed undesirable. Limitations of the study include lack of randomization of the GA and NL groups which is clinically difficult.

This pilot study found that a RR database can be used successfully to study important research questions. When other groups of patients are entered into this database it will define other peri-operative factors which will minimize recovery room events.

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# SASKATCHEWAN ANAESTHETIC MACHINES AND RELATED MONITORS - A HOSPITAL PREVALENCE STUDY

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**INTRODUCTION:**

In recent years (1980 and 88) Manitoba initiated a Manitoba Anaesthetic Machine Program to accommodate the Canadian Standards Association Z168.3-M1980, "Continuous Flow Inhalational Anaesthetic Apparatus (Anaesthetic Machines) for Medical Use." Manitoba's most recent survey was reported by R.M. Friesen et al in June 1989. Saskatchewan has a similar size population base with a wider and more even geographical distribution. A prevalence study was done in the summer of 1989 by the authors to determine the Saskatchewan situation for anaesthesia machines.

**METHOD:**

All hospitals and one private clinic in the province were surveyed in this prevalance or snapshot study. Phase One was an initial letter of explanation with an accompanying questionnaire to each hospital in the province as outlined by the Saskatchewan Hospitals Association (SHA). Each hospital with an anaesthetic machine (save one) was visited on site to corroborate the questionnaire to ascertain the availability and function of: number of anaesthetic machines present, machine type and age, frequency of use in preceding twelve months, maintenance methods, and ancillary monitoring equipment at each site.

The hands-on machine evaluation included medical gas supply (wall and machine), pressure gauges, yokes, oxygen fail safe, oxygen flush method common gas outlet, oxygen monitor, back bar lock-out mechanism, flow meters, vaporizers, ventilators, pressure alarms, carbon dioxide ($CO_2$) absorbers, breathing circuits, and waste anaesthetic gas scavenging systems.

Ancillary monitors reviewed included electrocardiogram (EKG), non-invasive blood pressure (NIBP), pulse oximeter ($SaO_2$), end-tidal capnography ($ETCO_2$) and temperature (Temp).

The last preventative machine maintenance provided by individuals outside the anaesthesia department or hospital was determined.

Finally, each hospital, clinic and aforementioned group was provided with an individualized and general summary of the study.

**RESULTS:**

Ninety-seven hospitals (16 urban, 81 rural) were included for a total of 191 machines (and 1 clinic machine). 141 machines were used in the preceding twelve months. Of these 141 active machines 136 (96%) had had preventative maintenance in the past twelve months. It is interesting that 15/59 (42%) of the inactive machines had also been serviced.

The following table outlines the monitoring devices available with each active anaesthetic machine.

TABLE 1

| | n | % |
|---|---|---|
| Anaesthetic Machine Monitors/alarms | | |
| Oxygen monitor ($F_iO_2$) | 119/141 | 84 |
| H/L pressure monitor | 38/141 | 27 |
| Spirometer | 24/141 | 17 |
| Oxygen pressure fail safe | 121/141 | 85 |
| Patient monitors | | |
| Electrocardiogram | 131/141 | 93 |
| Automated non invasive BP | 91/141 | 65 |
| Temperature | 23/141 | 16 |
| Pulse oximetry | 79/141 | 56 |
| Capnography | 52/141 | 37 |

13% (25/191) of the machines were manufactured before 1970, 41% (79/191) of the machines were manufactured from 1970 to 1980, and 46% (87/191) were manufactured after 1980. Some form of back bar lock out device was present on 83% (117/141) of active machines. Scavenging, active or passive, was present on 83% (117/141) of the machines in use in the last year.

**DISCUSSION:**

This prevalence study gives an indication of what anaesthetic machines and related monitors exist in Saskatchewan, a province of one million as of the summer of 1989.

We now have a reasonable idea of what we currently possess. It is now time for remedial action to update both machines and monitoring equipment. Up-to-date monitors may be as important or more important than up-to-date machines as long as the stated specific safety measures are present.[4]

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# RECOVERY AFTER NEUROLEPTANALGESIA FOR CATARACT SURGERY

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Introduction: Sedation as an adjunct to regional analgesia in the elderly can result in confusion, restlessness during surgery and prolonged recovery. Cataract surgery is increasingly performed on short stay patients where rapid induction and recovery are desirable and where adverse effects should be minimal. The recovery and amnesic effects of short-acting narcotics such as alfentanil and fentanyl in combination with diazepam have not been adequately assessed in the elderly. We used a pre-test and post-test questionnaire to assess cognitive and neurobehavioural recovery and amnesia in a double-blind randomised comparison of alfentanil/diazepam and fentanyl/diazepam combined with retrobulbar block for cataract surgery.

Methods: Institutional approval and informed consent were obtained for this study of 70 patients undergoing unilateral cataract surgery with retrobulbar block and neuroleptanalgesia. Each patient was examined and interviewed in the pre-anaesthetic assessment clinic. Patients over 50 years, without a history of memory or cognitive deficit, were eligible for study and completed the pre-test questionnaire. Patients were then randomised to either (GROUP A) alfentanil (5 µg/kg) plus diazepam (0.1 mg/kg), or (GROUP F) fentanyl (1 µg/kg) plus diazepam (0.1 mg/kg). Study drugs were prepared in advance with each narcotic diluted in a water soluble emulsion of diazepam and normal saline to 10 ml and administered IV as 0.1 ml/kg at a rate of 0.03 ml/kg/min. Bupivacaine 0.25% was used for retrobulbar block. During surgery ECG, blood pressure and pulse oximetry were continuously monitored. In the recovery room each patient completed the first post-test questionnaire and 24 hours later an identical questionnaire was completed. Data were analyzed by multiple chi-square comparisons (significant $p = 0.05$) of 10 pre-test categoric questions and 40 descriptor questions of memory and cognition. In addition adverse outcomes and standard pain and recovery scores were recorded.

Results: The results of the pre-test questionnaire showed that 31% of patients had disturbing dreams and napped during the day, 26% of patients were prone to nausea, 23% were forgetful and 6% showed mild confusion. All of these were related to age and were unaltered by anaesthesia. The recovery scores for alfentanil/diazepam were higher than fentanyl/diazepam upon admission to the recovery room but pain scores did not differ. Recall of retrobulbar injection was found in 54% of patients in both groups, whereas during surgery was found in 97% of patients in GROUP A and 89% in GROUP F. Pain during retrobulbar injection was recalled by 11% of patients in the recovery room but only 4% the following day. Postoperative nausea and vomiting was uncommon (<3%) in both groups. Cognitive assessment did not show any difference for GROUP A between pre-test and the recovery room and 24 hour post-tests. For GROUP F there was a small deterioration in cognitive function in both post-tests. Blinded assessment of surgical conditions and postoperative wellbeing were independently made and showed better analgesia and greater patient co-operation during surgery and wellness after surgery in GROUP A patients. Patients assessed their return to normal after 9 hrs in GROUP A and after 17 hrs in GROUP F while 89% of patients in GROUP A and 67% in GROUP F rated their anaesthesia as excellent. However 20% of GROUP F patients rated their anaesthesia as only fair compared to none in GROUP A.

Discussion: The combination of alfentanil and diazepam provides superior conditions compared to fentanyl with diazepam for cataract surgery and is safe for use in elderly patients. Recovery is faster and more complete, there are no significant changes in cognition or memory and patient satisfaction is greater. Although the deterioration of cognition after fentanyl/diazepam was small, this persisted for up to 24 hrs. Amnesia following injection was similar in both groups.

"AN IMPROVED SYSTEM FOR NARCOTIC CONTROL IN THE OPERATING ROOM"

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**INTRODUCTION:** The legal control of opiates is a universal concern in pharmacy and anaesthesia practice. Several concerns regarding narcotic control within the operating room (O.R.) can be raised, but the major concern of the Department of Pharmaceutical Services is accountability. (Accountability was defined as the degree of dose correlation compared to narcotics administered.)

The purpose of this project was first, to determine the extent of the narcotic accountability problem in the O.R. under the current system. Second, a new system of control was implemented. Finally, the new system was evaluated for narcotic accountability and impact upon staffing requirements.

**METHOD**

(i) The original or baseline method consisted of an anaesthetist signing out all or most of a days opiate requirements in conjunction with the first patient on their list. A narcotic inventory was done every eight hours by nursing staff.

(ii) The new system, evaluated several features common to successful O.R. narcotic control systems outlined in the literature.[1,2,3] In essence it is an anaesthesia controlled system outlining professional responsibility and accountability for narcotic agents. In so doing it liberates the O.R. nursing staff from the responsibility of narcotic inventories. In practice narcotic "kits" containing standardized narcotic inventories were prepared by pharmacy and dispensed to anaesthetists. Prior to each case the anaesthetists were to remove a kit from a locked cabinet. Inside each kit was an administration record slip, on which the patient's name, anaesthetist's name and the dose administered were to be indicated. Following each case the used kit was to be deposited in a locked cupboard. Used kits were retrieved, reconciled and repackaged in the main pharmacy. Discrepancies were confirmed within 24 hours with the anaesthetist involved.

**RESULTS**

(i) A baseline two-week audit found an O.R. narcotic accountability of 18% (59 narcotic logs with 327 patients).

(ii) A second O.R. narcotic audit was undertaken during the pilot study; the new system provided narcotic accountability of 83% (157 narcotic logs for 187 patients) over two weeks of operation. The discrepancies may be explained by a failure of the anaesthetists to follow policies of the pilot study. On one day the system was bypassed and narcotic accountability returned to 18%.

(iii) Workload measurement studies showed incremental full time equivalent (FTE) requirements for a pharmacy clerk and a pharmacist of 0.54 and 0.017, respectively.

**DISCUSSION** The baseline narcotic audit of 18% indicated a significant problem in the present system. The new system outlined above was generally well accepted by the anaesthetists, and increased narcotic accountability was recognized. Modifications to the system are being considered by the Department of Pharmaceutical Services in an effort to satisfy both ease of operation and accountability needed by law.

**CONCLUSIONS** Based on the results of this study it is concluded that current practice provides limited narcotic accountability in the operating room. It was recommended that a new system be implemented, with staffing requirements recognized. In addition, it was recommended that a committee be formed with representatives from Anaesthesia, Pharmacy and Administration, to further monitor an improved narcotic contol system in the operating room.

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# FEWER ADVERSE OCCURRENCES DURING REGIONAL THAN GENERAL ANAESTHESIA

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Introduction. The purpose of any quality assurance (QA) program is to assess differences in the risk to the patient between one method or practitioner and another and to suggest possible improvements. This is done by monitoring a defined set of complications and observing differences in their incidence between various groups. It has been the conventional wisdom, dating from the observations of Dripps and others,[1] that the relative complication rate between regional and general anaesthesia alone is not significant with respect to outcome. This study indicates that this may not be true for a number of common anaesthesia-related problems.

Methods. The method for concurrently gathering and assessing quality assurance data has been previously described.[2] A QA monitoring form listing 61 adverse patient occurrences (APOs) and other clinical parameters was attached to the anaesthesia record and filled out by the anaesthesia provider for every patient anaesthetized. Patient name and number, type of anaesthesia, ASA physical status, anaesthetizing location in the hospital, and anaesthesia providers were also recorded. For patients with an APO, a brief description of the occurrence – its cause, treatment, and acute outcome – was documented on the back of the QA form. The QA forms were retrieved daily and checked against the operating schedule to confirm completeness of reporting. The APOs were evaluated as avoidable or unavoidable, based on written criteria. Treatment of the APO was evaluated as appropriate or inappropriate. The QA data and assessments were then entered into a database using Reflex, a flat file database capable of cross tabulation. Differences in the responses to types of anaesthesia were evaluated using the chi-square test. Differences were considered significant when $p<0.01$.

Results. (Table). QA forms were received for 96% of the patients anaesthetized. Data were collected from 13,281 patients undergoing anaesthesia at a university-affiliated hospital from July 1, 1988 to June 30, 1989: 9544 patients received general anaesthesia, 2540 regional anaesthesia, and 1197 patients, not the subject of this study, received managed anaesthesia care. There were 3139 ASA Class I, 6010 Class II, 3296 Class III, 764 Class IV, and 54 Class V patients in the study. The distribution of complications by ASA class was not significantly different between types of anaesthesia. The rate of APOs was 8.72% for patients undergoing general anaesthesia and was significantly higher than the 3.86% rate with regional anaesthesia. When the APOs related exclusively to general anaesthesia (*eg*, airway management problems) and those related exclusively to regional anaesthesia (*eg*, block failure) were subtracted from the respective totals, the differences were still significant. The relative incidence of bradycardia 30% below and hypertension 30% above preoperative values was not significantly different between regional and general anaesthesia; however, severe hypotension, ischaemia, dysrhythmia, cardiac arrest, and death were either absent from or occurred significantly less often in the regional anaesthesia group. Specifically, there was a 2.3% incidence of cardiovascular occurrences associated with general anaesthesia as opposed to 0.9% with regional. Nausea and vomiting followed 1.3% of all general anaesthetics, but significantly fewer, 0.1%, regionals. Respiratory problems such as postoperative ventilatory support, bronchospasm, and hypoxaemia were also significantly more frequent with general anaesthesia. Multiple adverse events (2 or 3) were no more likely during regional than general anaesthesia. Adverse events were assessed as preventable 29.6% of the time with general and 32.2% of the time with regional anaesthetics.

Discussion. Clearly, there is a significant overall difference in the overall adverse occurrence rates between regional and general anaesthesia, even when the differences uniquely found in only one or the other are removed. For whatever reason, regional anaesthesia was less than half as likely, in our institution to be associated with adverse intraoperative events. It is equally clear that more remains to be done before the underlying cause of this difference can be stated, *eg*, prospective matching of groups by age, operation, duration of surgery, and surgeon. These kinds of data are often not a part of the standard quality assurance database, the primary purpose of which is to point toward potential problems and solutions. In summary, in this study, regional anaesthesia appeared to be relatively free of serious problems in the short run, but its effect on long-term outcome could not be assessed. The data in this study point toward an important potential difference between types of anaesthesia that warrants further investigation.

Table: Comparison of Adverse Occurrences

| Group: | General Anaesthesia | Regional Anaesthesia |
|---|---|---|
| Cases (n) | 9544 | 2540 |
| APOs (n)* | 832 | 98 |

*$p<0.01$ between anaesthetic groups

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# EFFECTS OF SALINE DILUTION AND I.V. CATHETER SIZE ON THE INFUSION OF PACKED RED BLOOD CELLS

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## INTRODUCTION

Current guidelines distributed by the Canadian Red Cross Society recommend addition of 50 mls of normal saline to a unit of packed erythrocytes if one wishes to increase the infusion flow rate. When rapid transfusion of blood is required, many anesthetists will add significantly more saline to a unit of packed erythrocytes in the hope of decreasing viscosity and increasing the flow rate.Although a few studies have determined the intravenous flow rates of crystalloid solutions[1,2]only one study has investigated the factors involved in the rapid infusion of packed red blood cells.It did not address the issue of total time required to transfuse the units of erthrocytes, since reconstitution yields units of packed cells with different total volumes.

The purpose of this study was to determine the optimal volume of saline that would yield the highest flow rate and the shortest time for complete transfusion of a unit of packed red blood cells while minimizing equipment and stress-related hemolysis. We also examined the effect of catheter size on these three variables.

## Methods

A 3X5 in vitro factorial design was used to assess the effects of dilution (none, 100 and 200 mls of normal saline) and catheter size (20,18,16 and 14 gauge and 16 gauge central line) on flow rate time to infuse 90% of total volume and hemolysis of packed red blood cells. Fifteen units of recently outdated packed erythrocytes were obtained from the hospital blood bank. Each was randomly assigned to one of the fifteen experimental conditions. They were weighed before and after dilution; Blood was also sampled after dilution and after infusion for measurement of free hemoglobin levels, an index of hemolysis. This was obtained from the supernatant plasma using a spectrophotometric technique. The transfusion apparatus consisted of an 82 inch non-vented Y-type blood administration set combined with a blood-warming extension and a blood warmer set at 37 degrees Celsius. The appropriate i.v. catheter was attached to the end of the blood-warming set and fixed to the inside wall of a clear plastic volumetric container. All units were infused under 300mm Hg delivered by an infusion pressure cuff. Volume infused and blood temperature were recorded every thirty seconds. Data were subjected to descriptive statistics and analysis of variance using a P-level of less than 0.05.

## Results

Dilution of units of packed cells with normal saline was found to significantly increase the flow-rate of the infusion (Table 1). There was not always a significant difference between 100mls and 200mls dilurion. This increased flow rate did not succeed in decreasing the time needed to infuse 90% of the total volume on the reconstituted packed red blood cells. There were no significant differences in the time required to infuse 90% of the total volume for the three levels of dilution.

The catheter size and length were found to significantly influence the flow rate of packed red blood cells; the smaller catheter yielding slower infusion rates (Table 2). A similar and significant difference was found when the time to infuse 90% of the total volume was examined: small gauge catheters took longer than did the larger catheters. The 16 gauge central line catheter did not perform any better than the 20 gauge catheter.

Free hemoglobin levels are currently pending.

## Discussion

It is interesting to note that despite obtaining increased flow rates when diluting packed erythrocytes with normal saline, this does not result in faster delivery of the mass of red blood cells to the patient.In situations where the patient requires both volume and erythrocytes, it seems advantageous to reconstitute packed cells with normal saline. For the patient who requires erythrocytes but is at risk for volume overload, it would seem prudent and equally efficacious to not reconstitute the packed cells.

Once again the important role of catheter size has been confirmed:larger catheters yield higher flow rates. This is often the variable that is the most easily controlled by the anesthetist. The relatively low flow rates obtained with the 16 gauge central line catheter present yet another argument for selecting peripheral lines over central lines for the infusion of blood products.

This study represents an in vitro attempt to examine the influence of volume of dilution and catheter size and length on the rapid infusion of packed red blood cells. Further studies need to be done to examine the influence of these factors under other situations which also mimic clinical situations.

Table 1

| Dilution Volume (mls) | Flow Rate (mls/min) | Time To Infuse 90% Vol. (seconds) |
|---|---|---|
| 0 | 64.6 | 199.8 |
| 100 | 109.7 | 181.8 |
| 200 | 142.2 | 188.6 |

Table 2

| Catheter Size (gauge) | Flow Rate (mls/min) | Time to Infuse 90% Vol. (seconds) |
|---|---|---|
| 20 | 75.7 | 246 |
| 18 | 95.9 | 179 |
| 16 central | 66.6 | 237 |
| 16 | 133.0 | 154 |
| 14 | 156.2 | 126 |

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# BALLOON FLOATATION IS MORE IMPORTANT THAN FLOW-DIRECTION IN POSITIONING "FLOW-DIRECTED" PA CATHETERS

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Pulmonary artery catheters (PAC's) are usually inserted supine with pressure monitoring. Over 80 percent of the time the catheter tip will lie in a branch of the right PA, presumably because the higher blood flow of the right lung carries the balloon tip in its current. For certain procedures such as right pneumonectomy it would be useful to position the PAC in the left PA. The objectives of this study were: (1) to ascertain in a randomized clinical trial whether lateral positioning could influence the location of the PAC tip, and (2) to evaluate with in-vitro simulation those factors that determine the dynamics of floatation of the balloon-tipped PAC.

## METHODS

Part 1: With institutional approval and informed consent, 33 patients undergoing elective coronary artery bypass surgery were randomized to have PAC's inserted in either the supine or right-side down position. Following introducer sheath insertion into the right internal juglar vein in the supine position, the PAC (American Edwards Paceport 7.5F) was inserted with the catheter curve to the patient's right, with the patient either supine or right-side down. Once a wedge waveform was obtained the balloon was deflated and the patient placed supine. The PAC tip position was verified by chest x-ray.

Part 2: A plexiglass model of the PA outflow tract and bifurcation was constructed and connected with PVC tubing to a cardiopulmonary bypass pump. With saline circulating through the system at various flow rates the PAC was advanced through the system. The influence of lateral positioning of the system and varying PAC size and direction of its natural curve were studied. Selective clamping of either branch of the PA bifurcation was performed and dye injected into the system to follow the effects of the altered flow patterns on balloon movement.

## RESULTS

Part 1: In five patients the PAC tip was withdrawn during the case and found to be in the main PA; these were excluded. In all 14 "supine" patients, the PAC tip was found to be in a branch of the right PA. Of the 14 "right-side down" patients, seven PAC tips were in the left PA. This was significant (P=0.003), Fisher exact test.

TABLE Results

| | Location of the PAC Tip | |
|---|---|---|
| | Left | Right |
| Supine | 0 | 14 |
| Right-Side Down | 7 | 7 |
| | (P=0.003) | |

Part 2: In the in-vitro model, the PAC tip always floated to the upward side, regardless of PAC size and changes in direction of the natural curve of the tip. Clamping the upward limb of the bifurcation did not prevent the tip from floating upward. Injection of dye into the circuit revealed floatation of the tip upward into an area of turbulence proximal to the clamp.

## DISCUSSION

Lategola and Rahn (1951)[1] described the use in dogs of a balloon-tipped catheter that could be inserted percutaneously and floated into the pulmonary vasculature without the need for fluoroscopic guidance. Swan et al (1970)[2] reported on the use of a similar system in humans. Studies have shown the PAC tip to be in the right PA after at least 80 percent of supine insertions. The results of this study show that in the right-side down position the PAC tip floats into the left PA significantly more often than in the supine position. This likely indicates that the effect of floatation of the air-filled balloon in the column of blood is more important than the effect of the increase in blood flow to the dependent lung.

The in-vitro model confirmed the effect of upward floatation of the balloon with the circuit in the lateral position. This predominated over the effect of PAC curve and size. Clamping the upward limb of the bifurcation, thus diverting the flow to the downward limb, did not prevent upward floatation, emphasizing the importance of this effect over flow-direction.

Right-side down positioning of the patient during PAC insertion significantly increases the likelihood of its locating in the left PA. Further refinement of the technique by identifying other factors involved in PAC floatation dynamics may lead to greater reliability in predicting its ultimate location.

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## A COMPARISON OF $CO_2$ LASER IGNITION OF THE XOMED, PVC AND RUBBER TRACHEAL TUBES

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Introduction: The use of laser is increasing in medicine and surgery due to their power, precision and hemostatic effects. However the high energy density of the surgical laser when used in proximity to combustible tracheal tubes during airway surgery can convert the tubes into veritable "blow torches." The result may be extensive burns to the patient. In an attempt to reduce the likelihood of such fires, the Xomed Laser-Shield™ tracheal tube (Jacksonville, FL, USA) was introduced. It is marketed as being "$CO_2$ laser resistant." To assess its superiority to conventional tracheal tubes, we compared its combustibility to polyvinylchloride (PVC) and red rubber (RR) tracheal tubes.

Methods: Size 7.0 mm ID Xomed Laser-Shield™, Mallinckrodt (Glens Falls, NY, USA) Hi-Lo PVC and Rusch RR (W. Germany) tracheal tubes were studied. A Cooper (Santa Clara, CA, USA) $CO_2$ laser and Zeiss (W. Germany) operating microscope with a 400 mm lens and "joy stick" micromanipulator were used to focus the laser beam perpendicularly onto the tracheal tubes. Five L/min of oxygen flowed through the tracheal tubes which rested on wet towels in air during the study. The laser was set to the continuous mode of operation and actuated until an intraluminal (blow torch) fire occurred. Ten trials each at 15, 17 and 20 watts were done for the PVC, RR and Xomed tracheal tubes. ANOVA and Scheffe tests were performed to detect significant differences between groups. A $P<0.05$ was considered necessary to rule out the null hypothesis.

Results: The times to blow torch ignition of the PVC tracheal tubes were (Mean±S.D.) 1.73±0.80, 1.76±0.73 and 1.53±0.42s at 15, 17 and 20 watts respectively. For the Xomed tracheal tubes, blow torch ignition occurred at 85.93±80.80, 42.51±49.35 and 20.30±39.32s at 15, 17 and 20 watts respectively. Laser contact with the RR tubes resulted in a candle like flame on the exterior of the tracheal tube after 11.91±6.00, 5.48±3.94 and 2.90±3.33 sec after 15, 17 and 20 watts respectively. Blow torch fires of the RR tracheal tubes occurred after 24.49±2.64, 25.41±4.60 and 21.92±5.60 sec at 15, 17 and 20 watts respectively. The differences in the times to combustion of the PVC vs. Xomed tracheal tubes achieved statistical significance at 15 and 17 watts ($P<0.05$). Intraluminal and extraluminal tracheal tube fires occurred after a significantly shorter time of laser exposure with the RR than with the Xomed tracheal tube at 15 watts ($P<0.05$). At 17 watts, extraluminal ignition of the RR tracheal tubes was noted after a significantly shorter interval of laser exposure than that for blow torch combustion of the Xomed tracheal tubes ($P<0.05$). At 20 watts there were no statistically significant differences in the times to combustion of the three tracheal tubes tested.

Discussion: The precision, power and hemostatic effects of the laser have led to its increased use in surgery. Other advantages of laser surgery over more conventional forms of treatment include reduced postoperative pain and edema. A survey of otolaryngologists active in laser airway surgery noted that fires are the most common serious complication of laser airway surgery.[1] The frequency of laser induced airway fires has been reported by Snow et al.[2] to be 0.57% making them one of the most common adverse events in clinical anaesthesia.

The seriousness of laser induced tracheal tube fires has led to the commercial development of special tracheal tubes for this application. The Xomed Laser-Shield™ tracheal tube was one of the first designed for laser surgery. It is fabricated from silicone which has a coating containing metallic particles. Our study shows that at 15 and 17 watts, a significantly longer duration of laser fire was required for ignition of Xomed tracheal tubes than PVC tubes. However at 20 watts of laser power, the time to combustion of the Xomed tracheal tube was not significantly different from that of the PVC tube. Similarly, while at 15 watts a longer period of laser contact was required for blow torch ignition of the Xomed tracheal tubes than for the RR tubes, at 17 and 20 watts there was no statistically significant difference in the time to intraluminal combustion of these tracheal tubes. Furthermore, the Xomed is much more expensive than the RR or PVC tracheal tubes.

Previous studies using the same experimental design by our group have shown that even at a power output of 70 watts with a duration of 1 min tracheal tube shafts may be adequately protected from the $CO_2$ laser. This can be accomplished by the careful wrapping of combustible tracheal tube shafts with self adhesive, 1/4 inch wide, 3M (Minneapolis, MN, USA) no. 425 aluminum,[3] or Venture (Rockland, MA, USA) 1 mil copper foil tapes[3] in an overlapping spiral manner. Alternatively the Laser-Guard[4] protective coating may be used. The latter consists of a self adhesive rectangular sheet of embossed silver foil to which a layer of sponge has been bonded. The stainless steel shaft of the Mallinckrodt Laser-Flex tracheal tube has also been shown to offer excellent protection from the $CO_2$ laser at high power.[5]

We conclude that the RR, PVC or Xomed tracheal tube provide inadequate protection from the $CO_2$ laser and should not be used for airway surgery. While the Xomed tracheal tube has been marketed as a "laser resistant" product, we determined that under the experimental conditions used, it did not offer a significant degree of safety beyond that of conventional RR and PVC tracheal tubes. We recommend wrapping tracheal tubes with the appropriate metallic foil tape, the use of the Laser-Guard™ or the Mallinckrodt Laser-Flex™ tracheal tube instead.

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# EFFECT OF HAEMOGLOBIN CONCENTRATION ON THE ACCURACY OF PULSE OXIMETRY

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## INTRODUCTION

The measurement of oxygen saturation by pulse oximetry is based on the finding that oxygenated and deoxygenated blood absorb infrared and red wavelengths to different extents.[1] It is not known whether the operation and accuracy of pulse oximeters is independent of the absolute haemoglobin concentration [Hg]. To examine this question, we performed the following in vitro study.

## METHODS AND MATERIALS

A simple finger model was devised to measure the oxygen saturation using two commercially available oximeters (Nellcor and Puritan Bennett/Datex). These measurements were compared to a direct measurement of oxygen saturation obtained with a Hemoximeter (Radiometer OSM2b). Venous blood, obtained from one of the authors, was divided into three aliquots to study the effect of [Hg]. The first aliquot was undiluted ([Hg] = 160 g/L), the second was diluted with plasma to a [Hg] of 100, and the third to a [Hg] of 50. Each aliquot was divided into two: one portion was fully oxygenated using an IL237 tonometer and the second was deoxygenated. Oxygen saturations between 50 and 100% were prepared by mixing the appropriate volumes of oxygenated and deoxygenated blood. A 1 ml sample of blood from each [Hg] and oxygen saturation was placed in the model and the space above the blood filled with nitrous oxide. Pulses were delivered manually to the model at 150 per minute. Once the oximeter measurement was constant for at least 20 seconds, a sample of blood was removed anaerobically to measure the oxygen saturation in the Hemoximeter.

The oxygen saturations determined by the oximeters were compared to those obtained by the Hemoximeter for each [Hg] using least squares linear regression analysis. The % error for each oximeter at each [Hg] was determined by calculating the difference between the oximeter and Hemoximeter, multiplying by 100 and dividing this difference by the value from the Hemoximeter.

## RESULTS

The % error in oxygen saturation was greater at oxygen saturations of 50% than at saturations of 100% (Figure). The absolute differences between the Nellcor and Puritan/Bennett Datex oximeters were less than 10% at saturations of 50% for all three [Hg]. The % error at a [Hg] of 100 g/L was < 7% while the % error at a [Hg] of 160 overestimated the saturation by 30-37%, and at a [Hg] of 50 g/L underestimated the saturation by 7-15%.

## CONCLUSION

The results of this in vitro model indicate that the % error associated with pulse oximetry depends on both the [Hg] and the oxygen saturation. The % error increases as the oxygen saturation decreases and is greater with a [Hg] greater than 100 g/L than it is with a [Hg] less than 100 g/L.

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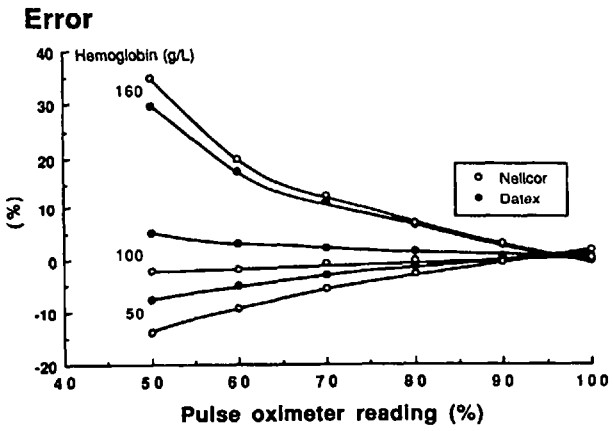
FIGURE



## A COMPARISON OF END-TIDAL AND TRANSCUTANEOUS PCO, MEASUREMENTS DURING ANAESTHESIA

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INTRODUCTION: Transcutaneous $CO_2$ ($TcCO_2$) monitoring may provide an alternative technique for continuous monitoring of ventilation. A randomized, prospective study was performed to determine the accuracy of the new Sensormedic™ $TcCO_2$ monitor in anaesthetized patients, by comparing the $TcCO_2$ measurements with arterial ($PaCO_2$) and end-tidal $CO_2$ ($ETCO_2$) measurements.

METHODS: Twenty-two adult ASA I-II patients undergoing elective surgery under general anaesthesia in the supine position with endotracheal intubation and mechanical ventilation were studied. All patients gave written informed consent to the protocol approved by the Hospital Human Procedures Experimental Committee. Patients greater than 60 years of age, with lung disease or obesity were excluded. General anaesthesia was maintained with fentanyl, isoflurane and $N_2O$:$O_2$ in a 2:1 ratio. Minute ventilation was adjusted by changing the respiratory rate in a randomized cross-over design, to achieve three different levels of $ETCO_2$ (Low: 28-30 mmHg; Medium: 34-36 mmHg; and High: 40-42 mmHg). Following a 10 minute steady-state period at each level, $TcCO_2$, $ETCO_2$ and $PaCO_2$ were measured. End-tidal gas samples were analyzed with an on line mass spectrometer, $PaCO_2$ was analyzed with a Corning 178 apparatus and the $TcCO_2$ monitor was pre-calibrated at 41°C. Additional measurements included heart rate and mean arterial pressure (Dinamap 1846P), oxygen saturation and nasopharyngeal temperature. Data were analyzed by linear regression and unpaired t-test; statistical significance was assumed when $p<0.05$.

RESULTS: Fifty-seven data sets with a $PaCO_2$ ranging from 28-62 mmHg were analyzed. The correlation between the regression lines comparing $ETCO_2$ and $TcCO_2$ with $PaCO_2$ was excellent (Fig.1 and 2). Comparison of the slopes of both regression lines showed a significant difference ($p<0.001$). Fig. 3 represents the gradients of $ETCO_2$ and $TcCO_2$ with $PaCO_2$ in the Low, Medium and High ranges. In the High $CO_2$ range, there was a significantly smaller $TcCO_2$-$PaCO_2$ gradient while the $ETCO_2$-$PaCO_2$ gradient was greatest.

DISCUSSION: Our data shows that the Sensormedic™ $TcCO_2$ monitor is a more accurate technique of monitoring $CO_2$ in comparison to capnography. Although we realize that this technique will not replace capnography for mechanically ventilated patients, it may provide excellent continuous monitoring in non-intubated patients.

Fig. 1 CO2 MEASUREMENTS
Arterial vs Endtidal

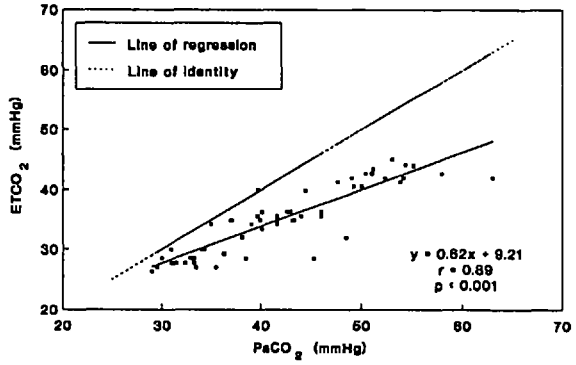



Fig. 2 CO2 MEASUREMENTS
Arterial vs Transcutaneous

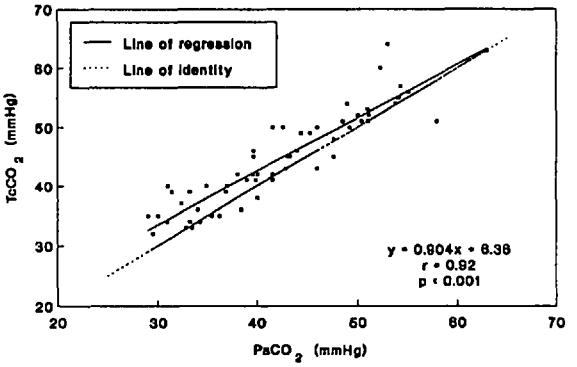
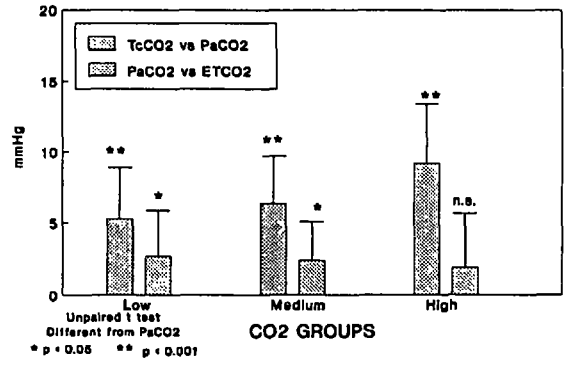



Fig. 3 MEASURED CO2 GRADIENTS
Mean ± SD



# RISK FACTORS FOR NAUSEA AND VOMITING AFTER GENERAL ANAESTHESIA

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## Introduction:

Post-operative nausea and vomiting is widely reported to be common and in most patients is not considered a serious adverse outcome[1]. However the published rates vary greatly which in certain situations such as during menstruation may exceed 50 percent[2]. There have been very few studies that were large enough to examine the numerous potential demographic, patient, anaesthetic and procedural interactions for these outcomes. We studied a database[3] of 3,483 patients (20.2%) who experienced nausea after general anaesthesia and 2339 patients (13.6%) who vomited and compared them with patients without these outcomes.

## Methods:

A total of 17,201 patients in the General Anesthesia Prospective Clinical Trial[3] were studied. Univariate chi-square analysis was performed for each outcome and each of 100 risk factors,including: age, sex, ASA, weight, obesity index, co-existing diseases, concurrent drug therapy, smoking, surgical procedure and duration, and premedicant and anaesthetic drugs. Those risk factors that were significant ($p = 0.05$) were then subjected to stepwise logistic regression analysis to determine if these were independent risks.

## Results:

There was very little difference in risk between nausea and vomiting except for degree. The risk of nausea and vomiting was increased in patients < 40 years, in females, after narcotic and after certain procedures, particularly laparoscopy, cholecystectomy and endocrine surgery. Patients with various types of cardiovascular, respiratory, endocrine and neurological diseases generally were not at risk or had a reduced risk of nausea and vomiting. Patients with hepatic or gall bladder disease had an increased risk of nausea and vomiting. Patients taking cardiac drugs or steroids or who smoked were not at risk of nausea and vomiting but patients taking antihistamines were.

TABLE: Univariate Risk Ratio (RR)

| | Nausea RR | P | Emesis RR | P |
|---|---|---|---|---|
| Female vs Male | 2.3 | $<10^{-6}$ | 2.0 | $<10^{-6}$ |
| ASA 1+2 vs 3+4 | 1.7 | $<10^{-6}$ | 1.7 | $<10^{-6}$ |
| Age <40 vs >40 | 1.3 | $<10^{-6}$ | 1.4 | $<10^{-6}$ |
| Gall Bladder disease | 1.7 | $3.6^{-6}$ | 1.4 | 0.021 |
| Laparoscopy | 1.8 | $<10^{-6}$ | 1.9 | $<10^{-6}$ |
| Cholecystectomy | 1.6 | $1.4^{-4}$ | 1.6 | 0.002 |
| Endocrine surgery | 1.5 | 0.010 | 1.6 | 0.010 |
| Vascular surgery | 1.6 | 0.007 | ns | 0.140 |
| Plastic surgery | 1.3 | $2.9^{-6}$ | 1.3 | $3.6^{-3}$ |
| Gynecol surgery | 1.3 | $<10^{-6}$ | ns | 0.143 |

Multivariate stepwise logistic regression confirmed that sex, age, ASA, gall bladder disease, laparoscopy and cholecystectomy were significant independent risk factors for both nausea and vomiting at $p < 0.05$. If a more stringent significance level of $p < 0.01$ is used, sex, age, and laparoscopy remain significant.

## Discussion:

Nausea and vomiting are more likely to occur in young healthy females undergoing laparoscopy or cholecystectomy. The use of narcotics before or during anaesthesia increases the risk of these outcomes but premedication with diazepam does not alter the risk. The risk of nausea and vomiting in young females undergoing laparoscopy is increased four-fold if performed during menstruation[2] and is at least twice the risk of the independent variables reported here. The potential for hormonal effects to interact with these risk factors needs further study.

## References:

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## FENTANYL BLUNTS THE HAEMODYNAMIC RESPONSE OF CHILDREN TO LARYNGOSCOPY

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**Introduction:** The major stress during induction of anaesthesia in most patients is laryngoscopy and tracheal intubation. Children are at risk of complications (e.g.: dysrhythmias, intracerebral haemorrhage) because of this stress response, but most investigations of this reaction involve adults. Fentanyl supplementation of an IV anaesthetic induction has been shown to blunt this pressor response in adults, but its effect in children is unknown.[1,2] Based on these adult studies, we hypothesized that 3 mcg.kg.-1 of fentanyl would attenuate this sympathetic response in healthy children.

**Methods:** After Hospital Ethics Committee approval and informed consent, 30 elective, ASA I-II physical status children of age 2 to 12 years were randomly assigned to 2 groups. Subjects were excluded if they had cardiac disease, respiratory disease, or one of the study drugs to be used was deemed inappropriate. **Baseline values:** Systolic blood pressure (SBP), and diastolic blood pressure (DBP) were measured with an appropriate blood pressure cuff by Korotkoff sounds and heart rate was determined by palpation in the Day Care Surgical Unit (DCSU) in a routine manner. On arrival in the operating room, the subject's HR, SBP, DBP, and mean blood pressure (MBP) were monitored with a Dinamapp® non-invasive blood pressure monitor (NIBP). The average of the values obtained in the DCSU and the first two values determined by the NIBP, which were obtained one minute apart, are the baseline values. **Induction:** During the first minute, the children were sedated by inhaling 70 percent N2O and 30 percent O2 and an IV catheter was inserted. Subsequently, the N2O was discontinued and the patients breathed, as tolerated, 100 per cent O2, for the remainder of the induction. During induction, the patients' haemodynamic variables were monitored every minute with the NIBP unit. The final values were measured 1.9 minutes after intubation. Both groups of patients were administered 0.1 mg/kg of vecuronium and 5 mg/kg of sodium thiopentone 2.0 and 1.8 minutes before tracheal intubation, respectively. Fentanyl, 3 mcg/kg, was administered IV 2.1 minutes before intubation. The trachea was intubated within a 15 second time period by a senior anaesthesia resident or anaesthetist. After intubation, anaesthesia was maintained for 2 minutes with 70 percent N2O, 30 percent oxygen and 1.5 percent halothane delivered through a coaxial circuit and ventilation was controlled to maintain normocapnia. Subjects were not stimulated during this period. Sample size was determined with a beta of 0.10. Data were compared using One-Way ANOVA, Two-Way ANOVA, ANCOVA, and Chi-square analysis, where appropriate. All results were accepted as significant if $P < 0.05$.

**RESULTS:** There were no significant differences between the groups' weight, age and gender. The haemodynamic stress response peaked 1 minutes after tracheal intubation (Figure). Fentanyl attenuated the induction pressor response; HR was reduced by 11 bpm, $P < 0.05$ (ANCOVA, covariates were baseline heart rate and age), and SBP was reduced by 20 mmHg, $P < 0.001$ (ANCOVA). By ANCOVA, the HR portion of the pressor response was modified by baseline HR. A higher baseline HR resulted in a greater pressor response of 0.4 bpm/bpm, $P < 0.025$. By ANCOVA, the SBP segment of the pressor response was increased by patient age. Older patients SBP response increased by 2.6 mmHg/yr. $P < 0.01$.

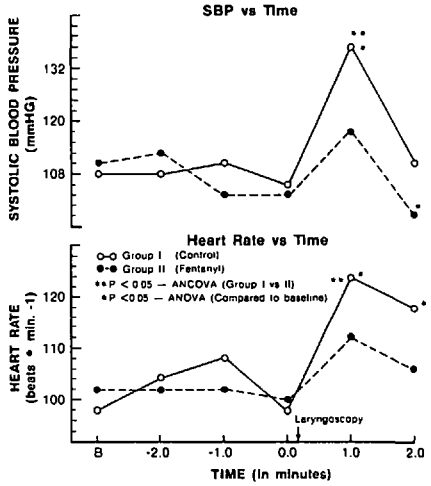


**Figure:** The heart rate and systolic blood pressure at rest (time = B, baseline), during induction of anaesthesia, and before and after tracheal intubation in children treated with thiopentone alone (Group I), and in combination with fentanyl (Group II).

**Discussion:** Haemodynamic stability is desirable during anaesthesia. Fentanyl, 3 mcg/kg, administered IV 2 minutes before tracheal intubation blunted the pressor response associated with laryngoscopy and intubation in healthy children. This was expected, based on adult investigations. We administered fentanyl 2 minutes before laryngoscopy. Whether this is the optimal time to give fentanyl before intubation is unknown. In addition, we do not know whether the effect of fentanyl on induction haemodynamic variables is superior to an equi-anaesthetic dose of sodium thiopentone. It was interesting to observe in children what is commonly obsered in adults' pressor responses. That is, older subjects had a greater rise in SBP and a child with a higher baseline HR, had a greater increase in HR. The results of this study could be applied to the management of children who are at risk of complications related to increased HR and blood pressure.

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# POSTOPERATIVE APNOEA IN FORMER PRETERM INFANTS: DOES ANAEMIA INCREASE THE RISK?

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It is very common to have premature infants with a low haematocrit (Hct) scheduled for minor surgical procedures in which no or minimal blood loss is anticipated. Episodes of apnoea and bradycardia occur frequently in premature infants, with the incidence inversely correlated with postconceptual age and weight.[1] This study determines whether the incidence of postoperative periodic breathing (PB), apnoea and bradycardia is increased in infants with preoperative Hct < 30%, and examines the adequacy of other factors that affect oxygen availability to the tissues in former preterm infants.

Methods: Preterm infants (gestational age ≤ 37 wks) 44-60 wks postconceptual age undergoing inguinal hernia repair were studied. All were required to have a preoperative Hct value of at least 25%. Following inhaled induction of anaesthesia, blood was drawn for measurement of Hb, Hct, reticulocyte count, % foetal Hb, 2,3-DPG and ATP levels. Anaesthesia was maintained with $N_2O$, $O_2$, halothane (ET ≤ 1.0%) and atracurium with controlled ventilation. Residual neuromuscular blockade was reversed at the end of surgery, and the trachea was extubated when the child was fully awake. In the postoperative period, the pattern of respiration and heart rate were continuously monitored and recorded for at least 12 h using an impedence pneumograph.[1] The incidence of postoperative apnoea, PB, and/or bradycardia in patients with Hct < 30% and those with Hct ≥ 30% were compared using Fisher's exact test or two-sample t-test as appropriate.

Results: To date, 24 children were studied. The results are presented in the table.

Discussion: For many years, a haematocrit of 30 has been the minimally acceptable level for elective surgery. More recently, anaesthetists became willing to accept children with lower Hct rather than subjecting them to the risk of blood transfusion. The former pre-term infant, however, is handicapped in his ability to compensate for the reduced oxygen carrying capacity that results from anaemia.[2] Because of the increased % of foetal Hb, decreased 2,3-DPG and inability to significantly increase cardiac output, oxygen flux is impaired. Previous studies in non-surgical patients have shown that this can result in tachycardia, dyspnoea, pallor, diminished activity, feeding difficulty, poor weight gain and even apnoeic attacks.[3]

Our results show that anaemia in former preterm infants can increase the incidence of postoperative apnoea. Many anaemic infants had a high percentage of foetal haemoglobin, which shifts the $O_2$ dissociation curve to the left and decreases the oxygen availability to the tissues. The threshold for requiring preoperative correction should be lower in these infants than in otherwise healthy full-term infants. If surgery cannot be deferred long enough to allow for correction of anaemia, these infants must be observed and monitored carefully in the postoperative period.

Table: Demographic data, haemotologic profile and postoperative complications in infants with haematocrits ≥ 30% and < 30%

| | Hct ≥ 30% (n = 19) | Hct < 30% (n = 5) | P |
|---|---|---|---|
| **Gestational age** | | | |
| mean ± SD | 33.5 ± 2.7 | 32.4 ± 3.2 | >.4[b] |
| range | 28 - 36 | 28 - 36 | |
| **Postconceptual age** | | | |
| mean ± SD | 45.5 ± 4.6 | 43.6 ± 5.5 | >.4[b] |
| range | 40 - 54 | 34 - 51 | |
| **History of apnea** | 4 (21%) | 1 (20%) | > .99[a] |
| **Hematologic Profile** | | | |
| Hematocrite % range | 32.7 - 39.1 | 27.6 - 29.7 | |
| Reticulocytes % mean ± SD | 2.32 ± 1.34 | 4.42 ± 2.49 | <.02[b] |
| Fetal Hb % mean ± SD | 36.7 ± 15.0 | 61.2 ± 33.8 | <.03[b] |
| ATP µm/dl mean ± SD | 50.8 ± 5.6 | 43.0 ± 3.3 | <.008[b] |
| 2,3 DPG µm/ml mean ± SD | 1.55 ± 0.28 | 1.27 ± 0.21 | >.07[b] |
| **Postoperative Complications** | | | |
| Brief apnea | 0 | 0 | |
| PB > 1% | 0 | 1 (20%) | >.2[a] |
| Prolonged apnea | 4(21%) | 4 (80%) | <.03[a] |
| Bradycardia | 0 | 1 (20%) | |

a = Fisher's exact test b = two-sample t-test

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## THE EFFECT OF DIFFERENT $N_2O$ CONCENTRATIONS ON MAC IN INFANTS AND CHILDREN

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Introduction. $N_2O$ reduces the MAC for volatile anesthetics in adults. With the increased requirements for volatile anesthetics in infants and children, $N_2O$ may not reduce halothane MAC in this age group to the same degree as observed in adults.[1] The purpose of this study was to measure how $N_2O$ alters the MAC of halothane anesthesia in infants and children. The effect of three different $N_2O$ concentrations on halothane MAC also provided information to predict whether $N_2O$ contributes to MAC in an additive manner as suggested by Eger or in a non-linear fashion as suggested by Cole.[2,3]

Methods. After informed written parental consent was obtained, 49 unpremedicated infants and small children who required elective surgery were studied. All patients received a mask inhalation induction with halothane and nitrous oxide and oxygen via a semi-closed circle system. Following induction of anesthesia, endotracheal intubation was performed and the anesthetic levels adjusted to pre-determined end-tidal $N_2O$ and halothane levels. End-tidal and inspired gas concentrations were measured from a secondary lumen for obtaining gas samples from the distal end of the endotracheal tube (Sheridan®) and recorded using a Perkin-Elmer mass spectrometer®. Ventilation was controlled during the study period.

The infants and children were divided into four groups to assess the MAC of halothane during 0%, 25%, 50% and 75% $N_2O$. At each $N_2O$ level, the study group was initiated after an opposite paired response had occurred (move-no move or vice versa). The halothane concentration selected for each patient was based on responses of the previous child in the study. Halothane levels were increased or decreased by 0.1 to 0.2 vol% depending on whether the previous child had moved or not moved in response to the surgical incision. Using this up and down method, the purpose of the study was to bracket an end-tidal concentration for halothane at each $N_2O$ concentration that would represent MAC. The results were analyzed by one way analysis of variance to compare differences between halothane levels, age, weight, and end-tidal $CO_2$ between the four groups. A regression analysis was used to determine the relationship between the MAC levels for halothane at each $N_2O$ concentration. Results are expressed as mean ± SD.

Results. The mean age and weight of infants and children in the study was 13.2 ± 7 mos and 10.4 ± 2.5 kg respectively. The ages and weights of the children were not significantly different among the four groups. The mean end tidal $CO_2$ during the study period was 29 ± 4 mmHg. During the study period, the mean duration of constant end-tidal halothane levels was 10 ± 3 minutes (the minimum period was 6 minutes). End-tidal $N_2O$ levels and halothane MAC for each study group are defined in Table 1.

The MAC for halothane decreased significantly as increasing $N_2O$ concentrations were administered. A regression analysis for all four patient groups extrapolated through all the data sets yielded a linear relationship (Fig 1). The $r^2$ value for this relationship was 0.87.

Discussion. The MAC of halothane in oxygen in this study (0.94 ± 0.08 vol %) was similar to the MAC value determined by Gregory et al in a study of infants of similar age.[1] Based on regression analysis, $N_2O$ appears to contribute in a linear fashion to halothane MAC. This linear contribution of $N_2O$ is similar to the findings in healthy adults when 30% and 70% $N_2O$ are added to enflurane anesthesia, but different than data obtained by Cole et al in a study that assessed multiple $N_2O$ levels in rats. The MAC value predicted for $N_2O$ in infants and children is approximately 105% similar to a study of adult volunteers under hyperbaric conditions. While anesthetic requirements for halothane and isoflurane are increased in infants, the predicted MAC of $N_2O$ in infants and small children suggest that the MAC of $N_2O$ is not significantly different between infants and adults.

In summary $N_2O$ appears to contribute in an additive manner to halothane MAC in infants and children at 25, 50 and 75% $N_2O$ concentrations. The MAC of $N_2O$, unlike halothane and isoflurane, may not be increased in infants and small children.

Table 1

| Group | n | Mean $N_2O$ (Vol %) | Halothane MAC (Vol %) |
|---|---|---|---|
| 1 | 11 | 0 | 0.94 ± 0.08 |
| 2 | 13 | 24.8 ± 1.4 | 0.78 ± 0.12 |
| 3 | 12 | 49.8 ± 1.5 | 0.44 ± 0.10 |
| 4 | 13 | 73.4 ± 2.7 | 0.29 ± 0.06 |

Figure 1

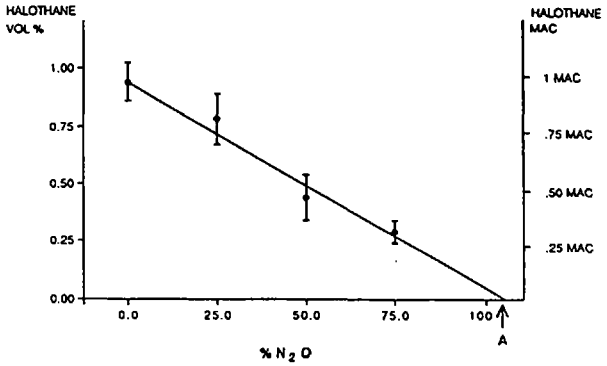


Fig. 1 Relationship of different concentrations of $N_2O$ to halothane MAC for four patients groups. "A" represents the predicted MAC of $N_2O$ from regression analysis.

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# TRANSDERMAL SCOPOLAMINE PATCHES REDUCE POSTOPERATIVE EMESIS IN PEDIATRIC PATIENTS UNDERGOING STRABISMUS SURGERY.

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## Introduction

It has been reported many pediatric patients vomit after strabismus surgery. Vomiting is unpleasant and has associated potential hazards of dehydration and contamination of the surgical wound. Many investigators have been trying to find an effective method for preventing this undesirable postoperative complication. We have therefore adopted the use of transdermal scopolamine patches (Scopoderm TTS, Ciba) which are normally employed to prevent motion sickness[1]. This is the first report of transdermal scopolamine being applied for pediatric patients.

## Method

Informed consent was obtained from the parents of 50 children, who had an ASA physical status of 1 or 2, and were aged between 1 and 11 years. They were randomly assigned to either a control or a transdermal scopolamine-treated group, each containing 25 subjects. The dose of scopolamine was reduced from half to one-fourth depending on age (a full sheet of patch contains 1.5 mg of scopolamine). The scopolamine patch was placed behind the ear on the evening prior to surgery.

Anesthesia was induced with halothane with 67% nitrous oxide in oxygen. After administration of either pancuronium or vecuronium, the trachea was intubated and ventilation was controlled. Prior to eye manipulation, 0.01 mg/kg atropine was administered intravenously. Anesthesia was maintained with 0.5-1.0% halothane with 40% nitrous oxide in oxygen. Upon completion of surgery, all patients were administered neostigmine and atropine to reverse the effects of residual muscle relaxants. The trachea was extubated when spontaneous ventilation was adequate and the gag reflex was present. None of the patients were given any antiemetic drug or analgesics postoperatively. Oral intake of liquid was allowed when the patients felt thirsty at least 1 h after surgery. Postoperative observation in the recovery room and in the ward was completed by nurses, who were unaware of the treatment regimen given to each patient. We recorded the incidence of vomiting, written down on the nurses' charts. Retching and nausea were not taken into account, since they left no evidence while the nurses were not present. The scopolamine patches were peeled off on the first postoperative day. Statistical analysis of data was performed utilizing the chi-squared test, and statistical significance was assigned at $p < 0.05$.

## Results

Between the two groups, there was no significant difference with respect to age, sex or fasting time. The number of postanesthetic vomiting episodes varied from zero to 7 times in the control group. The incidence in the transdermal scopolamine-treated group was 16%, which was significantly lower than that in the control group, 48% ($p=0.0161$). No patient complained of visual disturbance or dry mouth upon arrival at the operating room.

## Discussion

The use of droperidol for prevention of postanesthetic emesis is well established[2] Droperidol, however, causes prolonged sedation and may result in delay of oral intake. In contrast, because transdermal scoplamine patches do not have such an effect, they are considered to be the best strategy for prevention of postanesthetic vomiting in pediatric patients undergoing strabismus surgery. The incidence of vomiting in the transdermal scopolamine-treated group, 16%, is the lowest among reports that have been published hitherto[2,3,4]. A transdermal therapeutic system has an advantage of delivering a constant low dosage of drug over a prolonged period, unlike intravenous anti-cholinergic drugs which also act as antiemetics for a shorter period.

In conclusion, transdermal scopolamine appears to reduce the incidence and degree of vomiting in pediatric patients undergoing strabismus surgery.

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# UNLIMITED CLEAR FLUID INGESTION BY INFANTS UP TO 2 HOURS BEFORE SURGERY IS SAFE

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**Introduction:** The appropriate length of time healthy infants should abstain from clear fluids and solid foods before elective anaesthesia is unknown. Most texts recommend a fast of at least 4 hours before surgery. Van der Walt et al investigated healthy infants and they concluded that milk products should not be ingested less than 4 hours before surgery, but limited clear fluids (5% dextrose and 20% Poly-Joule (10 ml.kg$^{-1}$)) could be safely ingested 3-4 hours before surgery.[1] Recent investigators of preoperative fasting have concluded it is safe for children to ingest restricted clear fluids less than 3 hours before their operation.[2,3] We hypothesized that healthy infants could safely ingest unlimited clear fluids up to 2 hours before elective surgery.

**Methods:** After approval of the Hospital Ethics Committee, 150 healthy infants, ages 0-24 months, ASA physical status I-II, were enrolled into this study of elective surgical patients. Patients were excluded if they were being treated with medication known to affect gastric contents or they had a history of gastrointestinal disease. After obtaining parental consent, subjects were randomized to one of three groups. Following our usual practice, the infants abstained from solids on the day of surgery, were permitted bottled formula or milk up to 6 hours before surgery or breast milk up to 4 hours before surgery, and were permitted unlimited clear fluids up to 2, 2.5 or 3 hours before surgery. Clear fluids were defined as fluids which are clear aqueous solutions at 37°C. Suspensions and emulsions were not considered clear fluids. The ingestion of fluids on the day of surgery was closely monitored by nursing staff and parents. Anaesthesia was induced with a technique deemed most appropriate by the attending anaesthesiologist. After the establishment of adequate and stable level of anaesthesia, a 10 or 12 Fr. Salem gastric tube was passed orally into the stomach by a blinded investigator. Gastric tube position was confirmed by auscultation and the stomach contents were aspirated with the patient and gastric tube in several positions. Gastric contents were visually inspected for particles and the volume of gastric fluid was measured with a 10 ml syringe. Gastric pH was assessed with pH paper (Merck pH 0-14 and pH 0-2.5). Gastric contents less than 0.5 ml were assigned the value of 0.5 ml. In this study "risk" factors for aspiration pneumonia were defined as: (1) intragastric pH $\leq$ 2.5 and fluid volume $\geq$ 0.4 ml.kg$^{-1}$, and (2) intragastric fluid volume $\geq$ 1.0 ml.kg$^{-1}$. Sample size was determined with a beta of 0.1. Data was compared using One-Way ANOVA, Student's t test, Kruskal-Wallis ANOVA, Mann-Whitney-U test, Chi-Square analysis and Fisher's exact test, where appropriate. The relationship between gastric fluid volume and pH and possible confounders (gender, age, weight, length of fast, volume ingested, milk ingestion and in-patient/out-patient status) was done with forward stepwise linear regression analysis. Values were considered significantly different if $P < 0.05$.

**Results:** There were no signficant differences between the groups with respect to age, weight, gender, ASA physical status, in-patient and out-patient status, milk ingestion and volume of clear fluid ingestion. There was a significant difference between the groups with respect to length of fast, $P < 0.0001$ (Table I). There was no significant difference between the groups with respect to gastric fluid volume aspirated and gastric pH (Table II) and "risk" factors for aspiration pneumonia (Table III). Five of the thirty-six patients who ingested bottled formula or milk had curds in their gastric aspirate. None of the eight patients who ingested breast milk had particulate gastric matter. The only potential confounder that affected gastric fluid volume and pH was in-patient/out-patient status. In-patient's had a significantly higher pH, $P < 0.001$.

**Table I-Volume Ingested and Fast**

| Group | Vol.Ingested (ml/kg) mean + SD (range) | Fast (hr) mean + SD (range) |
|---|---|---|
| 3 hr.fast | 15±10 (2-47) | 3.4±0.7 (1.3-6.0)* |
| 2.5 hr.fast | 19±15 (1-69) | 2.7±0.6 (1.4-4.5)* |
| 2 hr.fast | 20±13 (1-64) | 2.2±0.7 (1.0-5.0)* |

* $P < 0.0001$

**Table II-Gastric Contents**

| GROUP | n | Volume (ml/kg) mean+SD (range) | pH Mean±SD(range) |
|---|---|---|---|
| 3 hr.fast | 50 | 0.25±0.80 (0.03-5.78) | 2.0±1.0 (1.3-6.0) |
| 2.5 hr.fast | 50 | 0.15±0.14 (0.03-0.52) | 2.3±1.3 (1.2-6.0) |
| 2 hr.fast | 50 | 0.21±0.37 (0.04-2.37) | 2.4±1.3 (1.2-7.0) |

**TABLE III-"Risk" Factors for Pulmonary Acid-Aspiration Syndrome**

| GROUP | Gastric Volume $\geq$ 0.4 ml.kg$^{-1}$ & pH $\leq$ 2.5 | Gastric Volume $\geq$ 1.0 ml.kg$^{-1}$ |
|---|---|---|
| 3 hr.fast | 2/50 | 1/50 |
| 2.5 hr.fast | 6/50 | 0/50 |
| 2 hr.fast | 5/50 | 2/50 |

**Discussion:** Based on these results, we now permit healthy infants to ingest unlimited clear fluids up to 2 hours before surgery. The presence of curds in a significant number of the infants who ingested bottled formula or milk on the day of surgery is unacceptable. This practice needs to be reviewed.

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# THE EFFECT OF GENERAL ANAESTHESIA ON POST-TONSILLECTOMY VOMITING

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**Introduction:** One of the commonest paediatric surgical procedures is tonsillectomy. When we began to consider management of children undergoing tonsillectomy on a Day Care Surgical basis, post-operative vomiting was of concern to us, but little was known of its incidence. To clarify this, we prospectively studied 300 children undergoing elective tonsillectomy at our institution. We hypothesized that the choice of anaesthetic technique would not affect post-operative vomiting after tonsillectomy.

**Methods:** After Hospital Ethics Committee approval and informed consent, 300 elective, ASA I-II physical status children of age 2 to 12 years undergoing tonsillectomy or adenotonsillectomy were randomly assigned to 3 groups. Subjects were excluded if they had cardiac disease, respiratory disease, or any of the drugs to be administered was relatively or absolutely contraindicated. Appropriate monitoring was established upon arrival in the operating room. After sedation with nitrous oxide, the patients underwent either an inhalation induction with halothane or an IV induction with 5 $mg.kg^{-1}$ thiopentone. After induction of anaesthesia the subjects were randomized into either group D, M or S (see below) and were administered 0.08 $mg.kg^{-1}$ vecuronium IV. Randomization was both blocked and stratified in order to ensure an equal distribution of patients among the groups upon completion of the study. After tracheal intubation ventilation was supported to maintain normocapnia. Group D had their anaesthesia maintained with 70 percent nitrous oxide and 1.5 percent halothane, and they were given 1.5 $mg.kg^{-1}$ meperidine (Demerol) IM about 10 minutes before the end of the operation. Group M was the same as Group D except their narcotic was 0.1$mg.kg^{-1}$ morphine IV at induction. Group S underwent balanced anaesthesia with 70 percent nitrous oxide, 30 percent oxygen plus sufentanil, 0.5 $mcg.kg^{-1}$ IV bolus at induction and a 0.2 $mcg.kg^{-1}.hr^{-1}$ infusion. Satisfactory neuromuscular blockade was maintained with intermittent 20 $mcg.kg^{-1}$ vecuronium boluses. Droperidol, 25 $mcg.kg^{-1}$ IV, was administered to all patients at induction. Upon completion of surgery, gastric contents were aspirated with an orogastric tube, muscle relaxation was reversed by 60 $mcg.kg^{-1}$ neostigmine with 20 $mcg.kg^{-1}$ atropine IV and the airway was suctioned clear. Group D and M were extubated before their airway reflexes returned and Group S patients were extubated when able to protect their airways. For the remainder of the study, the patients were treated comparably. Postoperative analgesia in the recovery room was achieved, when indicated, with morphine 0.05 $mg.kg^{-1}$ IV q10min.

On the wards, analgesia was achieved with 1 $mg.kg^{-1}$ codeine IM or p.o., whichever was most appropriate. Vomiting in the recovery room and on the wards was recorded by the nursing staff in a routine fashion. Excessive vomiting was treated with 1 $mg.kg^{-1}$ dimenhydrinate (Gravol) IM, when indicated. Parents were contacted the day after surgery by a blinded research assistant and asked how often their child vomited on the day of and the day after surgery. In this study excessive vomiting was defined as vomiting greater than 3 times on the ward. Demographic data was analyzed with ANOVA and Chi-Square analysis where appropriate. The incidence of vomiting, the incidence of excessive vomiting, and the number emesises were compared using Chi-Square analysis. Results were accepted as significant if $P<0.05$.

**Results:** There were no significant differences between the groups' weight, age, gender, length of surgery, and surgical procedure performed. The patients who underwent a balanced anaesthetic had a higher incidence of vomiting in the recovery room (Table I). Forty-nine percent of the patients vomited on the ward and eight percent of the ward patients had excessive vomiting. The choice of anaesthetic and the choice of induction technique did not significantly effect vomiting on the wards (Table II).

**Table I-Vomiting in the Recovery Room**

| Group | Incidence-Vomiting | Number of Emesis |
|---|---|---|
| D-Meperidine | 3/100 | 3 |
| M-Morphine | 2/100 | 2 |
| S-Sufentanil | 16/100* | 21* |

* $P<0.01$, Chi-Square analysis

**Table II-Vomiting on the Wards**

| Group | Incidence-Vomiting | Incidence-Excessive Vomiting (> 3 times) |
|---|---|---|
| D-Meperidine | 50/100 | 6/100 |
| M-Morphine | 51/100 | 6/100 |
| S-Sufentanil | 45/100 | 12/100 |
| IV Induction | 70/150 | 16/150 |
| Inhalation Induction | 76/150 | 8/150 |

**Discussion:** Ideally, the side effects of surgery and anaesthesia are kept to an acceptable minimum. We observed an unacceptably high incidence of vomiting in children after tonsillectomy. The administration of droperidol and intraoperative gastric emptying did not decrease vomiting to acceptable levels. Superior methods of decreasing vomiting after tonsil surgery need to be found. Parents of children undergoing tonsillectomy on an out-patient basis should be aware that many children vomit after this operation and a significant number of children will develop excessive vomiting, which may require post-operative hospitalization.

# A COMPUTER CONTROLLED INFUSION OF PROPOFOL FOR INDUCTION AND MAINTENANCE OF ANAESTHESIA IN CHILDREN

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Introduction:-

Five studies have evaluated propofol as an induction agent in children down to the age of one year[1-5] and found it to be satisfactory with a low incidence of cardiovascular and respiratory side effects. No study in children has employed continuous infusion of propofol for maintenance of anaesthesia, which has proved successful in adults[6]. A computer controlled infusion system based on a pharmacokinetic model has been developed which has been applied successfully to healthy adults[7] The aim of the study was to evaluate this system in healthy children.

Methods:-

18 children, age one to thirteen years, ASA grades one or two, presenting for in-patient general surgical, urological and orthopaedic operations were studied. Ethics Committee approval was obtained and written informed consent from each child's parents or guardian. The children were premedicated with oral temazepam 0.3 $mg/kg^{-1}$, or trimeprazine elixir 2 $mg/kg^{-1}$. EMLA cream was applied under an occlusive dressing one hour pre-operatively.

Monitoring consisted of ECG, precordial stethoscope, pulse oximeter and Dinamap automatic blood pressure recorder.

The infusion system consisted of a Psion 2 computer interfaced with the Ohmeda 9000 infusion device. The real time pharmacokinetics model used to drive the system employed adult pharmacokinetic data and adjustments were made solely on the basis of weight.

Anaesthesia was induced by selecting a suitable target blood concentration of propofol. This was initially limited to 9.9 ug/ml but was later increased to 14.0 ug/ml.

Peri-operatively, the target blood concentration was reduced to a value appropriate to the level of surgical stimulation, usually 10-12 ug/ml. Nitrous oxide 67% and oxygen 33% was delivered via facemask and analgesia was provided by an appropriate regional nerve block or a titrated intravenous injection of papaveretum.

Peripheral venous samples were collected for whole blood propofol concentration by gas chromatagraphic analysis using a flame ionization detector.

Results:-

Figure 1 is plotted from analysis of 104 results taken with the pump operating at high flow rates to maintain a steady predicted plasma propofol concentration. Based on the adult pharmacokinetic model, the system overestimates the blood propofol level, reflecting the higher clearance values of propofol in healthy children. The computer controlled infusion system produced satisfactory quality of anaesthesia and no supplementation with volatile agents was required during any of the procedures. When the target propofol concentration was limited to 9.9 ug/ml, patient movement and breath-holding occurred on surgical incision, but this did not occur when the higher target concentration of 14.0 ug/ml was used for induction.

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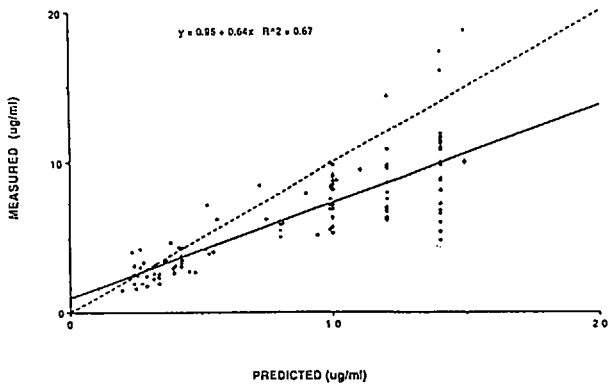


Discussion:-

This study has demonstrated the safe application of a computer controlled propofol infusion for induction and maintenance of anaesthesia in healthy children. There was a low incidence of respiratory side effects and marked cardiovascular stability. The relationship between predicted and measured blood concentrations of propofol demonstrates the increased clearance of propofol by children. New pharmacokinetic parameters are therefore required which reflect more accurately the distribution and elimination of propofol in paediatric use.

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# LIQUID CRYSTALLINE TEMPERATURE MONITORING: DOES IT ESTIMATE CORE TEMPERATURE IN ANAESTHETIZED PAEDIATRIC PATIENTS?

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**INTRODUCTION:** Paediatric anaesthetists are faced daily with the task of maintaining body temperature in their patients. Implicit in this task is the accurate measurement of core temperature with the use of noninvasive monitors. Various sites, invasive and noninvasive, have been used to measure temperature. Core temperature sites like esophageal, rectal, axillary and tympanic membrane (gold standard)[1] have been used. Liquid Crystalline Temperature (LCT) strips have been utilized since 1978 to measure temperature intraoperatively and have been met with varying enthusiasm.[2,3,4] This study was designed to evaluate the accuracy of a central, corrected forehead LCT strip in estimating core temperature in anaesthetized infants and children.

**METHODS:** After approval from our Ethics Committee, 71 ASA I or II infants and children undergoing elective surgery were studied. All patients were fasted and unpremedicated. General anaesthesia was induced with thiopentone 5mg/kg, vecuronium 0.1 mg/kg, and fentanyl 2 mcg/kg. After the trachea was intubated, anaesthesia was maintained with either a caudal or lumbar epidural and isoflurane, 0.5-1.5 MAC. Standard temperature conservation methods were used, including passive humidification and a warming blanket. After induction, an estimated core temperature LCT strip with a correction factor of 1.5°C was placed on the forehead. Thermocouple probes were used to measure tympanic, axilla, rectal, oesophageal, finger, forearm, and forehead (on either side of the LCT strip) temperature. Recordings of temperature were made every ten minutes for the first 90 minutes of the surgery. Demographics are reported as means ± S.D.. Differences between groups were compared with use of one-way ANOVA and SNK tests for multiple comparisons. Differences within groups were compared with use of repeated measure and SNK. Statistical significance ( $p<0.05$) was accepted.

**RESULTS:** The mean (±S.D.) age and weight was 55.0±45.8 mo and 20.1±14.7 kg, respectively. Mean LCT differed significantly from all measured sites, except oesophageal at 0,10, 80 and 90 minutes ($p<0.001$) (fig 1). Mean LCT was ≈2.5°C greater than tympanic temperature ($p<0.001$) while forehead RT and LT were ≈5.5°C less than tympanic temperature ($p<0.0001$) (fig 2). Even after subtraction of the correction factor (1.5°C), mean LCT was ≈1.0°C greater than and statistically different from tympanic temperature ($p<0.001$). Forehead RT did not differ significantly from forehead LT (fig 3).

**DISCUSSION:** Compensated LCT forehead measurements failed to estimate core temperature. Previous investigators have shown good correlation between tympanic, esophageal, rectal, and axillary temperatures in paediatric patients.[5] Graphically, the noninvasive LCT strip and core temperature curves are parallel. Thus, the temperature compensated LCT probe should be adjusted downward by 2.5°C to enhance accuracy. Since normothermia was maintained, further studies are required to determine the accuracy of the LCT strip during mild hypothermia.

**ACKNOWLEDGEMENT:** We thank Sharn Inc. for providing the LCT strips.

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Figure 1

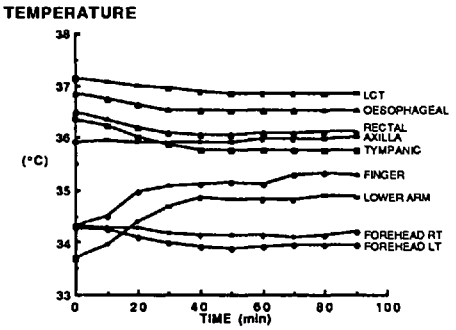



Figure 2

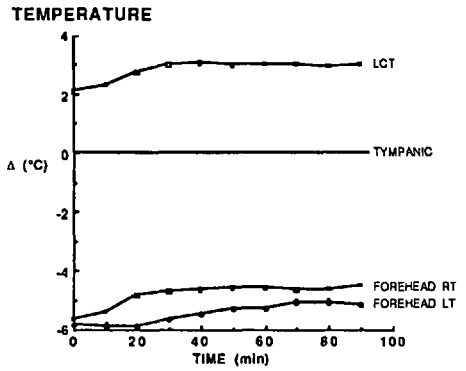
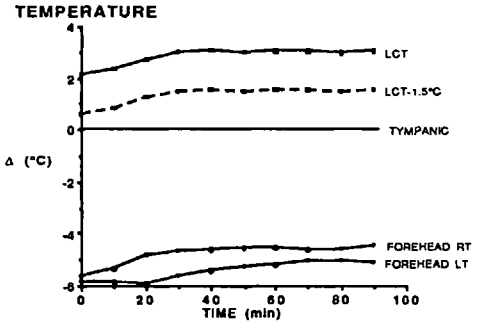



Figure 3



## IDENTIFICATION OF THE EPIDURAL SPACE WITH AN IV MICRO-DRIP INFUSION SET IN INFANTS AND CHILDREN

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Introduction:

Forty years have passed since the introduction of the lumbar and thoracic epidural anaesthesia for operations on infants and children in Canada[1,2] , epidural anaesthesia via the lumbar or thoracic route is not popular at present . The main reason of unpopularity of the lumbar or thoracic epidural anaesthesia in this age group seems to be derived from the difficulty of locating the epidural space and concern for the unintentional dural punctures .

To overcome this difficulty , the use of an iv micro-drip infusion set for an identification of the epidural space described in adult patients[3,4] was tried in infants and children.

Methods:

The identification of the epidural space by this method was tried in 270 infants and children(< 6 yrs). The sites of puncture were in the lumbar region in 237 cases and in the thoracic region in 33 cases . The age distribution is shown in the table .

A sterile IV micro-drip infusion set was added to the standard epidural tray. The set was prepared with saline in usual manner as for an intravenous infusion. The infants and children were kept still under general anaesthesia during the puncture . Following the insertion of the epidural needle into the interspinous ligament, the infusion set was connected to the needle hub. The micro-drip chamber was kept about 1 meter above the puncture site. The clamp of the infusion set was fully opened( No dripping should be observed if the tip of the needle was in the interspinous ligament ). While an assistant was observing the drip chamber, the needle was slowly and carefully advanced. At the first sight of running of drip ( an objective sign of loss of resistance ) , immediately the anaesthetist was notified and he stoped advancing the needle , and the clamp was closed . Before an administration of local anaesthetic solution or an insertion of the epidural catheter , correct placement of the needle was confirmed in a standard method .

Results:

The epidural space was accurately located by this method in 269 cases; on the first attempt in 261 cases and on the second attempt in 8 cases. Inadvertent dural punctures identified by the appearance of CSF occurred in three cases ( all patients < 3 months ). These dural punctures occurred within the first 30 cases in this series . In these cases of dural puncture , the needle was withdrawn and reinserted into the adjacent intervertebral space and the epidural space was identified successfully on the second attempt in all three cases. One possible subdural extra-arachnoidal injection of local anaesthetic solution occurred to a neonate . Although no dripping of CSF was noticed , after the injection of local anaesthetic, respiratory arrest occurred and unusually high sensory blockade was observed. The neonate recovered without sequelae after 6 hours of mechanical ventilatory support.

Table : Age distribution of lumbar and thoracic epidural anaesthesia in infants and children .

| Age (year) | < 1 | 1 | 2 | 3 | 4 | 5 | Total |
|---|---|---|---|---|---|---|---|
| Lumbar route | 106 | 46 | 22 | 25 | 18 | 20 | 237 |
| Thoracic route | 26 | 3 | 2 | 0 | 0 | 2 | 33 |
| Total number | 132 | 49 | 24 | 25 | 18 | 22 | 270 |
| Success rate* (%) | 97 | 100 | 100 | 100 | 100 | 100 | 98.5 |

* Success rate of correct identification of epidural space without prior dural puncture .

Discussion:

This method of epidural space identification seems to be useful and reliable in infants and children , especially in those older than 3 months of age .

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# DOES THE HAEMOGLOBIN CONCENTRATION PREDICT POST-OP APNEA IN EX-PRETERM INFANTS?

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## INTRODUCTION:

One of the mechanisms proposed to explain post-operative apnea in the ex-preterm infant is that a reduction in oxygen ($O_2$) delivery depresses the immature respiratory centre. Red blood cell transfusions (RBC) have been shown to decrease the incidence of apnea (AP) and periodic breathing (PB) in ex-preterm infants, although most of the improvement was noted in infants with higher levels of AP and PB.[2] In contrast, others have found no clinical benefit from RBC.[3] Steward noted that the haemoglobin concentration [Hgb] in ex-preterm infants was less than it was in full-term infants, and that 22% of the ex-preterm infants developed apneas.[4] To determine whether a relationship exists between the [Hgb] and the incidence of post-operative respiratory depression in ex-preterm infants, the following study was undertaken.

## METHODS:

The medical records of 77 ex-preterm infants (<37 weeks gestation) who underwent surgery in our institution were reviewed. Patient sex, body weight, gestational age (Gest), post-conceptual age (PCA), [Hgb], the frequency of RBC at the time of the procedure, and anaesthetic technique were recorded. The incidences of AP and bradycardia (B) after surgery were recorded. The infants were monitored with an Edentec 2000 apnea monitor. Apnea was defined as a respiratory pause $\geq$ 15 seconds in duration. Body weight, gestational age, PCA, and [Hgb] were analyzed using Students unpaired t-test. Nominal data were analyzed using Chi-square analysis with the Yates correction for continuity. Statistical significance was accepted for $p < 0.05$.

## RESULTS:

Of 77 ex-preterm infants studied, 60 (71%) had neither Ap nor B (Group 1), and 17 (29%) had Ap alone, B alone, or both (Group 2). Gest, PCA, and body weight were similar in the 2 groups (Table 1). Pre-operative [Hgb] and the incidence of RBC transfusion was similar between the 2 groups (Table 1). Two infants (12%) in Group 1 received transfusion, ([Hgb] of 134 and 117 $g \cdot L^{-1}$), while 4 infants (7%) in Group 2 received RBC. RBC were not given intra-operatively to any of the infants. One infant (6%) in Group 1 and 7 infants (12%) in Group 2 had a pre-operative Hgb < 100$g \cdot L^{-1}$.

## DISCUSSION:

In a previous study, we noted the presence of post-operative respiratory depression in ex-preterm infants less than 44 weeks PCA.[5] In this cohort of infants, post-operative complications could not be predicted by the presence of an abnormal Hgb. Six infants in our series had Hgb < 100 $g \cdot L^{-1}$ and none of these infants experienced post-operative cardio-respiratory difficulties. The results of the present study indicate that the Hgb concentration in ex-preterm infants with post-operative cardio-respiratory depression is similar to that found in ex-preterm infants without post-operative depression. RBC transfusion is not without hazard and our results indicate that a transfusion may not attenuate post-operative respiratory depression in ex-preterm infants. We do not recommend RBC transfusion in ex-preterm infants for the purpose of attenuating cardio-respiratory depression. Cardio-pulmonary monitoring is required after surgery in these infants until 12 hours apnea free.

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Table 1

| | GROUP 1 | GROUP 2 |
|---|---|---|
| Gest. age (wks) | 29.8 ± 3.4 | 31.8 ± 3.9 |
| PC age (wks) | 44.8 ± 6.7 | 47.2 ± 6.1 |
| Weight (kg) | 3.9 ± 1.3 | 4.5 ± 1.4 |
| Hgb ($g \cdot l^{-1}$) | 127.8 ± 26.5 | 118.6 ± 16.2 |
| RBC trans (%) | 12% | 7% |

Data are mean ± SD

## MINUTE VENTILATION DURING MASK HALOTHANE ANAESTHESIA IN INFANTS

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Introduction: Minute ventilation has been used to assess changes in ventilatory control by deriving parameters of respiratory drive and timing. Mean inspiratory flow ($(V_T/T_I)$ is an assessment of respiratory drive whereas inspiratory time ($T_I/T_{tot}$) is a measure of timing.[1] Few studies have described these parameters in infants during halothane anaesthesia. The following study used non-invasive pneumotachography in infants undergoing elective surgery.

Methods: With institutional ethics approval and informed parental consent, 6 ASA 1 fasted infants undergoing elective inguinal hernia repair were studied. Intravenous anaesthesia (pentothal 5 $mg \cdot kg^{-1}$) was induced in 4 infants and inhalational anaesthesia was induced in 2 infants. Unintubated infants breathed spontaneously from modified Jackson-Rees anaesthesia circuit. Anaesthesia was maintained with 70% $N_2O$ and 2% halothane in oxygen. Mouth pressure (Honeywell) and flow (Fleisch) were recorded on tape (Hewlett-Packard) and played back at a sampling frequency of 50 Hz for computerized breath-by-breath analysis. End-tidal $CO_2$ was recorded (Puritan-Bennett/Datex 254 airway gas monitor). Minute ventilation was described by $V_T$, RR, $V_T/T_I$ and $T_I/T_{tot}$. The course of surgery was divided into 3 stages representing the extremes of respiratory depression: preincision (A); surgical stimulation (B) and emergence. Data was expressed as ± SD which summarizes the course of surgery. $V_T/T_I$ post-induction (A) was 5.71 ± 0.2 $ml \cdot kg^{-1} \cdot s^{-1}$.

Statistical difference was assessed with ANOVA. A p value of 0.05 was accepted. A representative record is shown in Figure 1. Table 1 summarizes the data for the group.

Results: Surgical stimulation caused an increase in $V_T/T_I$ (7.83 ± 0.37 $ml \cdot kg^{-1} \cdot s^{-1}$). However during emergence there was a rapid increase in $V_T/T_I$ (9.34 ± 1.29 $ml \cdot kg^{-1} \cdot s^{-1}$). Inspiratory timing ($T_I/T_{tot}$) was not statistically different at stage A, B and emergence. RR decreased during emergency because of a prolongation of $T_{tot}$. Table 1 summarizes the data for the group (x ± SD) for the three stages of anaesthesia. Durging emergence there is a statistically significant decrease in RR and an increase in $V_T/T_I$ and $V_T$.

Conclusion: Halothane anaesthesia resulted in a reduction in respiratory drive ($V_T/T_I$) which was rapidly reversed during emergence. In contrast, inspiratory timing was not significantly different between the stages of anaesthesia.

Acknowledgement: Supported by the Physicians Services Foundation Incorporated.

Reference:

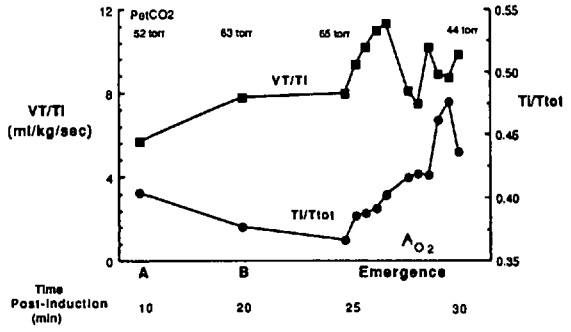
1. Milic-Emili J. Lung 1982; 160:1-17

TABLE

| | PRE-INCISION | SURGICAL STIMULATION | EMERGENCE |
|---|---|---|---|
| $V_T$ ($ml \cdot kg^{-1}$) | 3.0 ± 0.8 | 3.0 ± 0.9 | 6.0* ± 1.3 |
| RR (bpm) | 62.63 ± 11.12 | 71.76 ± 16.88 | 58.20+ ± 1.05 |
| $V_T/T_I$($ml \cdot kg^{-1} \cdot s^{-1}$) | 8.14 ± 2.12 | 8.905 ± 1.9 | 15.81* ± 4.0 |
| $T_I/T_{tot}$ | 0.38 ± 0.04 | 0.38 ± 0.05 | 0.37 ± 0.04 |

*stat different from stage A
+stat sign from stage B

FIGURE



# INTERNAL JUGULAR VENOUS CANNULATION IN CHILDREN UNDER 5 YEARS OF AGE.

M.F. Smith, FRCPC, British Columbia Children's Hospital and the University of British Columbia

## INTRODUCTION

The placement of a reliable central venous catheter for management of children undergoing major surgery has been achieved by several different routes. Following early success with direct cannulation of the internal jugular vein, we undertook to evaluate our experience with this technique.

## METHODS

All children under 5 years who required central venous cannulation were included in the study, provided there had not been an internal jugular venous line inserted previously in the neck. 104 children underwent 112 cannulation attempts.

Under anaesthesia, the patients were positioned in 15 to 20 degrees Trendellenberg with the head turned away from the side to be used and a rolled towel placed under the shoulders to reduce the concavity of the lateral neck. At the anterior border of the sterno-mastoid muscle and at the level of the prominence of the thyroid cartilage a skin incision was made and a 22 gauge finding cannula was introduced at 30 degrees to the skin in the direction of the ipsi-lateral axilla. If the vessel was not found, progressively more medial approaches were taken, palpating the carotid artery before each pass. Once found, in cyanosed and polycythemic patients, the pressure was recorded to verify venous cannulation prior to the insertion of a dilator. Using the Seldinger technique, the catheter chosen was then inserted.

## RESULTS

The patients in the series varied in age from 1 day to 4 years 10 months and in weight from 2.4 to 21.2 kg. 35 (34%) of the patients were less than 1 year and 9 (9%) were less than one month in age.

Of the 112 attempts made to cannulate the internal jugular vein directly, 103 (92%) were successful in placing a satisfactory line. Cannula insertion failed in 6 attempts on the first side but succeeded when the other side was used. In one patient weighing 3.4 kg., attempts failed bilaterally and surgical cannulation of the right atrium was required. Puncture of the carotid artery was identified in only 1 patient.

In the 26 patients aged 1 month to 1 year, successful cannulation was achieved in 26 of 29 attempts (89%). In the patients aged under 1 month, cannulation was successful in 8 of 11 attempts (72%).

No significant complications were recognized in the immediate peri-operative period in either successful or unsuccessful sites of cannulation. Minor venous bleeding was seen in one third of the patients who received heparin for cardiopulmonary bypass. No significant hematomas were recognized.

## DISCUSSION

The approach to the internal jugular vein from the anterior border of the sternomastoid was chosen to allow location of the vein from a direction away from the carotid artery. The skin incision was made relatively higher in the neck than in adults to avoid trauma to the cupola of the lung.

The results of our study compare favourably with other reported series. However, several clinical observations were made and deserve further mention.

A slow and delicate introduction of the preliminary cannula usually found the vessel most efficiently. In approximately 50% of the patients, particularly in the smaller infants, the vessel was discovered during gradual withdrawal of the first cannula.

It was recognized during the study that fairly reliable positioning of the cannula tip at the atrio-caval junction was obtained by measuring the length of the cannula from the skin penetration site to a point 1 cm below the manubrial notch in children less than 10 kg and 2 cm below the manubrial notch in children greater than 10 kg.

## REFERENCES

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# PRE-USE TESTING OF COAXIAL CIRCUITS: THE PERILS OF PETHICK

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INTRODUCTION:
Several tests are recommended by the manufacturers of coaxial (modified Mapleson D) circuits. Pethick (1975) described a test to establish the integrity of the inner delivery hose which involves pressing the oxygen flush valve and observing the reservoir bag deflate [1]. We critically evaluated Pethick's test to determine its' accuracy.

METHODS:
Three different brands of coaxial circuits were used: the Bain™, the CoAx-2™, and the CPRAM™. Testing was done in three steps. Firstly, Pethick's test was applied with and without the mask elbow adapter [2]. Secondly, faults were created in the circuits and Pethick's test repeated. Thirdly, faulty CPRAM circuits were used on spontaneously breathing subjects (the principal investigators) and end-tidal carbon dioxide monitored to look for clinically significant changes.

RESULTS:
The CPRAM™ required correct placement of the elbow adaptor to show a positive Pethick's test. The others did not. Pethick's test did not detect leaks <10litres/min or obstructions <95% of the lumen area. When used on awake human subjects, proximal leaks just sufficient to be detected by Pethick's test made no difference to the ETCO2. Proximal transection did increase respiratory rate, but this occurred before the $ETCO_2$ changed.

DISCUSSION:
Pethick originally described his test as a way of detecting proximal disconnects in coaxial circuits. For this use it remains valid. It does not, however, prove to be a complete test of inner tubing integrity. Circuit faults undetectable by Pethick's test may be small and apparently insignificant in our study of awake subjects in the short term. This may not be so for anaesthetised patients over longer periods. However, ethical considerations preclude testing this hypothesis. Our awake subjects reported discomfort at 5-10 minutes, which anaesthetised patients could not. The earliest objective effect was increased respiratory rate. This occurred before changes in either inspired or expired $CO_2$ were measurable with our system.

We conclude that Pethick's test can fail to detect major faults in the CPRAM™ circuit, the clinical effects of which will not be immediately apparent with spontaneous respiration.

1. CASJ 22:115

2. Anesthesiology 59:489-490

# AGONIST AND ANTAGONIST OF OXYGEN FREE RADICAL

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It is wellknown that polymorphnuclear leukocyte plays important oxidative bactericidal roles due to oxygen free radical and simultaneously injuries cell membranes followed by various pathological disease. In this experiment, we studied antagonistic or agonistic substances of oxgen free radical of PMN.

## METHODS

Adding 3% dextran to heparinized venous blood of healthy human, the blood was placed quietly for 30 minutes in room temperature. The serum was centrifuged at a rat of 1200 rpm for 10 minutes. The erythrocyte in the sedimentation was destroyed by low osmolarity fluid and then PMN of $1 \times 10^7$ were taken after adding Hanks' solution. Phorbol 12-Myristate 13-Acetate (PMA) was used as stimulator and measured by cytochrome reduction method. Experiment was grouped as followed.

G1) PAF alone
G2) PAF + PMA
G3) PAF + CV 6209
G4) PMA + Endotoxin
G5) PMA + Verapamil
G6) Temperature between 0°C and 50°C

## RESULTS

G1) PAF ($10^{-5}$, $10^{-7}$, $10^{-9}$M) alone activated oxygen free radical after 30 minutes. But the velocity of activation was very slower comparing with PMA alone.

G2) Combination of PMA and PAF ($10^{-5}$, $10^{-7}$, $10^{-9}$M) accerelated activation of oxygen free radical. $10^{-7}$ M of PAF revealed 8.3% increase of activation of oxygen free radical than PMA alone.

G3) PAF antagonist CV 6209 ($10^{-4}$M) suppressed about 21% of activation of oxygen free radical stimulated by PAF ($10^{-5}$M) without PMA.

G4) Each concentration of 0.0075 mg, 0.075 mg, 0.75 mg of endotoxin revealed 56%, 66%, 63% increase of activation of oxygen free radical, respectively than PMA alone.

G5) 0.1 mg of verapamil revealed about 53% decrease of activation of oxygen free radical than PMA alone and 0.01 mg of Verapamil revealed 17% decrease of activation of oxygen free radical than PMA alone.

G6) Oxygen free radical recorded marked production between 30°C-40°C and the peak level was 37°C. On the other hand, the level of 0°C, 10°C, 20°C, 25°C, 45°C, 50°C inhibited the procuction of oxygen free radical.

| Temp(°C) | OD actual values | Index of activation changes |
|---|---|---|
| 0°C | 0.033 | 3.3 |
| 10°C | 0.033 | 3.3 |
| 20°C | 0.103 | 10.3 |
| 25°C | 0.427 | 42.6 |
| 30°C | 0.915 | 91.4 |
| 37°C | 1.001 | 100.0 |
| 40°C | 0.932 | 93.1 |
| 45°C | 0.423 | 42.3 |
| 50°C | 0.058 | 5.8 |

## CONCLUSION

Verapamil, CV 6209 and low temperature below 25°C were effective on inhibition of oxygen free radical production, but PAF or endotoxin promoted activation of oxygen free radical.

## REFERENCES

1) Yoshikazu Miura: Research Communications in Chemical Pathology and Pharmacology, Vol. 64 (No. 2), 331-341, 1989
2) Akira Yuo et al: The Journal of Immunology, Vol. 142, 1678-1684, 1989
3) Koichiro Takeshige et al: Clinica Chimica Acta, 92- 329-339, 1979

# PHONOCARDIOGRAPHIC MONITORING USING A SPECIAL ENDOTRACHEAL TUBE

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## INTRODUCTION

Auscultation of the heart sounds is routine both in clinical medicine and anaesthesia practice. In particular, esophageal and precordial stethoscopes are in common use during surgery for heart sound and respiratory monitoring. Unfortunately, these methods suffer from disadvantages, the precordial units being difficult to reliably attach to the anterior chest wall, and the esophageal units suffering from potential problems such as placement into the trachea or into an esophageal diverticulum, entanglement with the endotracheal tube and trauma to the oropharynx and varices.

We report here on an endotracheal tube (ETT) designed to eliminate the need for a separate stethoscope.

## DESIGN

The ETT is specially constructed unit with a wide-bore cuff inflation line. The cuff is acoustically connected to a leak-free microphone by a three-way valve (stopcock) after inflation with air using a syringe. Inflation pressures are kept to about 25 cm $H_2O$, using a standard ETT cuff pressure monitor (Portex). A standard audio preamplifier (gain=100) amplified the microphone signal to an amplitude suitable for recording using a Marantz professional cassette recorder. A set of earphones allowed the phonocardiogram (PCG) to be monitored intraoperatively. In selected cases, the amplified ECG and PCG signals were also digitized by computer (12 bits, 1000 Hz) for further analysis (heart sound segmentation and power spectral analysis).

## EVALUATION

The system was evaluated clinically at two centres in 15 surgical patients. No special problems were met in placement of the tube. In all cases the PCG was heard with remarkable clarity. Simultaneous recordings were taken from an esophageal stethoscope in two cases, but they were barely audible at the gain settings used for the ETT system. Similarly, two recordings taken using a conventional ETT with a small-bore cuff inflation line were inaudible. The Figure shows the PCG recorded by computer in one patient.

## DISCUSSION

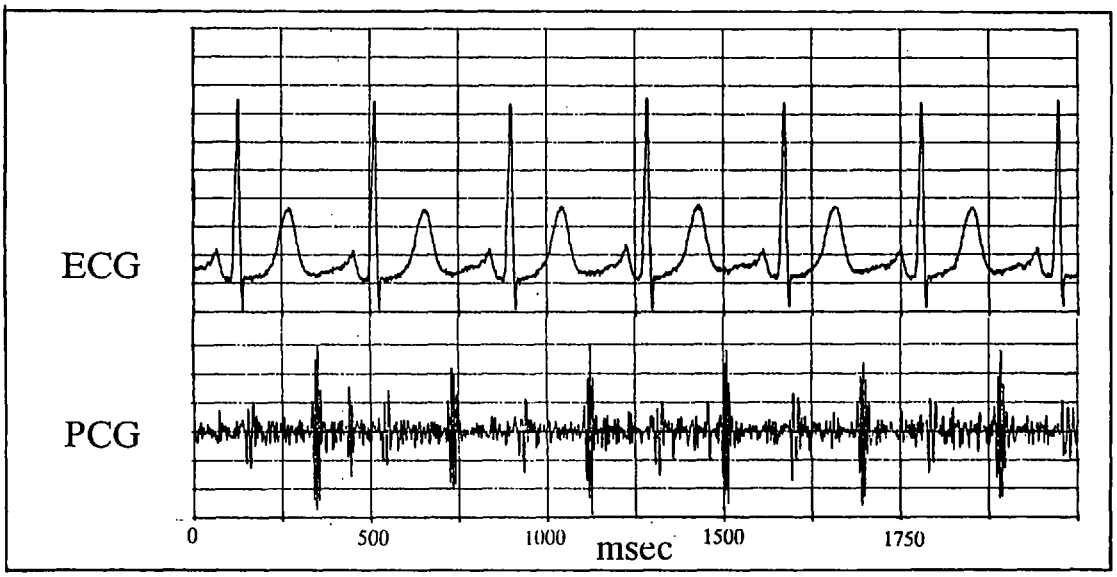
This method of PCG recording eliminates the need for precordial and esophageal stethoscopes in intubated patients. It is an easy and reliable method of obtaining the PCG in surgical patients. The clarity of the signals obtained in this way may facilitate the use of surgical PCG as an indicator of myocardial function [1]. Further studies using computer-based signal analysis techniques [2,3] will likely add further value to the PCG signals obtained.

## REFERENCES

[1] Anesthesia and Analgesia 68:385, 1989
[2] CRC Critical Reviews in Biomedical Engineering 15:211, 1988
[3] IEEE Transactions on Biomedical Engineering 34:485, 1987

## FIGURE

Sample phonocardiogram recording obtained intraoperatively. *Top*: Electrocardiogram (ECG). *Bottom*: Phonocardiogram (PCG).



# THE EFFECT OF ULINASTATIN ON THE RELEASE OF GRANULOCYTE ELASTASE DURING HYPOTHERMIA WITH SURFACE COOLING

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Granulocyte elastase is an enzyme released from the granulocyte lysosome during inflammatory diseases, shock, etc.and is believed to be playing an important role in the inflammatory destruction of tissues and lowering of cellular functions. It's very interesting to know the change of the serum granulocyte elastase during hypothermia. In the present study, we have measured the plasma level of granulocyte elastase and investigated the effect of Ulinastatin, on the plasma activity of granulocyte elastase.

Subject and Methods : Patients undergoing open heart surgery under hypothermia were enrolled in the present study, but emergency cases of surgery or patients with severe preoperative cardiac failure were excluded. Anesthesia was induced with thiamylal and maintained by closed circuit ether. After monitoring of ECG, EEG, intraarterial catheter, esophageal and rectal temperature, surface cooling and rewarming was performed using ice or warm water. Surgical operation was done at the lowest temperature. After resuscitation, rewarming was begun. The patients were divided into three groups, group U-I with intravenous injection of 6000 u/kg of Ulinastatin before cooling, group U-II with the additional dosing after warming to 30°C ,and the untreated group. (group C) Blood samples were drawn six times, before cooling, after cooling to 30°C, at the lowest temperature, after resuscitation, after warming to 30°C , and then after completing warming, in order to detect granulocyte elastase (GLE) and $\beta$-glucuronidase ($\beta$-gl). At the same time, changes in hemodynamic parameters, arterial blood gas and volume of urine were compared.

Results : (1) Blood pressure did not differ significantly between the three groups except that after resuscitation, it was significantly higher in group U-I than group C. (2) The plasma levels of GLE increased significantly in group C and group U-I at the end of rewarming. In contrast, in group U-II, there was no marked change. (3) The serum levels of -gl increased significantly in the three groups at the end of rewarming (35°C ), compared with the baseline level. (4) The volume of urine increased significantly in group U-I and U-II as compared with group C during rewarming.

Discussion : Hypothermia is sometimes referred to as controlled shock, in which peripheral and organic microcircuit is an important factor. GLE is one of protease, and has been shown to increase during extracorporeal circulation and hemodialysis. As the mechanism of secretion of this enzyme,it has been suggested that release of elastase occurs as a result of sequestration of neutrophils into the lungs due to activation of complements. Since elastase lyses elastin and fibronectin, it induces tissue degeneration and destruction through increased activities. So, it's very important to know the change of GLE activities and suppress it in order to prevent postoperative disorders in the vital organs. In the present study, GLE increased only after release of occlusion in all three groups, suggesting that the increases in GLE were induced not by the stimulation of hypothermia but by some mechanical stimulation or hypoxia during circulatory arrest. Ulinastatin has been shown to inhibit a variety of proteases and exert anti-shock effect, and has been reported to the inhibit increases in GLE activities significantly during extracorporeal circulation. In the present study, the release of GLE was significantly inhibited in Group U-II. The reason for not inhibiting in Group U-I is probably that the half-life of Ulinastatin is relatively short (approximately 45 min) and may require additional dosing to achieve this effect. In the groups treated with Ulinastatin, the volume of urine increased significantly, suggesting that the peripheral circulation was maintained at a good level. It is believed that inhibition of granulocyte elastase is important for prevention of postoperative pulmonary complications and circulatory depression.

References : 1.Antonsen S, Brandslund I, Clemensens, et al : Neutrophil lysosomal enzyme releae and complement activation during cardiopulmonary bypass. Scand. J. Thorac Cardiovasc Surg 21 : 47-52, 1987
2. Zheutlin LM, Thonar EJMA, Jacobs ER, et al : Plasma elastase levels in adult sespiratory distress syndrome. J. Crit Care 1 : 39, 1986

AN EVALUATION OF A SIMPLE, IN-LINE FLUID WARMING DEVICE. T. Hackmann, FRCPC, D.J. Steward, FRCPC. Department of Anaesthesia, British Columbia's Children's Hospital and the University of British Columbia.

INTRODUCTION:

It is important that intravenous infusions of blood or other fluid should be warmed if they are to be infused rapidly or administered to small infants. Commonly used blood warmers require the addition of special tubings which add a considerable dead space to the infusion system, and may take some minutes to assemble in an emergency.

Recently a simpe fluid warming device (ANIMEC™ Infusion Warmer, Elltec Co., Ltd.) has been available consisting of a dry warmer through which the standard I.V. tubing can be channelled. This takes very little time to attach and does not add to the dead space of the infusion line (see figure 1).

We have studied the performance of this device in warming a crystalloid solution from room temperature or whole blood from 4°C at various flow rates.

METHOD:

The fluid to be warmed was run from a constant infusion pump (IVAC™ 560) at rates ranging from 10 to 999 ML/hour. The ANIMEC™ infusion warmer was applied to the I.V. tubing according to the manufacturers guidelines. The temperature of the delivered fluid was measured immediately distal to the warmer and at a distance of 30 cm and 60 cm downstream using needle thermister probes (MONATHERM™ model 6000 with #3001-1580 myocardial temperature sensors). The thermister needle insertion sites were sealed with collodion, and care was taken to maintain the entire perfusion system free of air bubbles.

Although the manufacturer recommends the use of flow rates in excess of 180 ml/hour we also investigated lower flow rates in order to determine the usefullness of this device in pediatric patients.

The manufacturer warns of the danger of overheating if the infusion is interrupted and then resumed. To simulate this and assess the result we stopped the infusion for periods of 1 and 5 minutes each, with the warmer left switched on. We then recorded the maximum subsequent temperature at the distant sites, in a separate experiment we recorded the temperature of the fluid within the tubing inside the warmer during interruptions of flow.

RESULTS:

The temperature of the delivered fluid at each site at various flow rates is shown in figures 1 and 2. At low flow rates crystalloid solution exited the warmer at over 30°C but cooled by the time it reached the 30 cm and 60 cm measurement sites. The maximum warming effect was seen at a flow of 200 ml/hour, when fluid at 32.5°C was delivered. When the flow was interrupted for 1 or 5 minutes higher peak tempertures were recorded but these never exceeded 37.5°C.

Blood temperature measure at 30 cm and 60 cm downstream was over 18°C at all flow rates. However at low flow rates ( 20 ml/hour) the blood was heated to potentially damaging levels within and when exiting the device. Optimal and safe blood warming was seen at flow rates of 150-250 ml/hour.

DISCUSSION:

We have demonstrated that the ANIMEC infusion warmer effectively raises the temperature of crystalloid solutions from that of the room to over 30°C when the flow rate is between 75 and 600 ml/hour. At higher flow rates the device was less effective. At low flow rates the warm fluid exiting the warmer cooled toward room temperature before reaching the measurement sites 30 and 60 cm downstream

The simplicity of this device, its ease of rapid attachment, and lack of increased fluid dead space make it attractive for use in pediatric patients. It will provide warmed blood (30°C) at a rate adequate to replace the blood volume of a 3 kg infant over 1 hour. In the emergency situation it permits blood or other infusions to be warmed without changing or adding to the infusion line system. This may be useful in the operating room or other intensive care area if there is a sudden unanticipated need to infuse fluids. If very rapid transfusion of blood is necessary, one of the previously described blood warmers with a larger heat exchange capacity is recommended.

Figure 1
Performance Warmer/Crystalloid at Room Temperature

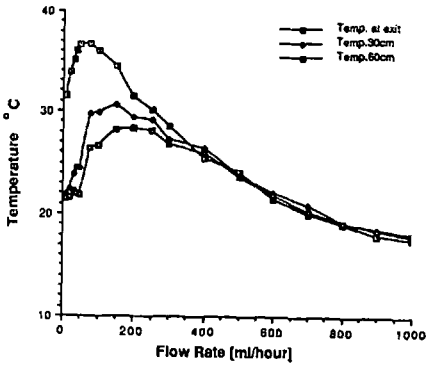
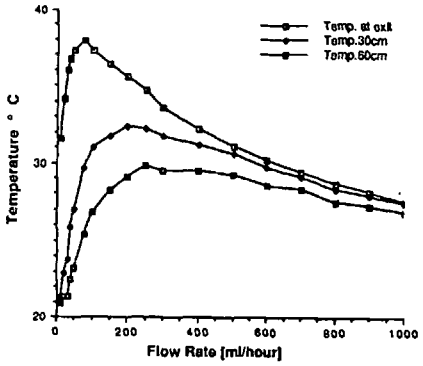



Figure 2
Performance Warmer - Blood at 4°C



# CLINICAL APPRAISAL OF THE LARYNGEAL MASK AIRWAY

J R Maltby FRCPC, R G Loken FRCPC, N C Watson, FRCPC
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The purpose of this study was to evaluate the clinical effectiveness of the laryngeal mask airway (LM airway).[1-3] This new device is intermediate in design and function between an oropharyngeal airway and an endotracheal tube. It is made of medical grade silicone and is designed to withstand repeated autoclaving and multiple use. A tubular oropharyngeal airwy is fused at its distal end to an oval silicone mask which lies in the hypopharynx, and the inflatable rim or cuff provides an airtight seal around the laryngeal inlet.

## Methods

Three specialist anaesthetists, none of whom had previously used the LM airway, administered general anaesthesia using this device to 250 patients aged 14-87 yr. All obstetric patients, and emergency patients with a suspected full stomach were excluded. Each patient's sex, age, weight, neck movement, dentition, and anticipated ease of intubation were recorded. Anaesthetic techniques and drugs were similar to those which would have been used for the same procedures if face-mask or endotracheal anaesthesia had been used. The LM airway was passed under light inhalational anesthesia; neuromuscular blocking agents were only used for procedures for which muscle relaxation would be required to provide good operating conditions. Following induction the anaesthetist positioned the patient's head as if a laryngoscopy were to be performed. A lubricated, deflated LM airway was inserted into the mouth and advanced blindly over the tongue into the pharynx until resistance was felt. The cuff was immediately inflated with air and positive pressure was applied to the reservoir bag in order to observe chest movement and to test the efficiency of seal over the larynx. Efficiency was graded as perfect (easy inflation of the lungs with no audible leak); satisfactory (easy inflation, small leak); or unsatisfactory (obstructed ventilation, large leak, or both). If placement was unsatisfactory after three attempts the LM airway was abandoned, and laryngoscopy and endotracheal intubation were performed. At the conclusion of surgery the laryngeal mask was left *in situ* until the patient responded to verbal commands. The cuff was then deflated and the patient was asked to remove the device.

## Results

The LM airway was used for a wide variety of surgical procedures, with either spontaneous or controlled ventilation (Tables I and II). The seal produced by the inflatable rim of the mask around the patient's larynx was satisfactory in most patients. When the LM airway was in place a clear airway was maintained without mandibular support.

TABLE I Demographic and operative details

| | |
|---|---|
| Age(yr) | 42±19 (14- 87) |
| Weight(kg) | 71±17 (39-160) |
| Anaesthesia (min) | 67±60 (10-280) |
| Values are mean ± SD (range) | |
| Surgery | |
| ENT, face | 21 |
| arm | 29 |
| trunk | 16 |
| cholecystectomy | 10 |
| lower abdomen | 65 |
| cystoscopy, TURP | 20 |
| D & C | 41 |
| leg | 44 |
| other | 4 |
| total | 250 |

TABLE II Insertion and efficiency

| | |
|---|---|
| LM insertion | |
| easy | 187 |
| >1 attempt | 61 |
| impossible | 2 |
| Neuromuscular blocker | |
| used | 101 |
| not used | 149 |
| LM efficiency | |
| perfect | 164 |
| satisfactory | 74 |
| abandoned | 12 |
| Failures (n = 12) | |
| failed insertion | 2 |
| obstructed airway | 5 |
| large leak | 5 |
| Ventilation (n = 238) | |
| spontaneous | 143 |
| controlled | 95 |

## Discussion

The LM airway does not require laryngoscopy for its insertion, it cannot be misplaced in the esophagus, it relieves the anaesthetist's hands from holding a face-mask, and it is well tolerated during emergence from anaesthesia. However, perfect protection of the airway cannot be guaranteed, and its use is not recommended for patients who may have a full stomach.

## References

1 Br J Anaesth 1983; 55: 801-4.
2 Anaesthesia 1985; 40: 356-61.
3 Anaesthesia 1989; 44: 238-41.

## MEASUREMENT OF RESPIRATORY WORK IN A BREATH BY BREATH ANALYSIS USING NEW BEDSIDE RESPIRATORY MONITORING SYSTEM

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(I) Purpose

The measurement of respiratory work has recently become the subject of much research, because we can evaluate the performance of ventilators and SIMV, PSV and CPAP systems on the basis of excess work of breathing using this parameter. However, accurate measurement of respiratory work requires special experimental apparatus and techniques. The continuous monitoring of this parameter at bedside is not available for every patient who receives ventilatory care in ICU.

Recently we have developed a new bedside respiratory monitoring system which is able to measure respiratory work of breathing consisting of total respiratory work, total resistive work and inspiratory resistive work in a breath by breath analysis.

In this study, we demonstrated the features of this new system for measuring respiratory work, and evaluated the ventilator performance, PSV and CPAP systems provided by several kinds of ventilators using this parameter.

(II) Features of new bedside respiratory monitoring system

The most outstanding features of this system integrating an ultrasonic flow meter and $CO_2$ analyzer are the compact, light-weight sensor, which are capable of accurate and stable long-term measurement without the influence of humidity, because this flow meter employing propagation time of ultrasonic wave pulse eliminates sound verocity factor. In addition to this, this system is able to measure 14 different kinds of respiratory and metabolic parameters, including end-tidal $Pco_2$, $\dot{V}co_2$ and $V_D/V_T$ ratio. This system is also capable of both graphic and numerical indication and hard copying of the screen displays and trend recording. Another important point is that it is possible to clean and sterilize the sensor portion with disinfectant. The sensor is completely disassembled and no tools are needed for reassembly.

Respiratory work was computed as the integral of the product of airway pressure and volume based on the pressure volume curve and the compliance obtained from this respiratory monitor. Total respiratory work, total resistive and inspiratory resistive works were measured respectively.

(III) Clinical experiments and applications

(1) Comparison between controlled ventilation and triggered ventilation: Three compartments of works indicated passive work on the controlled ventilation, on the other hand, inspiratory resistive work showed excess work on the triggered ventilation.

(2) Effect of different sizes of endtracheal tubes on the respiratory work: The level of excess work increased as the diameter of tube decreased. When 4 mm inner diameter of tube was applied, the excess work generated by the smallest tube was about 16 times greater than that of the control.

(3) Study of CPAP and PSV mode of ventilator: The level of pressure support at 5 $cmH_2O$ eliminated the excess work caused by the CPAP systems. Furthermore, the changes in the level of pressure support 5 to 10 $cmH_2O$ showed passive work which indicated active ventilatory support to the patient.

(VI) Conclusion

Since our first report about increased excess work and $\dot{V}o_2$ caused by SIMV presented in London in 1982, respiratory work and oxygen cost of breathing has become an important parameter for evaluating the ventilatory modes and the performance of ventilators. The new bedside respiratory monitoring system which is able to measure respiratory work could make a big difference in clinical bedside applications.

# INTRAOPERATIVE CARDIAC OUTPUT MONITORING BY TRANSTRACHEAL DOPPLER TUBE

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INTRODUCTION The recent development of a system for monitoring patients during surgery has been remarkable. For monitoring, a non-invasive system is desirable. Typically, thermodilution with catheterization in the pulmonary artery is widely used to measure cardiac output. This method though highly reliable, is invasive. Therefore, there have recently been many reports on the non-invasive monitoring of cardiac output.

In this study, we have applied a cardiac output measuring device with a transtracheal doppler tube (TTD) to patients and we have evaluated its usefulness. The TTD cardiac output measuring device has been developed by ABCOM. U.S.A. In principle, it measures the cardiac output by inserting a intratrachea of the patient. This tube is located in the area where there is a maximum velocity of the blood flow in the ascending aorta. At this point, the diameter and the area of the ascending aorta are measured. By multiplying this area by the ultrasonically determined average blood flow velocity in the ascending aorta, the cardiac output can be continuously monitored.

In the present study, we simultaneously measured the cardiac output with both the TTD method and the thermodilution method in patients under general anesthesia. Thereafter we compared the two results.

METHOD 10 patients were studied including 7 males and 3 females, all in ASA status II-III. Their ranged in age from 43 to 69 years old and in body weight from 42 to 73kg. 9 cases had undergone open abdomen surgery and one had had open heart surgery. Anesthesia combined with epidural anesthesia or by high dose fentanyl anesthesia.

After introducing the general anesthesia, the TTD tube was inserted into the pulmonary artery. During the operation, cardiac output was monitored by the TTD and the thermodilution methods and the results of both assays were compared.

RESULTS The cardiac output by the thermodilution and TTD methods were compared at 40 points of measurement. the cardiac output was 2.4-8.3 L/min. At a risk factor of 0.1%, there was a direct correlation with a coefficient 0.85.

The following regression equation was deduced.

$$Y = 0.61X + 1.3$$

Where Y = TTD cardiac output and X = thermodilution cardiac output.

The values in the TTD method tended to be lower than those of the thermodilution method.

DISCUSSION In this study, the measurement acquired by the TTD method showed a good correlation with the measurement acquired by thermodilution. During operations, the circulation is very changeable because of the effects of anesthetics, bleeding, transfusion and cardiovascular agents. The most important requirements for such a monitoring system are non-invasiveness, ease in handling, accuracy and measurement in real-time. So far, only the cardiac output of patients in serious condition has been measured. Moreover, the evaluation of the cardiac function by thermodilution catheters is invasive and non-continuous. there have been many reports on complications which they have caused. The TTD method reported herein can be performed simply by per os intubation while allowing continuous measurement of the cardiac output. This can be used as an adequate method for continuously and chronologically monitoring the changing kinetics of the circulatory system.

With this method, it is essential to adequately place the transducer on the tip of the intratracheal tube in the position where it can catch the maximum blood flow in the ascending aorta. As a results, the position of the tube must be corrected after insertion. However, with practice, one can correct the position quickly to begin measuring. In fact, during an operation, we experienced a decreased sensitivity in measurement caused by a subtle positional change in the tube. However, we were able to easily correct this problem.

Before removing the tube, we observed tracheal mucous membrane adjacent to the transducer by using a bronchofiberscope. However, we observed no abnormality such as reddening. We did not observe any other complications caused by the TTD tube.

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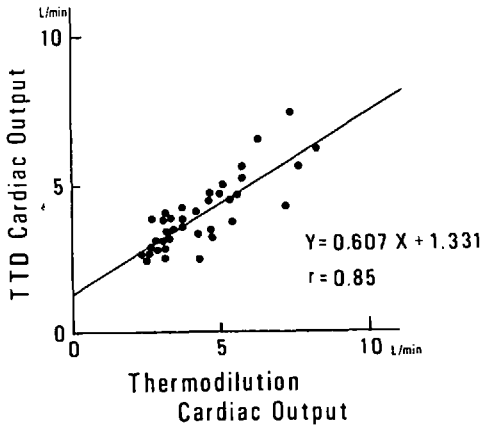
2 Anesthesiology, 71; 11-15



# EVALUATION OF ESOPHAGEAL TEMPERATURE MEASURED BY GASTRIC TUBE WITH THERMISTER

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## INTRODUCTION

Since body temperature is an important information for the optimal patient care during anesthesia and in the ICU, rectal or esophageal thermistor is commonly used to measure core temperature. The rectal temperature, however, sometimes underestimates the core temperature during the abdominal surgery, since abdominal cavity is exposed to the ambient temperature. The esophageal thermistor is prefered in these cases. The new gastric tube (Thermosump) has been developed, to which thermistor probe is incorporated 25 cm from the tip of the tube. The purpose of the present study was to evaluate the accuracy and the safety of this thermistor-incorporated gastric tube in the animal model and during surgery.

## SUBJECTS AND METHOD

1) Six dogs were anesthetized with pentobarbital, and Thermosump,a conventional esophageal thermistor,and a pulmonary artery catheter were inserted. Esophageal temperature measured by Thermosump,by a conventional esophageal thermistor,and pulmonary artery blood temperature were measured every 15 minute for 3 hours. Suction of gastric contents was done intermittently and total amount was measured. Gross findings on esophageal mucosa were examined after necropsy.

2) In 59 patients (ASA physical status 1-2), who underwent elective surgery, esophageal temperature by Thermosump, bladder temperature by Foley catheter, which is incorporated with thermistor, and rectal temperature by conventional thermistor were measured every 15 minute during operation. Informed consent were obtained from all patients before the study. Gastric content was collected intermittently, and total amount was measured. Complication such as bleeding and difficulty to insert the tube were evaluated.

## RESULTS

1) Esophageal temperature by Thermosump correlated well with those measured by conventional esophageal thermistor ($r = 0.99$), and pulmonary arterial blood temperature ($r = 0.99$), in dogs. No difficulty was found to suction the gastric contents There was no visible damage found on the esophageal mucosa at necropsy.

2) The correlation between the temperature measured by Thermosump, and those by rectal thermistor or bladder thermistor in patients was relatively poor ($r = 0.79$, and 0.60, respectively). During abdominal surgery, bladder temperature was significantly lower than that by Thermosump, resulting in the poor correlation ($r = 0.50$). During the surgery of extremities, correlation between the temperatures measured was much higher ($r \geq 0.80$). There was no difficulty found to insert the tube, and to aspirate the gastric contents. No complication was found associated with this study.

## DISCUSSION

Body temperature is one of the important informations for optimal patient care in the OR and the ICU. Among several body temperature currently measured, core temperature such as tymanitic temperature, esophageal and rectal temperature, and pulmonary blood temperature by means of pulmonary arterial catheter, is prefered during anesthesia and for critical patient care, since it represents the metabolic state of the patients, and thermoregulating system. During abdominal surgery, however, rectal temperature and bladder temperature are often affected, since the abdominal cavity is exposed to ambient temperature, resulting in the underestimation of core temperature. Although esophageal temperature is known to correlate well with core temperature, it is sometimes difficult to insert it with a gastric tube. For this reason, a gastric tube with thermistor probe was developed recently. The present study demonstrated that the esophageal temperature measured by Thermosump correlated well with pulmonary arterial blood temperature and there was no difficulty found to insert it and collect gastric contents. This tube is useful to monitor core temperature in the patients who undergo abdominal surgery, and need core temperature monitoring.

**Table Comparison of esophageal temperature with rectal and bladder temperatures**

| | total | type of surgery | |
|---|---|---|---|
| | | abdominal surgery | extremities |
| | (n =59) | (n = 33) | (n = 26) |
| ET[1] vs RT[2] | 0.79 | 0.78 | 0.81 |
| ET[1] vs BT[3] | 0.60 | 0.50 | 0.80 |

all values are coefficient of correlation ($p < 0.001$)
1. esophageal temperature
2. rectal temperature
3. bladder temperature

# CONTINUOUS EPIDURAL ANAESTHESIA FOR OBSTETRICS AFTER MAJOR SPINAL SURGERY

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INTRODUCTION: The guidelines for continuous epidural anaesthesia (CEA) for obstetrics in patients with previous major spinal surgery are unclear. Both the safety and efficacy of the procedure have been questioned. However the literature in this field is sparse, with only 2 reports containing >3 patients[1,2]. The current paper outlines our experience with 18 patients requesting CEA for labor with previous spinal surgery. This includes 21 attempts since 3 had CEA in 2 pregnancies, which is the largest collection of such cases reported to date. We have also performed long-term follow-up interviews which have not been previously reported in this situation.

METHODS: After institutional approval, the charts of 18 patients with previous major spinal surgery who requested CEA for labor analgesia were reviewed. The levels of surgery and presence of any musculoskeletal, neurologic or cardiopulmonary symptoms were noted. The peripartum course was examined for the ease of CEA insertion; quality of anaesthesia; local anaesthetic requirements; and occurrence of complications. Thirteen of the patients were also contacted 8 weeks to 8 years after their last pregnancy to ascertain the degree of satisfaction with their anaesthetic management and presence of any long-term complications that may be attributable to the CEA.

RESULTS: Seventeen of the 18 patients had previous spinal fusion with Harrington instrumentation for idiopathic scoliosis. The remaining patient had a lumbar laminectomy for spinal stenosis and subsequent excision of a herniated disc in the area. The lower level of surgery ranged from L1 to S1. Low back pain was present in 2 since their surgery but none had any neurologic or cardiopulmonary dysfunction. A total of 21 CEA (2 pregnancies in 3 patients) were attempted during labor. In 3 cases the CEA was later extended for use during a caesarean section. The peripartum results are shown in TABLE 1. In only 1 patient was it impossible to enter the epidural space (lack of palpable spines; only bone was encountered). Of the remaining CEA attempts, 12 were performed easily but 8 required >1 try. Eleven of the 21 attempts produced satisfactory analgesia with usual doses of local anaesthetic (0.25% bupivacaine for labor and lidocaine $CO_2$ for delivery). Nine others had "suboptimal" anaesthesia, with inadequate analgesia of either the abdominal or perineal areas and/or larger than normal local anaesthetic requirements. In 4 of these 9 cases, either using the larger doses or supplementation with lidocaine $CO_2$ produced complete analgesia. Of the 3 cases in which the CEA was used for a caesarean section, 2 had normal local anaesthetic requirements and 1 had larger than usual demands. There was no association between the level of surgery and ease of insertion or quality of CEA. The long-term interview revealed high patient satisfaction with their management and no long-term complications. However there was low back pain for a few days after delivery in 2 patients with multiple insertion attempts.

DISCUSSION: This paper indicates that CEA is usually successful in obstetrical patients with prior major spinal surgery for labor, vaginal delivery and caesarean section. Satisfactory analgesia was achieved in 15 of the 21 attempts. However larger than usual doses or a more concentrated solution were needed in 4 of these, suggesting that 0.25% bupivacaine may not be adequate and 0.5% bupivacaine or lidocaine $CO_2$ may be more appropriate. Our results are similar to those of Hubbert[1] and Crosby et al[2], who reported satisfactory analgesia in 10/17 and 7/9 CEA attempts. In the former study, successful CEA occurred in 4/5 of the patients with the lower limit of surgery above L3 but in only 6/12 of those with levels below this. Our lack of correlation between the ease of insertion or quality of anaesthesia and the surgical level was therefore surprising and may be at least partly due to the uncertainty of the level (usually obtained by history or physical examination). There were no significant short-term complications and no long-term complications occurred (even when followed for up to 8 years). Therefore CEA appears to be safe and usually effective in these patients and they should not be automatically denied CEA due to their previous surgery.

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TABLE 1:

| NUMBER OF ATTEMPTS | QUALITY OF ANALGESIA | NUMBER OF EPIDURALS |
|---|---|---|
| 1 | satisfactory | 7 |
| 1 | suboptimal* | 5 |
| >1 | satisfactory | 4 |
| >1 | suboptimal* | 4 |
| >1 | none+ | 1 |

* see RESULTS for definition
+ unable to enter epidural space

## CHEST WALL MOTION DURING HALOTHANE ANAESTHESIA IN INFANTS

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Introduction: Calibration of the respitrace in patients unable to cooperate with the isovolume maneouvre has been problematic. Several investigators have used the normal variation in breathing patterns to calibrate the respitrace.[1-3] In this study the variation in breathing pattern induced by anaesthesia was used to calibrate the respitrace in infants breathing spontaneously during mask halothane anaesthesia.

Methods: With approval from the institutional ethics committee and informed parental consent, 6 ASA 1 infants undergoing elective inguinal hernia repair were studied. Anaesthesia was induced with thiopental 5 $mg \cdot kg^{-1}$ in 2 infants and with halothane in 3 infants. Anaesthesia was maintained with 70% $N_2O$ and 2% halothane in $O_2$. Unintubated infants breathed spontaneously through a modified Jackson-Rees circuit. Mouth Pressure (Honeywell) and flow (Fleisch pneumotachograph) were measured. Flow was mathematically integrated to volume. Chest wall excursion was measured with inductive plethesmography (Respitrace). Data were recorded on a Hewlett-Packard 4 channel tape recorder and played back at a sampling frequency of 50 Hz for computerized breath-by-breath analysis. Respitrace calibration factors (CF) were obtained using the least squares method and polynomial regression analysis. The relationship between the measured and the predicted $V_T$ was described by polynomial regression, and the $r^2$ value. The CF were used to partition $V_T$ into rib cage (RC) and abdominal compartments.

Results: The mean ± SD for age and weight was 2.5 ± 0.5 months and 5.75 ± 0.58 kg, respectively. The $r^2$ describing the relationship for the predicted and measured $V_T$ ranged from 0.4-0.95. A representative figure validating the CF is shown in Figure 1. One patient had a complete paradox of RC and the respitrace could not be calibrated. Two patients demonstrated a partial paradox of the RC. However, 3 patients exhibited synchronous motion RC and abdominal compartments. The RC contribution to $V_T$ ranged from 50-90%. The figure corresponding to data in Figure 1 is shown in Figure 2. This result is in contrast to the predominance of the abdominal contribution previously shown in older children.[4]

Supported by the Physicians' Services Institute Foundation.

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FIGURE 1

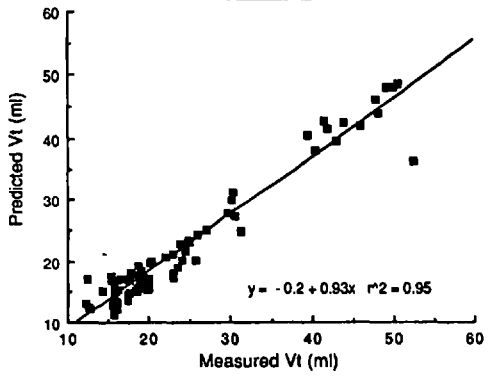
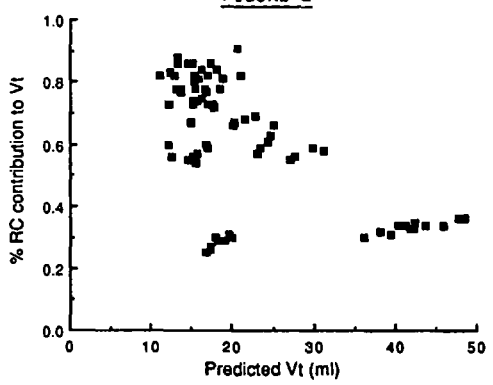



FIGURE 2



# ATTENUATION OF CARDIOVASCULAR RESPONSES TO INTUBATION WITH COMBINATION OF LABETALOL AND SUFENTANYL

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## Introduction

Laryngoscopy and endotracheal intubation is often accompanied by significant increases in heart rate and arterial blood pressure.[1] Numerous methods have been used in an attempt to attenuate these responses but no single technique has gained widespread acceptance. Pretreatment with labetalol, a combined beta and alpha adrenergic blocker, attenuates the hemodynamic response to tracheal intubation. Sufentanyl, a potent narcotic analgesic also blunts the hemodynamic response to intubation. Large doses of sufentanyl may delay recovery from anesthesia and cause postoperative respiratory depression after short surgical procedures. The aim of this study was to examine the use of a combination of small doses of labetalol and sufentanyl during induction of anesthesia with respect to reducing the hemodynamic changes.

## Methods

The study was approved by the Institutional Review Board; informed consent was obtained from the patients. None of the patients had a history of hypertension, angina, congestive heart failure or asthma. Twenty-six ASA 1 and 2 patients were randomly assigned to one of four groups. Group 1 was a control group (no study drug; n=8), group II received labetalol 5 mg (n=6), group III received sufentanyl 0.5 mcg/kg (n=6), and group IV received labetalol 5 mg and sufentanyl 0.5 mcg/kg (n=6). All patients were premedicated with triazolam 0.25 mg sublingually. The blood pressure and heart rate were recorded by a Dinamap automatic blood pressure monitor. After baseline indices were recorded ($T_0$), all the patients were given 3 mg of d-tubucurarine IV followed by the study drug. Data collection was repeated after 5 minutes and anesthesia was induced with thiopental 4 mg/kg in group I and II patients and thiopental 2 mg/kg in group III and IV. All patients received succinylcholine 1.5 mg/kg to facilitate intubation. Laryngoscopy was initiated one minute later and the trachea was rapidly intubated. Anesthesia was maintained with 67% nitrous oxide ($N_2O$) and 33% oxygen ($O_2$) and ventilation was controlled to keep the end-tidal $CO_2$ between 30-35 mm HG. Blood pressure and pulse rate were recorded at 1, 3, and 5 minutes after intubation. Data were analyzed using analysis of co-variance. Significance was set at $p<0.05$.

## Results

Baseline hemodynamics (±SEM) for each group were comparable to the control group with heart rate (HR) of 80±10; systolic blood pressure (SBP) of 118±9; diastolic blood pressure (DBP) of 70±7. One minute after intubation, the HR, SBP, and DBP were significantly increased in group 1 and 2 patients, compared to group 3 and 4 patients. There was no significant differences in HR, SBP, and DBP between group 3 and 4 patients after 1 minute, 3 minutes, and 5 minutes after intubation. Three patients in group 3 and three patients in group 4 developed severe respiratory depression with a decrease in $S_aO_2<90\%$ before anesthetic induction requiring oxygen by mask.

## Discussion

Laryngoscopy and tracheal intubation cause an elevation in blood pressure and heart rate. The results show that sufentanyl 0.5 mcg/kg given five minutes prior to induction is effective in preventing the hemodynamic response to intubation. There was no advantage in adding 5 mg labetalol in combination with sufentanyl 0.5 mcg/kg. However, patients receiving sufentanyl 0.5 mcg/kg prior to induction may develop severe respiratory depression and need to be monitored closely.

## Reference

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| PULSE | BASELINE T0 | BEFORE INDUCTION T5 | +1 MIN | +3 MIN | +5 MIN |
|---|---|---|---|---|---|
| Group 1 | 80±10 | 83±15 | 107±22 | 91±18 | 87±17 |
| Group 2 | 85±10 | 88±11 | 107±13 | 106±11 | 101±8 |
| Group 3 | 71±9 | 59±9 | 79±12* | 67±7 | 62±4 |
| Group 4 | 82±12 | 75±11 | 84±12* | 76±8 | 69±5 |
| SBP | | | | | |
| Group 1 | 118±9 | 120±9 | 148±29 | 131±17 | 127±20 |
| Group 2 | 125±4 | 120±10 | 141±10 | 130±6 | 116±7 |
| Group 3 | 127±13 | 118±14 | 116±12* | 110±10 | 101±8 |
| Group 4 | 135±18 | 126±21 | 120±20* | 112±17 | 107±16 |
| DBP | | | | | |
| Group 1 | 70±7 | 73±11 | 99±24 | 87±23 | 78±24 |
| Group 2 | 76±7 | 75±10 | 92±18 | 73±9 | 61±11 |
| Group 3 | 73±14 | 68±10 | 67±10* | 53±10 | 49±5 |
| Group 4 | 73±9 | 65±13 | 65±14* | 49±8 | 50±8 |

*Significantly different from control $p<0.05$.

## HAEMODYNAMIC EFFECTS OF I.M. OPIOIDS FOR ANALGESIA DURING VENTILATOR TREATMENT AFTER OESOPHAGECTOMY

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Introduction: Prophylactic ventilator treatment has been a common procedure following oesophageal cancer surgery. Rather heavy sedation is required for ventilatory acceptance and pain relief during the treatment. The use of narcotic analgesics may contribute to circulatory instability during the first postoperative hours. In this study we have evaluated the effects of intramuscular buprenorphine, pentazocine and morphine on systemic and pulmonary haemodynamics immediately after the surgery.

Methods: This study received institutional approval and informed consent was obtained from each patient. Twenty-six ASA physical status I-II patients (20M/6F, age 52-77) undergoing oesophageal cancer surgery were entered into randomized, double-blind trial. All patients were inserted Swan-Gantz catheter on the day before surgery and control haemodynamic measurements were obtained including mean arterial pressure (MAP), heart rate (HR), cardiac index (CI), systemic vascular resistance (SVR), mean pulmonary arterial pressure (MPAP), pulmonary capillary wedge pressure (PCWP), central venous pressure (CVP), and pulmonary vascular resistance (PVR) . Following intramuscular administration of diazepam 5-10mg and atropine 0.5mg as premedication, anaesthesia was induced and maintained with nitrous oxide and enflurane in oxygen with pancuronium. Nasotracheal intubation was performed uneventfully. Any narcotic analgesics was not administered during surgery. The patients were transferred to the ICU immediately after surgery and mechanical ventilation was started using Servo 900C ventilator. The second haemodynamic measurements, respiratory rate, peak airway pressure and blood gas analysis were obtained when the patients spontaneously complained of pain or had fighting to ventilator and at the same time they received one intramuscular dose of buprenorphine 0.006mg/kg, pentazocine (0.8mg/kg or 1.5mg/kg), or morphine 0.3mg/kg. One hour later the third haemodynamic measurements and the respiratory and blood gas data were obtained. Pain was graded into four categories (absence of pain, discomfort on questioning, spontaneous complaints, and patients in obvious pain) and assessed. No other analgesics, sedatives or medications likely to potentiate or inhibit the study drugs were administered while the patient experienced satisfactory pain relief from the initial medication. Time to remedication was recorded and considered duration of adequate analgesia. The haemodynamic and respiratory data were compared using student's t test.

Results: Groups were similar with respect to age, sex, weight and ASA status. Seven patients received buprenorphine 0.006mg/kg (B), six received pentazocine 0.8mg/kg (P 0.8), seven received pentazocine 1.5mg/kg (P 1.5) and six received morphine 0.3mg/kg (M). The second haemodynamic data showed increases in MAP, HR and MPAP compared with the control data. In B and P 0.8 Groups, there were no significant changes between the second and third haemodynamic data. In P1.5 Group, HR and SVR increased significantly ($P<0.05$, $P<0.01$) and MAP increased slightly following the drug administration. In contrast, MAP decreased significantly ($P<0.01$) in M Group. Respiratory rate and peak airway pressure decreased following the drug administration in all groups. $PaCO_2$ increased significantly ($P<0.05$) in B Group. All patients reached absence of pain within one hour after the B administration. One patient in P0.8 Group, one in P1.5 Group and four in M Group had the grade of discomfort on questioning and tolerable slight fighting to ventilator. Durations of adequate analgesia were $14.8\pm8.8$(B Group), $6.6\pm2.8$(P 0.8 Group),$9.0\pm7.5$(P 1.5 Group) and $6.6\pm5.4$(M Group) hours respectively. No obvious side effects appeared in all groups.

Discussion: All patients had excellent or good pain relief within one hour after buprenorphine, pentazocine or morphine administration. However, there were considerable differences in haemodynamic response among the four groups. Large amount of pentazocine produced increases in HR and SVR, suggesting sympathetic cardiovascular effect which may lead to myocardial ischaemia in patients with coronary artery disease. In contrast, morphine produced a decrease in MAP. These drugs may be not suitable for analgesia in elderly patients with oesophageal cancer. Buprenorphine had no significant haemodynamic changes. Buprenorphine may be first choice drug for analgesia during postoperative ventilator treatment in patients with oesophageal cancer because of minimal circulatory effect, excellent pain relief and longer duration.

# OXYGEN MEDIATED COMPLEMENT ACTIVATION: AN IN-VITRO STUDY

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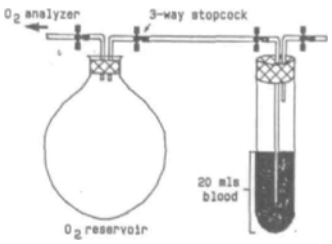
INTRODUCTION: The complement system is a group of plasma proteins which undergo sequential activation in a cascade fashion and which interacts to cause a variety of physiological and pathological effects. There are two pathways of complement activation, the classical and the alternate. C3a, C4a and C5a, the activated fragments of complement C3, C4 and C5 (anaphylatoxins) have several biological effects. Smooth muscle spasm, release of histamine and other active amines from basophils and mast cells, increase in vascular permeability, platelet aggregation, and initiation of formation of microaggregates.

Oxygen is critical for the efficient generation of energy by aerobic metabolism. Oxygen therapy is indicated whenever oxygen delivery to the tissues is impaired. One of the known hazards of oxygen therapy with high concentrations for prolonged periods is oxygen toxicity, the mechanism and pathology of which remain obscure. Oxygen has two unpaired electrons, each located on a different antibonding orbital. In the process of acting as an elecron acceptor, oxygen can form several reduced oxygen species which are toxic in nature. Some of the signs of pulmonary insufficiency seen as a result of unbalanced activation of complement are similar to those encountered in oxygen toxicity.

The use of pump-oxygenator systems has been associated with a complex array of postoperative clinical sequelae (Post Pump Syndrome) including coagulopathies, increase capillary permeability, increase accumulation of interstitial fluids, leucocytosis, fever, and profound organ dysfunction which is particularly manifest in the pulmonary, renal, and central nervous systems. The striking similarities between these findings and the known biologic activities of the complement-derived anaphylatoxins C3a and C5a suggest that these inflammatory mediators may precipitate in promoting some of these symptoms.

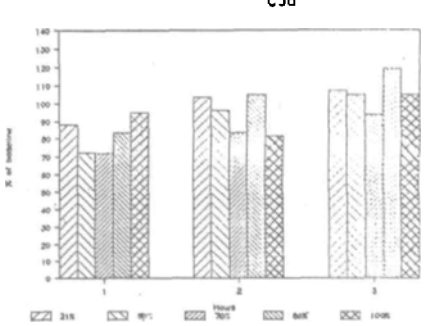
This study was designed to investigate whether an activitation of complement occurs with high concentrations of oxygen.

METHOD: With IRB approval and written consent from patients, we studied blood from twelve healthy male volunteers age 20-40. Five silicone coated test tubes, each filled with 20 ml of fresh anticoagulated blood taken from a single donor, were bubbled with different concentrations of oxygen (21%, 50%, 70%, 80%, and 100%) continuously for three hours. The gas mixtures were taken from the anesthesia machine and stored in breathing bags, then delivered to the test tubes with five plastic tubes connected to five pipet tips. A constant identical slow flow was achieved to prevent hemolysis. The gas mixtures were double checked with a Puritan Bennett paramagnetic oxygen analyzer. 5 ml of blood was transferred from the test tube to standard disodium EDTA tubes at one hour, two hours, and three hours. A baseline sample was taken before any oxygen was administered. Blood gases were also examined at these times to ensure adequate oxygenation. Plasma was separated immediately for C3a analysis on a later date by radioimmuno assay (Amersham). Results were analyzed using Students t test with Bonferroni's correction (p 0.05 was considered significant).




RESULTS: During this three-hour in-vitro study we were unable to detect any significant activation of complement C3 either with increased concentration of oxygen or with time.

DISCUSSION: In this in vitro model with carefully controlled gentle bubbling of different concentrations of oxygen through blood from healthy volunteers we were unable to detect any activation of anaphylatoxin C3a. This finding is in contrast to the findings obtained by other authors, i.e., a time dependent generation of C3a with a two-fold increase after 60 minutes with vigorous bubbling of 100% $O_2$ in a bubble oxygenator. As we conduct our study for three hours providing adequate oxygenation by gentle bubbling, we believe that the claimed activation may be due to the mechanical damage secondary to a huge blood gas interface with vigorous bubbling rather than the concentration of oxygen.

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## EFFECTS OF ENFLURANE ON ELECTRICAL ACTIVITIES IN THE HIPPOCAMPAL DENTATE GRANULE CELLS

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### INTRODUCTION

Enflurane was shown to depress the excitatory synaptic transmission and to increase the action potential discharges in the hippocampal CA1 pyramidal cells over a wide range of concentrations. Of interest is that enflurane has different effects on the excitability of hippocampal dentate granule cells from those on the CA1 pyramidal cell excitability. The excitability of dentate granule cells was increased by enflurane at low concentrations, but decreased at higher concentrations. Although recent studies showed that the inhibitory postsynaptic potentials (IPSP) of the CA1 pyramidal cells was markedly depressed by enflurane, the effects of enflurane on the synaptic inhibition of dentate granule cells remain uncertain. The aim of the present study was to examine the effects of enflurane on the dentate granule cell activities, especially on the strength of the synaptic inhibition, with the field potential analysis in freely moving rats.

### METHODS

Twelve male Wistar albino rats were used. The recording and stimulating electrodes were implanted under pentobarbital anesthesia into the dentate hilus and the perforant path, respectively. Two weeks after the electrode implantation, the animals in which the monosynaptic EPSPs and population spike (synchronized action potentials) components of the field potential can be well identified were chosen for the later experiments. After the control recording of field potentials, enflurane was evaporated in the observation box until the animals showed no response to the tail-pinch stimulation. Changes in the dentate field potentials and animal behaviors were observed before, during and after the enfluran anesthesia. The strength of recurrent synaptic inhibition in the dentate area was estimated by an analysis of paired-pulse depression.

### RESULTS

Shortly after an application of enflurane, animals showed a hyperactivity for several minutes. During this period, enflurane had little effect on the excitatory and inhibitory synaptic transmissions. As the animal fell into the deep anesthesia, however, the excitatory synaptic transmission was rapidly depressed. The strength of paired-pulse depression at an interpulse interval of 20 msec was markedly potentiated, showing an increase in the strength of GABAergic recurrent synaptic inhibition. In contrast, the late paired-pulse depression at interpulse interval of 100-5000 msec was not significantly affected by enflurane. While enflurane strongly potentiated the population spike amplitude, its latency was prolonged. When the air mixed with enflurane was replaced by fresh air, the depressed excitatory synaptic transmission recovered gradually. The potentiated paired-pulse depression and population spike amplitude also returned gradually to the control level as the animal recovered behaviorally from the anesthesia.

### DISCUSSION

Because of the depression of excitatory synaptic transmission and the potentiation of synchronized action potentials, enflurane seems to increase markedly the granule cell excitability even in a deep anesthesia. While it was shown that enflurane selectively reduced the IPSPs in the hippocampal CA1 and CA3 pyramidal cells, the present study showed that the recurrent synaptic inhibition of the dentate granule cells was potentiated, but not reduced, by an application of enflurane. It is possible, thus, that enflurane has differential effects on the synaptic inhibitions in the hippocampal CA1 area and the dentate area.

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# ANOTHER LOOK AT MATERNAL INSPIRED OXYGEN CONCENTRATION DURING CESARIAN SECTION

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**Introduction:** Many authors have shown that foetal arterial and venous $pO_2$ increase proportionally to maternal inspired oxygen concentration and the maternal $pO_2$.[1,2] This however, has only been studied with constant maternal inspired oxygen concentration through out the cesarian section. In many institutions including ours, anesthesiologists use a higher maternal oxygen concentration only for the period between the hysterotomy and birth which is usually much less than 3 minutes. This study was designed to see if there will be a difference on foetal $pO_2$ if high oxygen concentration for a short time period is used.

**Methods:** Our study was accepted by the Research and Ethics Committee of our institution. 20 patients with normal term pregnancies undergoing elective cesarian section were studied. Each patient was placed under general anesthesia using a standardized technique: preoxygenation with 100 % oxygen was started at the time the surgeon begun the abdominal prep, anesthesia was induced just before the surgeon was ready to incise the skin. Thiopental 4 mg / kg and succinylcholine 1 mg / kg were used. A rapid sequence induction was performed using a Sellick manoeuvre and tracheal intubation. Before the delivery, anesthesia was maintained with nitrous oxyde 50 %, oxygen 50 %, halothane 0.5 % and vecuronium 0.04 to 0.05 mg/kg. At the time of the hysterotomy, ten patients had the same anesthesia continued and ten patients had the nitrous oxyde cut off to provide 100 % oxygen (each patient having been assigned randomly beforehand to one of the two groups). After the delivery and after the umbilical cord had been clamped, the anesthesia consisted of fentanyl 100-250 g, nitrous oxyde 66% and oxygen 34%. Halothane was usually discontinued but used at concentrations of 0.25 - 0.5 % according to the clinical situation. The different parameters mesured were the time delays between the preoxygenation, the induction of anesthesia, the hysterotomy and birth. Arterial blood gases were done on the mother and on the arterial and venous umbilical cord at birth and the neonate was evaluated using the Apgar score. The patients were also interviewed within 3 days, after the cesarian section to try and elicite awareness. This was done using a standardised questionnaire (3). Statistical analysis was done using the Student's t test, the Mann Whitney U test, or the Chi square when appropriate. A value of $p < 0.05$ was considered significant.

**Results:** There was no statistical difference in our two groups with regards to the demographic results. All the different time delays mesured were also statistically similar between the two groups. The arterial maternal blood gases were statistically similar regarding the pH, $pCO_2$, and $HCO_3$ but showed statistical difference for $pO_2$ with 177.41 ± 42.26 mmHg for the 50% group and 280.99 ± 94.17 mmHg for the 100% group ( p = 0.007). The arterial and venous umbilical cord blood gases in the 2 groups were not statistically significant. Arterial pO2 were 19.33 ± 5.7 mmHg in the 50% group and 18.5 ± 7.34 mmHg in the 100% group. Venous pO2 were 31.1 ± 7.8 mmHg in the 50% group and 33% ± 10.76 mmHg in the 100% group. The Apgar scores were statistically different at one minute with modal scores of 9 for the 50% group (range 8-10) and 8 for the 100% group (range 3-9). The Apgar scores at 5 minutes were statistically different with modal scores of 10 for the 50 % group (range 9-10) and 9 for the 100 % group (range 4-10). The Apgar scores at 10 min. showed no significant difference with modal scores of 10 in both groups. Finally, there was no statistically significant difference in the frequency of awareness with 1 patient out of 10 reporting awareness in the 50% group and 4 patients out of 10 in the 100% group.

**Discussion:** Our study shows that although maternal arterial $pO_2$ increased significantly with those mothers breathing 100 % oxygen, the arterial and venous foetal $pO_2$ did not increase significantly compared to those mothers who breathed 50 % oxygen. Another difference that came out from our study is that Apgar scores were different at 1 and 5 minutes, but surprisingly they were lower in the 100 % group. This is explained by the fact that two neonates had low Apgar scores of 3 and 4, at 1 min. The one neonate with an Apgar score of 3 had a difficult birth because he was in a transverse position and the mother suffered a blood loss of 1.5 l at the time of delivery. We did not have any explanation in the case of the neonate with the Apgar score of 4. Concerning the frequency of awareness, 1 out of 10 patients in the 50% group and 4 out of 10 in the 100% group had some recall of events during the cesarian section, usually around the birth of the baby. Although this difference was not statiscally significant, it is tempting to consider it at least clinically significant until proven otherwise. A higher number of patients in both groups might have resulted in a statistically significant difference.

In conclusion, our study shows that there is no advantage in using 100 % maternal inspired oxygen concentration in the period between hysterotomy and birth to try and improve the foetal $pO_2$, unless one uses a high maternal inspired oxygen concentration through out the cesarian section. There is also some clinical suggestion that awareness might be more frequent in the group that received 100% inspired oxygen concentration.

**References:**

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# THE INVOLVEMENT OF ANESTHETISTS IN CRITICAL CARE MEDICINE

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Introduction: Anaesthesia is one of four major specialties committed to critical care medicine. There is a general impression however, that anaesthesia as a specialty is loosing interest in critical care medicine. Yet, there is little data available on how many anaesthetists are involved in practicing critical care medicine in Canada. We have undertaken a national manpower review with respect to the primary specialty of critical care physicians.

Methods: A self administered survey was mailed to the coordinators of intensive care units (ICU) in all hospitals across Canada. Nonresponders were sent a second questionnaire. Failure to return the second questionnaire resulted in telephone contact. For the purpose of the study, the data obtained included level (of acuity) of the ICU, specialty, years of experience and age of all physicians providing critical care. Level 1 critical care units (monitoring units) were excluded from further analysis because the nature of practice would not include anaesthetists. Physicians were then divided into anaesthetists and non-anaesthetists as well as by level of care (level 2 or 3) and compared with respect to age and years of experience using analysis of variance.

Results: The survey was mailed to 481 hospitals in Canada and encompassed 3264 ICU beds. The overall response rate was 84 percent. There was a greater than 70 percent response rate from all provinces. Included were 117 level 3 ICUs (highest intensity) and 194 level 2 ICUs (intermediate intensity). Results are presented in table 1. The discrepancy in number of respondents between years of experience and age in all categories was due to partial completion of the questionnaire. There were no significant differences between anaesthetists and non-anaesthetists in level 2 practice with respect to age and years of experience. However, anaesthetists in level 3 practice have significantly less years of experience than non-anaesthetists. There was no significant difference in ages between anaesthetists and non-anaesthetists in level 3 practice.

Table 1:
Physicians in Critical Care Practice by Level and Specialty

| | Age | |
|---|---|---|
| | Level 2 | Level 3 |
| Anaesthetists | 40.4 (64) | 39.5 (87) |
| Non-anaesthetists | 41.5 (431) | 41.4 (330) |
| | P = NS | |
| | Years of experience | |
| | Level 2 | Level 3 |
| Anaesthetists | 9.1 (59) | *7.2 (88) |
| Non-anaesthetists | 9.6 (388) | 9.2 (333) |

*$P < 0.05$

Mean (number)

Discussion: No differences between anaesthetists and non-anaesthetists with respect to age and years of experience were present in level 2 practice. However, anaesthetists in level 3 critical care practice had a significantly reduced years of experience for a similar mean age as non-anaesthetists. This appears to imply that anaesthetists engaged in level 3 critical care tended to retire from critical care and return to their primary specialty sooner than non-anaesthetists. Level 3 critical care tends to encompass for the most part university based and academic practice. The reasons for anaesthetists leaving level 3 practice is unclear but perhaps this phenomena should be investigated further if anaesthesia is committed to playing a role in critical care medicine.

# FACTORS AFFECTING HYPOMAGNESEMIA AFTER CARDIOPULMONARY BYPASS

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**Introduction**: Magnesium is known to be essential for celluar metabolism and intracellular signal transduction. Magnesium is thought to play important roles in the regulation of tension development in muscles, including smooth and cardiac muscles, and is also reported to prevent or to ameriolate ischemic injuries. It has been suggested that in ischemic myocardium magnesium levels are low, and that the administration of magnesium is an effective treatment for arrhythmias which are resistant to authentic antiarrhythmic agents. Magnesium is also able to relieve vasospasm. During cardiopulmonary bypass(CPB), it is important to prevent ischemic damage in organs, including the heart. It has been reported that the serum magnesium level decreases during and after CPB. We investigated the factors affecting this decrease.

**Methods**: Nine patients with ischemic heart diseases (56±8 y.o.), 20 with valvular heart diseases (50±3 y.o.) and 5 with congenital heart diseases (38±19 y.o.) were investigated. They were anesthetized with diazepam and fentanyl (100 μg/kg). Magnesium was not given during the entire course of the investigation, nor added to the priming solution for CPB. The cardiplegic solution contained KCl(20 mM) and insulin(5 U/L), but not magnesium. Patients were cooled to an esophageal temperature of 28°C during bypass. Blood samples were drawn through radial artery canulas, and serum magnesium levels were determined spectrophotometrically using the xylidyl-blue method (normal value=1.6-2.1 mEq).

**Results**: Serum magnesium concentration decreased significantly after CPB from 1.76±0.17 to 1.37±0.19 mEq/L ($p<0.001$). It reached a minimum on the 1st post-operative day (1.34±0.19 mEq/L), and remained low on the 2nd postoperative day (1.49±0.23 mEq/L). Preoperative physical condition affected post-operative hypomagnesemia. Hypomagnesemia was more marked in patients with a lower NYHA classification, and their recovery was retarded. Chronic diuretic therapy is known to be one of the major causes of hypomagnesemia. Although the preoperative magnesium levels remained normal even in those patients who received preoperative furosemide therapy, hypomagnesemia continued longer in patients who received preoperative furosemide therapy than in those who did not. The change of serum magnesium levels in patients with valvular heart diseases and those with ischemic heart diseases were compared. Patients classified as NYHA II and who did not receive preoperative furosemide therapy were selected from each group. Hypomagnesemia was more marked and continued longer in patients with ischemic heart diseases than in those with valvular heart disease. Neither age nor the duration of CPB affected postoperative hypomagnesemia.

**Discussion**: The serum magnesium level is reported to decrease 14-39 % after CPB, and to remain lower than preoperative values for 3-7 days. The present study confirms these observations, and further demonstrates that hypomagnesemia is more significant in patients with (i) a lower NYHA classification, (ii) preoperative furosemide therapy, and (iii) ischemic heart diseases. Because the magnesium levels in these patients remain normal before CPB, it seems likely that the hypomagnesemia after CPB reflects the intracellular magnesium deficiency which probably exists before surgery. In other words, serum concentrations of magnesium do not reflect the intracellular concentration of magnesium, which is more important in its biochemical and biophysiological roles. Although the complications directly caused by hypomagnesemia were not found in these patients, it is possible they may occur. Supplementary magnesium in the perioperative period seems to be required in patients with ischemic heart diseases, patients classified as NYHA III/IV or those receiving preoperative furosemide therapy.

# THE EFFECT OF GENERAL ANAESTHESIA ON POST-TONSILLECTOMY PAIN AND RESPIRATORY STATUS

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**Introduction:** The severity of post-operative pain and the incidence of adverse respiratory events after tonsillectomy complications are poorly documented. This lack of valid and reliable data came to light when we began to reconsider the management of children undergoing tonsillectomy on a Day Care Surgical basis. To evaluate pain and respiratory depression, we prospectively studied 300 children undergoing elective tonsillectomy. We hypothesized (1) that children undergoing tonsillectomy would have better pain control in the recovery room if administered IM narcotics in the operating room, (2) that post-operative pain management on the wards would be unaffected by intraoperative narcotics, and (3) that children administered a balanced anaesthetic would have an increased incidence of respiratory events post-operatively.

**Methods:** After Hospital Ethics Committee approval and informed consent, 300 elective, ASA I-II physical status children of age 2 to 12 years undergoing tonsillectomy or adenotonsillectomy were randomly assigned to 3 groups. Subjects were excluded if they had cardiac or respiratory disease, or if any of the drugs to be administered were relatively or absolutely contraindicated. We explained to each parent the use of a linear visual analogue pain scale (VAS) and gave each parent a copy of a VAS. The anchors for the 0 - 100 pain scale were no pain and worst pain imaginable, respectively. **Introduction**: Appropriate monitoring was established upon arrival in the operating room. After sedation with nitrous oxide (50 - 70 percent), the patients had an IV induction with 5 $mg.kg^{-1}$ thiopentone or an inhalation induction with halothane. After induction of anaesthesia, the subjects were randomized into either group D, M or S (see below) and were administered 0.08 $mg.kg^{-1}$ vecuronium. These narcotics and their pattern of use were selected since this respresents typical clinical practises by some of our staff. After tracheal intubation, ventilation was supported to maintain normocapnia. Group D had their anaesthesia maintained with 70 percent nitrous oxide and 1.5 percent halothane, and they were given 1.5 $mg.kg^{-1}$ meperidine (Demerol) IM about 10 minutes before the end of the operation. Group M was the same as Group D except their narcotic was 0.1 $mg.kg^{-1}$ morphine IV at induction. Group S underwent balanced anaesthesia with 70 percent nitrous oxide/30 percent oxygen plus sufentanil, 0.5 $mcg.kg^{-1}$ IV bolus at induction and a 0.2 $mcg.kg^{-1}.hr^{-1}$ infusion. Appropriate neuromuscular blockade was maintained with intermittent 20 $mcg.kg^{-1}$ vecuronium boluses. Upon completion of surgery, muscle relaxation was reversed by 60 mcg.kg-1 neostigmine with 20 $mcg.kg^{-1}$ atropine IV and the oral airway was suctioned clean. Group D and M were extubated before their airway reflexes returned and Group S were extubated when able to protect their airway. For the balance of the study, the patients were treated similarly. **PARR:** In the post-anaesthetic recovery room (PARR), patients were monitored continuously with a Nellcor pulse oximeter. Oxygen was administered by mask at 6-8 $L.min^{-1}$ for 10 minutes as tolerated and then only if indicated or the patient was still unconscious. For the purpose of this study severe hypoxemia, was defined as an oxygen saturation of less than 90 percent. Morphine, 0.05 $mg.kg^{-1}$ IV, was administered q10min, if the patients modified CHEOPS pain score, as determined by a blinded assessor, was greater than 7.[1] (The standard CHEOPS pain score had the behaviour rating for touching of the surgical site deleted). Respiratory rates were monitored every 5 minutes for three occasions and then every 15 minutes.
On the ward, the children were administered 1 $mg.kg^{-1}$ codeine q3-4h IM or p.o. as determined by the attending ward nursing staff. The first dose of codeine was given IM. On the day after surgery, the parents were contacted by phone by a blinded research assistant and asked to rate their child's pain on the day of surgery and the day after surgery using the linear analogue pain scale. The data was analyzed using One-way ANOVA, Kruskal-Wallis ANOVA, Chi-square analysis, Fisher exact test and ANCOVA. The acceptable alpha error was set at 0.05.

**Results:** There were no significant differences between the demographic data. Patients administered meperidine had the best pain control in the recovery room as evidenced by decreased pain scores and decreased narcotic administration (Table I and II). The administration of narcotics and pain scores on the wards were unaffected by the anaesthetic technique. Balanced anaesthesia with sufentanil was associated with significantly decreased respiratory rates in the recovery room ($P < 0.001$). Children administered meperidine had higher oxygen saturations in the PARR and the lowest incidence of severe hypoxemia, $P < 0.05$ (Table III). Two patients who were administered sufentanil were apneic in the PARR (this apnea responded to stimulation).

**TableI- Overall PARR Pain Scores**

| Group | Scores (Mean + SD) |
|---|---|
| Meperidine | 5.4 ± 0.7* |
| Morphine | 6.0 ± 0.8 |
| Sufentanil | 5.7 ± 0.8* |

$P < 0.01$, Kruskal-Wallis ANOVA; Me < S; S < Mo

**Table II-Morphine Administration in the PARR**

| Group | # of Morphine Doses Given |
|---|---|
| Meperidine | 28 |
| Morphine | 92 |
| Sufentanil | 43* |

* $P < 0.05$, Me < S; $P < 0.0001$ S < Mo

**Table III-Severe Hypoxemia in PARR**

| Group | Incidence-Oxygen sat<90% |
|---|---|
| Meperidine | 0/100* |
| Morphine | 9/100 |
| Sufentanil | 8/100 |

* $P < 0.05$, Fisher exact tests

**Discussion:** Narcotic-relaxant (balanced) anaesthesia leads to a rapid return of airway reflexes at the end of surgery in children. This is advantangeous at the end of tonsil surgery, but we have shown that this technique using sufentanil has increased complications (hypoxemia) in the recovery room. The administration of lower doses of narcotic (in this case morphine) also does not decrease the incidence of severe respiratory complications and is associated with increased pain in the PARR. In this study, the administration of adequate IM doses of narcotics (in this case Demerol) in the operating room best controlled pain in the PARR and was not associated with significant respiratory depression.

**References:** 1. Adv Pain Res Ther 1985; 9:395-402.

# ELECTIVE INTUBATION IN THE UNSTABLE CERVICAL SPINE PATIENT

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**Introduction:** Controversy exists regarding the optimal mode of endotracheal intubation in the patient with an unstable cervical spine[1,2]. There is no good evidence in the literature to suggest that one mode of lintubation is superior to another in preserving spinal cord function in this setting. A retrospective study was undertaken to compare the neurologic outcome of patients with unstable cervical spine injuries following airway instrumentation awake, or under general anaesthesia, in order to determine the safest mode of airway management.

**Methods:** A 10 year chart review of patients with unstable cervical spines, who required operative procedures, was conducted. Patients with complete cord injuries, either at, or adjacent to the level of spinal injury, were excluded. The sex and age of the patient, mode and level of injury, preoperative neurologic status, and associated injuries were recorded. From the anaesthetic records, the method of intubation, use and type of traction during intubation, and occurrence of technical difficulties during airway instrumentation, were retrieved. Immediate and late postoperative neurological deficits were recorded from the progress notes made by the neurosurgical resident or attending neurosurgeon. Chi-square analysis was used to test for statistical significance, which was asumed when $p<0.05$.

**Results:** Eighty-two charts were reviewed. Twenty patients with complete spinal cord injuries were excluded because their injury would have precluded assessment of possible changes in spinal cord function following airway instrumentation. Of the remaining 62 patients, there were 49 males (79%). The mean age was 36.5 years, with a range of 16 to 85 years. The mechanisms of injury included: 35 from MVA (56%), 16 from falls (26%), 10 sports related (16%) and one resulted from a blow to the head (2%). A total of 9 injuries occurred at the C1,2 level (15%), and the remainder were in the subaxial cervical spine (85%). There were 17 patients with neurological deficits (27%): 9 radiculopathies, 6 incomplete cord injuries, one thoracic cord injury and one peripheral neuropathy. Associated injuries consisted of other orthopaedic injuries in 9 patients and pulmonary contusions in two. Intubation occurred after induction of anaesthesia in 43 patients (69%), 19 patients were intubated awake (31%). Aids to intubation included: fiberoptic bronchoscope (9), lighted stylet (8), stylet (4), and rubber bougie (1). In-line stabilization was employed in 50 patients; tongs (25), halo (9), manual (16). In total, 8 intubations were deemed to be difficult, requiring multiple attempts. Postoperatively, there were no new neurologic deficits, 2 radiculopathies resolved, and 2 had improved following surgical stabilization. A summary of mode of intubation and neurological outcome is presented in TABLE 1. There were no differences ($p>0.05$) comparing neurologic outcome with intubation awake or under general anaesthesia.

**Discussion:** We reviewed elective intubation in 62 patients with unstable cervical spines and minimal neurologic injury. There was no evidence of new neurological injury, and endotracheal intubation did not adversely affect neurological function whether performed awake or under general anaesthesia. This is consistant with the literature regarding intubation in this patient population[3].

**References:**

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3. Anaesth Intens Care 1985;13:319-324.

Table 1 **MODE OF INTUBATION AND NEUROLOGICAL OUTCOME**

| | Anaesthetized | Awake |
|---|---|---|
| Total (n) | 43 (69%) | 19 (31%) |
| Neurologic deficit | | |
| Preoperative | 11 (18%) | 6 (10%) |
| Postoperative | 10 (16%) | 5 (8%) |
| New deficit | 0 (0%) | 0 (0%) |
| Resolution | 1 (2%) | 1 (2%) |
| Improved | 2 (3%) | 0 (0%) |
| Unchanged | 8 (13%) | 5 (8%) |

## ALFENTANIL IN MINOR SURGERY REQUIRING TRACHEAL INTUBATION: A MULTICENTRE TRIAL

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Introduction:

Alfentanil has an onset of narcotic effect three to four times faster than that of fentanyl, and an elimination half-life less than half as long. Pharmacokinetically it would appear to be ideally suited for short surgical procedures. This multicentre study involved an open, non-comparative clinical evaluation of alfentanil as an analgesic adjunct in intubated patients undergoing minor surgery.

Methods:

Patients scheduled for elective minor surgery, aged 12-60 years, of ASA physical status I-III and requiring tracheal intubation were studied. The induction sequence included droperidol 0.0175 $mg.kg^{-1}$, pancuronium 0.02 $mg.kg^{-1}$ IV and pre-oxygenation. Alfentanil 30-50 $ug.kg^{-1}$ IV (see Table) was administered at 25 $ug.kg^{-1}.min^{-1}$. Induction was completed with thiopentone 3-5 $mg.kg^{-1}$ and tracheal intubation facilitated with succinylcholine 1.5 $mg.kg^{-1}$. Anaesthesia was maintained with nitrous oxide/oxygen (70%/30%), and increments of muscle relaxants and alfentanil (see Table) as needed. Low concentrations (0.25%-0.50%) of enflurane or isoflurane were administered whenever alfentanil failed to maintain haemodynamic stability.

Monitoring included baseline and perioperative measurements of systolic, mean and diastolic blood pressures (SAP, MAP, DAP) and heart rate (HR), determination of recovery times, incidence of adverse experiences, and the anaesthetist's overall evaluation of the induction, maintenance, and recovery. The incidence of nausea and vomiting and the requirement for post-operative analgesics and/or anti-emetics were noted. Continuous data are presented as means ± SEM.

Results:

Twenty-three investigators enrolled 212 patients of mean age 33 ± 0.7 yrs. Most patients were ASA physical status I (89%) and 65% were female. Gynecological (43%), orthopaedic (28%) and dental (9%) procedures accounted for the majority. Duration of anaesthesia was 39.4 ± 1.4 min; the length of surgery was 26.1 ± 1.2 min. The initial and total dosages of alfentanil averaged 35.1 ± 0.5 and 44.7 ± 0.9 $ug.kg^{-1}$ respectively. Two-thirds (68%) of patients received at least one supplemental dose of alfentanil; the mean time to the first increment was 16 min. A potent inhalational supplement was administered in 50 cases (24%). Patients requiring inhalation supplement were more likely to be male (36% vs 17%), to weigh more (71 vs 66 kg), and to have undergone longer durations of anaesthesia (51 vs 36 min.) and surgery (36 vs 23 min.) than those receiving nitrous oxide/oxygen alone.

Haemodynamic changes were characterized by decreases in mean SAP, MAP, DAP and HR following alfentanil, intubation and surgical stimulation. These decreases never exceeded 13% below control values. Maximum decreases in blood pressures were observed at one minute post surgical stimulation, followed by rapid recovery to baseline values. Mean HR decreased by 6.5% following intubation and remained 6.5-9.8% below control values for up to 45 minutes.

Mean time from termination of surgery to awakening was 4.9 ± 0.3 min, to extubation 5.2 ± 0.3 min., to response to verbal commands 5.6 ± 0.3 min., and to orientation 11.7 ± 0.7 min. Two patients (0.9%) required naloxone for reversal of respiratory depression. Post-operative analgesics and anti-emetics were administered to 25% and 8% of patients, respectively. Intra-operative awareness was not reported by any patient.

The anaesthetists rated the induction, maintenance and recovery as either "good" or "satisfactory" in at least 95% of cases. "Unsatisfactory" ratings were given for 3% of the inductions, 5% during maintenance, and 1% of the recovery periods. Adverse experiences were reported in 66% of cases; most were considered "non-disturbing". Most frequently noted were hypertension (21%), tachycardia (18%), nausea/vomiting (16%), bradycardia (13%) and movement (11%). Chest wall rigidity occurred in 9 patients (4.2%). Clinically important hypotension was not reported. Adverse experiences considered "disturbing and possibly related to alfentanil" were reported for 11 patients (5.2%), including hypertension (1.4%), nausea (1.4%), vomiting (0.9%), bradycardia (0.5%), movement (0.5%) and chest wall rigidity (0.9%).

Discussion:

This multicentre trial evaluated alfentanil administered in a manner representative of current clinical practice. Alfentanil replaced the need for potent inhalation agents in 76% of procedures. Its use was associated with cardiovascular stability, rapid recovery times, and a low incidence of disturbing side effects.

Table Alfentanil dosage guidelines ($ug.kg^{-1}$)

| Length of Procedure | Initial Dosage | Increments | Total Dosage |
|---|---|---|---|
| ≤ 30 min. | 30 | 2.5 | ≤ 40 |
| 30-60 min. | 30-50 | 5-15 | ≤ 75 |

# A MULTICENTRE* EVALUATION OF ALFENTANIL AS AN ANAESTHETIC ADJUVANT IN SPONTANEOUSLY BREATHING PATIENTS.

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## Introduction

Alfentanil is a new opioid with a potency approximately one tenth that of fentanyl. It has a rapid onset of action with a short terminal half-life.(1) Previous studies indicate that when compared to fentanyl as the narcotic component of a general anaesthetic, its use results in a more rapid recovery.(2) The present multicentre study was designed to evaluate the clinical efficacy and safety of alfentanil as the narcotic component of anaesthesia in non-intubated, spontaneously breathing patients undergoing minor surgical procedures.

## Methods

221 ASA 1, 2 or 3 patients aged 12 to 60 years who were scheduled for minor procedures not requiring endotracheal intubation were studied in 21 centres. All patients were fasted for at least eight hours and were unpremedicated. Droperidol 0.0175 mg/kg was administered intravenously as an antiemetic. Three minutes later, anaesthesia was induced with alfentanil 8-15 ug/kg and thiopental 3-5 mg/kg. Maintenance was with 70% nitrous oxide in oxygen, and further increments of alfentanil (2.5 ug/kg) and thiopental were administered as required. If the anaesthetist considered an inhalational agent to be necessary to maintain anaesthesia, then 0.25 to 0.5% enflurane or isoflurane was utilized.

Peroperative cardiorespiratory measurements included ECG, systolic and diastolic blood pressures and respiratory rate.

Recovery times (taken from the discontinuation of nitrous oxide) included time to open eyes, to respond to verbal commands, and to orientation. PARR scores were assessed using a modification of the Aldrete system. Postoperative side effects were recorded, and an assessment of intraoperative awareness was made.

## Results

41 males and 180 females were studied, of whom 170 were ASA 1, 43 ASA 2 and one was ASA 3. Mean age was 34.2 ± 0.9 yrs and mean weight was 85.8 ± 3.1 kg. 147 patients underwent minor gynaecological procedures, and 34 underwent arthroscopies. The mean duration of anaesthesia was 20.3 ± 1.0 mins.

The mean induction dose of alfentanil was 14.3 ± 0.3 ug/kg and 47.5% of patients received at least one increment, with the mean total dose for all patients being 17.5 ug/kg. The induction dose of thiopental was 4.5 ± 0.1 mg/kg, and 57.5% of patients received at least one additional increment.

Cardiovascular variables remained stable throughout anaesthesia: heart rate decreased by a maximum of 8.6% at 15 minutes, and the mean maximum decrease in SBP was 11.7%, one minute following the administration of thiopental.

Respiratory rate was significantly lower than baseline at all points evaluated, falling from 16.0 breaths/min at baseline to 4.3 at one minute following thiopental.

53 (24%) patients received either enflurane or isoflurane and in this group of patients the mean ASA rating was lower and the mean anaesthetic time was longer (34.3 mins versus 16.0 mins).

The most frequent peroperative side effects considered 'disturbing' by the anaesthetist were movement (15.4%), chest wall rigidity (4.1%), laryngospasm (2.7%) and apnoea (1.8%). The mean recovery times were as follows: awakening 5.1 ± 0.3 mins, response to verbal command 6.5 ± 0.4 mins, and orientation 11.4 ± 0.7 mins. In the PARR, after 10 minutes, 98% of patients were either fully awake or arousable, 95% could breathe deeply and cough freely, and 94% were able to move all extremities. By 20 minutes, all patients were awake or arousable and 99% were able to move voluntarily and to cough freely.

Postoperative side effects included nausea (14.5%) and vomiting (9.5%), but only 4.1% of patients required an antiemetic. There were no instances of awareness during anaesthesia.

The anaesthetist rated 99.6% of inductions as 'good' or 'satisfactory' and one was evaluated as 'unsatisfactory'. Similarly, evaluations of maintenance were 90.7% 'good' or 'satisfactory' and 9.3% 'unsatisfactory'. Recovery was rated 'good' or 'satisfactory' in 99% of cases with two being categorized as 'unsatisfactory'.

## Conclusions

The use of alfentanil as the narcotic component of a thiopental/nitrous oxide anaesthetic for minor surgical procedures provided a satisfactory induction in all but one patient. Cardiovascular dynamics were stable, and maintenance was satisfactory in 91% of patients. Early recovery from anaesthesia was rapid, and later recovery was rated as at least satisfactory in 99% of patients. The most frequent side effects encountered were movement, chest wall rigidity, nausea, vomiting, laryngospasm and apnoea. An antiemetic was administered in only 4.1% of patients.

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* Complete list of participants to be published elsewhere

# INTRACELLULAR ACTION OF THIAMYLAL IN VASCULAR SMOOTH MUSCLE OF CANINE MESENTERIC ARTERY

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Thiobarbiturates have been demonstrated to have vasoconstricting and dilating effects on canine peripheral arteries[1] and rat aortas[2,3] in the range of clinical anesthetic concentrations. The object of this study was to investigate the possible intracellular action of thiamylal in order to clarify the mechanism of vasodilatation induced by thiobarbiturates.

## Methods

Helical strips of dog mesenteric arteries (0.8-1.0 mm, O.D.) were mounted to measure isometric tension. The effect of thiamylal on contractions induced by KCl(20 mM) and norepinephrine (NE, $10^{-5}$ M) were examined in Krebs' bicarbonate solution (Ca 2.5 mM; Sol. I) or in $Ca^{++}$-free Krebs' solution containing 2 mM EGTA (Sol. II) aerated with 5% $CO_2$ / 95% $O_2$ at 37.0 °C. The effect of thiamylal on caffeine (10 mM)-induced contraction was examined in Sol. II, following repeated application of caffeine and $Ca^{++}$ loading.

The effect of thiamylal on strips from small mesenteric arteries (0.4-0.6 mm, O.D.) without endothelium contracted with 20 mM KCl was examined in Sol. I. Then, the strips were exposed to saponin (25 μg/ml) for 20 min in the solution containing 2 mM EGTA (Sol. III) aerated with 100% oxygen to prepare the chemically skinned fibers. After stabilization of the contraction of skinned fibers induced by $Ca^{++}$ ($10^{-5}$ - $10^{-4}$ M), thiamylal was given in the cummulative concentrations.

## Results

The contractions induced by KCl and NE in normal media (Sol. I) and that by NE in Ca-free media (Sol. II) were significantly inhibited by thiamylal, $3x10^{-4}$ to $10^{-3}$ M. Caffeine-induced contraction was significantly inhibited by thiamylal over $10^{-4}$ M.

In KCl-contracted arteries with intact cells, thiamylal, $3x10^{-4}$ to $10^{-3}$ M, induced relaxation (Fig: Open circles), whereas, in Ca-contracted skinned fibers, thiamylal over $10^{-5}$ M induced significant relaxations, $ED_{50}$ being $1.52 \times 10^{-5}$ M (Fig: Closed circles).

## Discussion

It has been suggested by many investigators that barbiturates have Ca channel blocking action in vascular smooth muscles[1-4]. However, the present study revealed that thiamylal inhibits contractions elicited by release of $Ca^{++}$ from intracellular storage sites activated by NE or caffeine as well as contractions induced by $Ca^{++}$ influx through voltage-dependent or receptor-operated channels. Further, it was demonstrated that thiamylal inhibits Ca-induced contraction of skinned fibers, and that concentration of thiamylal necessary to induce relaxation was lower in skinned fibers than in intact cells. These findings suggest that the direct inhibitory effect on the contractile proteins or enhancement of Ca sequestration may contribute to the vasodilatations elicited by thiamylal.

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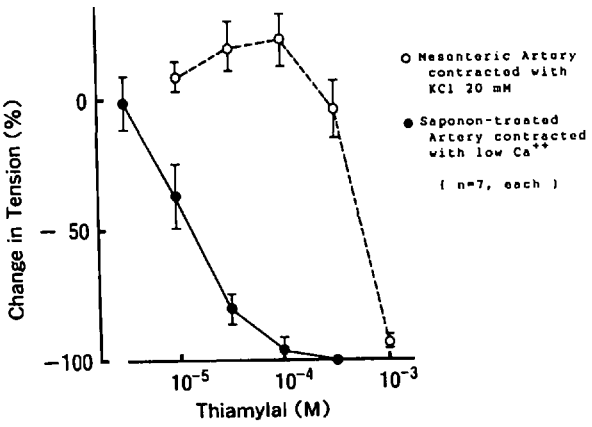


FIG: Change of tension induced by thiamylal. Open circles indicate intact fibers contracted with 20 mM KCl and closed circles indicate skinned fibers contracted with $Ca^{++}$ ($10^{-5}$ to $10^{-4}$M). n=7, each.

# EMERGENCE RESPIRATORY COMPLICATIONS IN CHILDREN: A COMPARISON BETWEEN HALOTHANE AND ISOFLURANE.

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## INTRODUCTION:

Respiratory complications during and following general anaesthesia are significant potential causes of morbidity and mortality, particularly in children, in whom a high ratio of minute ventilation to functional residual capacity, coupled with a high oxygen consumption, rapidly leads to dangerous hypoxaemia.

It has been demonstrated that when halothane and isoflurane are compared with respect to respiratory complications during induction of anaesthesia, isoflurane is associated with a higher incidence of coughing, breath holding, laryngospasm and arterial desaturation [1,2,3,4]. There have been no detailed studies that have compared the incidence of emergence airway phenomena between halothane and isoflurane. We have performed a prospective, randomized and observer blind comparison of the two agents during emergence from anaesthesia.

## METHODS:

Forty patients aged twelve to forty-eight months undergoing minor urologic surgery or inguinal or umbilical hernia repair were studied. Intravenous induction using sodium pentothal 5 mg/kg, atropine 0.02 mg/kg was followed by succinylcholine 1.5 mg/kg to facilitate endotracheal intubation. Anaesthesia was maintained with N20/02 67:33 delivered with a Mapleson D circuit with the patient breathing spontaneously. Patients were randomized to receive either halothane or isoflurane. All patients received a regional block for postoperative analgesia. At the end of the surgical procedure, the patients were given the selected volatile agent at an inspired concentration of 2MAC in 100% 02 for five minutes. They were then turned to the lateral position and extubated. An observer, blinded to the agent used, recorded the occurence of respiratory complications over the next fifteen minutes. A Nellcor N-10 pulse oximeter with paper recorder was placed on a toe for fifteen minutes.

Patients were excluded from the study if they had an abnormal airway, gastroesophageal reflux, chronic respiratory or cardiovascular disease, or if they had had a respiratory tract infection in the previous four weeks.

Age, weight, duration of anaesthesia and lowest SpO2 were compared using the unpaired Student's t-test. Frequency of complications was compared using the chi-squared test.

## RESULTS:

There was no statistically significant difference between the two groups with respect to age, weight, duration of anaesthesia, frequency of respiratory tract complication or lowest SpO2. The decreases in SpO2 which occurred took place during transfer from the operating room to the recovery room.

| | Halothane | Isoflurane | p |
|---|---|---|---|
| n | 20 | 20 | |
| Age (mo) | 27.0 ± 10.6 | 27.5 ± 9.3 | NS |
| Weight (kg) | 13.2 ± 2.4 | 13.4 ± 2.3 | NS |
| Duration (min) | 39.5 ± 16.3 | 36.5 ± 15.0 | NS |
| Coughing | 3 | 0 | NS |
| Breath Holding | 4 | 6 | NS |
| Airway Obst | 5 | 5 | NS |
| Laryngospasm | 0 | 0 | NS |
| No Complications | 11 | 11 | NS |
| Lowest SpO2 | 96.9 ± 1.9 | 96.6 ± 2.0 | NS |

## DISCUSSION

The results of this study indicate that there is no significant advantage of halothane or isoflurane with respect to respiratory tract complications during emergence from anaesthesia in young children with normal respiratory tracts.

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# DETERMINATION OF MAINTENANCE DOSE OF VECURONIUM IN CONTINUOUS INFUSION

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## Introduction

Vecuronium bromide(Vec.) is frequently used in continuous infusion because of non cumulative effect.
In order to maintain a uniform level of surgical relaxation a bolus dose injection followed by infusion of neuromuscular blocker has been used.
At that time frequent and large corrections of the rate of infusion are necessry because of big variances of neuromuscular blocker steady state infusion dose required(1).
The purpose of this study is to examinine (a)how to predict the opitimal maintenace dose of Vec. in continuous infusion and (b)recovery time from the stop the infusion of Vec. to the T25(25% of control twitch height) level, which is optimal stage for the administration of anticholiesterase.

## Method

Thirty four healthy(ASA 1 or 2) adult surgical patients(18-59 years) were studied after giving institutionally approved written informed consent. Premedication included atropin 1.0mg and diazepam 10mg p.o. an hour before operation. After obtaining a control measuring using mechanical twitch responses caused by the stimulation of the ulnar nerve supramaximally(puls width 0.3msec, 0.1HZ). Anesthesia was induced with thiopental (5mg /kg). Ninety seconds following the thiopental injection, each patients received an intravenous dose of Vec. 0.2mg/kg. following the intubation, ventilation was controlled with 2% ethrane and 70% nitrous oxide in oxygen.
Patients recovered to 10% of control twitch height(T10). At which time the Vec. infusion was started at various speed(0.01 -0.1mg/min). The infusion rate was adjusted to maintain 90-95% twitch depression. Measurements were taken of :(a) recovery time(RT) from complete block(T0) to 10% of control twitch height(T10) during the recovery in the first administration of Vec. :(b)mean maintenance doses in continuous infusion. :(c)recovery time from the time of stopping infusion to the T25.
In order to examine the relationship between RT and maintenance dose linear regression was determined between these two parameters.

## Results

Figure 1. shows close relationship between recovery time and maintenance dose(r=-0.86). From this regression line the formula to get the maintenance dose was obtained as follow.

maintenance dose (mg/min)=0.01054-0.0027xRT (min)

RT:Recovery time($T_0$-$T_{25}$)

Quick spontaneous recovery(9.8+1.1, mean+SE min). of neuromuscular transmission was followed after the termination of the infusion.

## Disccusion

The negative good correlation between recovery time and maintenance dose was observed. Rapid recovery from the block after the stop the infusion means that steady state of block was maintained during continuous infusion.
Using this formula it is possible to predict the optimal maitenance dose in continuous infusion of vecuronium.
Carefully observation with the recovery from the block caused by the first bolus injection of Vec. and measured T0-T25 recovery time are essential to determine the maintenance dose to keep 90-95% block in continuous infusion.

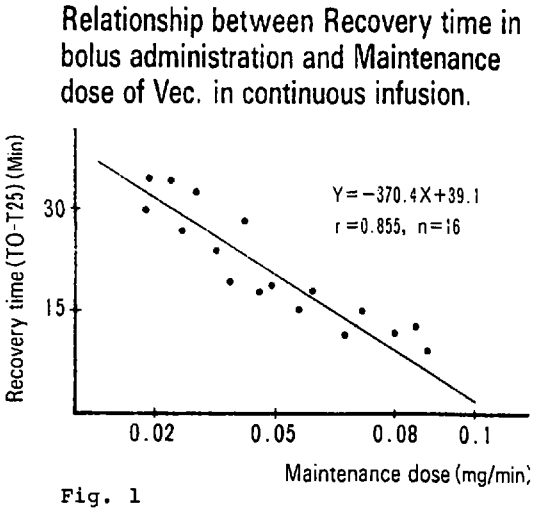


Fig. 1

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# TOTAL INTRAVENOUS ANESTHESIA DURING INTRACRANIAL SURGERY. CONTINUOUS PROPOFOL INFUSION IN COMBINATION WITH EITHER FENTANYL OR SUFENTANIL.

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**INTRODUCTION** In neurosurgery hemodynamic stability and early awakening after anesthesia are essential. Total intravenous anesthesia (TIVA) with propofol and short acting opioids has been used in neurosurgery (1,2), and the results confirmed these two prerequisites. The effects of propofol on intracranial pressure, cerebral hemodynamics and metabolism make it a suitable agent to be used in patients who are at risk for elevated intracranial pressure (3-5). This study was undertaken to compare fentanyl and sufentanil in combination with propofol in TIVA on hemodynamic parameters and on time of awakening after anesthesia.

**METHODS** Twenty two patients,between 20 and 65 years of age scheduled for intracranial surgery for a brain tumor and without cardiovascular disorders, were randomly divided in two groups A and B. On the evening before operation psychomotoric performance of all patients was tested by an orientation test (day and date) (test I), a countdown test (20 to zero) (test II), and an identification test of two coins with the fingers and the eyes closed (test III). All patients were premedicated with 10 mg diazepam orally 90 minutes before induction. Anesthesia was induced in all patients with propofol i.v. 2 mg/kg injected slowly over two minutes, and pavulon 0.1 mg/kg was given to facilitate intubation. Anesthesia was maintained with a continuous infusion of 12 mg/kg/hr for the first 10 minutes; then 9 mg/kg/hr for the next 20 minutes and thereafter 6 mg/kg/hr untill the end of the procedure. Pavulon was given intermittently as necessary. In group A, patients received fentanyl 10 mcg/kg at induction and analgesia was continued with a maintenance dose of 2 mcg/kg/min. Group B patients received sufentanil 1 mcg/kg at induction, and thereafter a continuous infusion of 0.2 mcg/kg/min. Ventilation was with oxygen in air at an $FiO_2$ of 0.30, and adjusted to maintain an end tidal $pCO_2$ between 25 and 28 mm Hg. Towards the end of the procedure the ventilation was adjusted to an end tidal $pCO_2$ of 40 mm Hg. After induction mannitol 1 gr/kg was given intravenously in 30 minutes, and the patient was placed in the head holder. One hour before the cessation of the propofol infusion the opioid infusion was stopped. The end of anesthesia was defined as the end of the propofol infusion.

During the procedure the mean arterial blood pressure (MAP) was continuously recorded and measured through a radial artery catheter. Heart rate (HR) was recorded from the ECG. If MAP increased more than 20% from the pre-induction value, a top-up dose of 4 ml opioid (200 mcg fentanyl or 20 mcg sufentanil) was given. If MAP remained still above 20% of pre-induction value for more than five minutes labetalol was given (never exceeding 200 mgr). After the end of the anesthesia no additional medication was given likely to affect recovery or hemodynamic parameters. The time from cessation of the propofol infusion to spontaneous ventilation was recorded and the patient was extubated. The psychomotoric performance tests were repeated every three minutes untill preoperative values were reached. Statistical comparisons were made using paired and unpaired Students-t-test and analysis of variance as appropiate. P value of $< 0.05$ was considered to be significant.

**RESULTS** The groups A and B were comparable as to age (46.9 ± 12.1 and 40.9 ± 11.4 years), weight (73.3 ± 17.0 and 68.8 ± 12.3 kg), sex ratio and duration of anesthesia (281.6 ± 85.3 and 292.6 ± 89.6 min). The number of additional opioid doses (18 in group A and 17 in group B) and labetalol doses (5 in both groups) did not differ significantly between the groups. The mean MAP and HR are listed in the Table. Between the two groups only MAP at the time of cessation of propofol infusion at the end of anesthesia showed significant difference (Table). Postoperative hypertension, defined by at least two consecutive arterial pressure readings in excess of 190 mmHg systolic and 100 mmHg diastolic, was not seen (6). The duration from the cessation of the propofol infusion to spontaneous ventilation was for group A and B 9.7 ± 5.0 and 8 ± 4.9 min respectively (n.s.). As to the performance of psychomotoric test I for group A it was 28.5 ± 16.4 min and for group B 20.1 ± 10.5 min. For the countdown test 39.0 ± 27.8 and 24.5 ± 11.2 min respectively and for the psychomotoric performance test III 44.5 ± 27.4 and 28.8 ± 15.3 min respectively. None of the tests showed statistical significance for the two groups.

TABLE Results (mean±SD)

| | MAP | | HR | |
|---|---|---|---|---|
| | GROUP A | GROUP B | GROUP A | GROUP B |
| pre-induction | 93.3±7.7 | 94.1±14.4 | 84.5±15.5 | 81.5±22.2 |
| 1 min post intubation | 89.1±11.8 | 92.0±14.2 | 79.1±12.5 | 75.5±13.8 |
| 1 min post head pins | 113.3±15.3** | 106.5±13.1 | 75.4±10.3* | 68.5±11.0* |
| cessation of opioid | 81.6±9.0 | 81.7±8.6** | 79.3±12.2 | 72.8±12.4* |
| cessation of propofol | 90.2±8.3 | 103.1±13.1**+ | 79.5±11.2 | 74.3±10.6 |
| 1 min post extubation | 104.9±18.5 | 109.9±21.4** | 85.9±12.1 | 83.8±12.6 |
| performance test III | 101.6±12.7 | 105.2±19.1* | 88.2±11.6 | 80.3±17.2 |

* $P < 0.05$, ** $P < 0.01$, differences within the group, compared to pre-induction value. + $P < 0.05$ , intergroup differences.

**DISCUSSION** Both techniques of TIVA during intracranial surgery provided satisfactory results as to hemodynamic stability and recovery from anesthesia.

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# SCALP INFILTRATION WITH BUPIVACAINE IN PAEDIATRIC BRAIN SURGERY

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Introduction: Stimulation of the scalp and periosteal nerve endings at craniotomy causes an increase in blood pressure and heart rate.[1] In some cases these effects may endanger the patient especially if there are cerebrovascular anomalies, vascular tumors or increased intracranial pressure.[2] By infiltrating the scalp with a local anaesthetic in order to block nerve endings one would anticipate the haemodynamic response could be prevented or at least diminished. A previous study of adults using a single dose of bupivacaine found a significant decrease in expected haemodynamic response.[1]

Our intent is to determine the efficacy and safety of bupivacaine scalp injections in children. We will attempt to establish the optimal dose that will blunt the haemodynamic response while ensuring this dose is below the toxic level.[3]

Methods: With ethics committee approval and parental consent, 17 patients have been studied in this ongoing prospective trial. Patients under 2 years or with previous scalp incision were excluded. Eligible patients were assigned randomly to one of three groups. Controls were infiltrated with 1:400,000 epinephrine (E) in saline in keeping with standard neurosurgical technique at this institution. Study groups received either a 0.125% or 0.25% solution of bupivacaine with 1:400,000 epinephrine. The anaesthetist was unaware of the infiltrate solution. Premedication was not given. Anaesthesia was induced with thiopental 5 mg/kg, fentanyl 5 µg/kg and pancuronium bromide 0.1 mg/kg. Another 2 mg/kg thiopental was given just prior to intubation. Anaesthesia was maintained using 30% $O_2$, 70% $N_2O$ and 1% isoflurane. End-tidal $pCO_2$ was maintained at 30 mm Hg. An arterial line was inserted for blood pressure monitoring and blood sampling. Up to 1 cc of assigned solution was injected along the proposed incision line by the neurosurgeon. Five minutes was allowed to elapse between scalp infiltration and incision.

The following six events were used for comparison: (1) pre-scalp infiltration (baseline heart rate and blood pressure), (2) post-scalp infiltration, (3) post-scalp incision, (4) scalp flap reflection, (5) craniotomy, and (6) dural incision. Heart rate and mean arterial pressure (MAP) were recorded for each event for periods ranging from 40 to 250 seconds (100 ± 35, mean ± SD). Sustained hypertension (> 20%) was treated with additional thiopental and/or isoflurane. Arterial samples were taken at 5, 10, 15, 20, 30, 60 and 120 minutes for bupivacaine levels. Following extraction of the plasma, bupivacaine was measured by high performance liquid chromatography (HPLC).[4]

Statistical significance ($p < 0.05$) was determined with one-way ANOVA and Student-Neuman-Keuls for multiple comparison.

Results: Demographic data are summarized in the Table. The infiltrate solution did not cause a significant change in MAP or heart rate despite the presence of epinephrine. Heart rates did not change significantly in the three groups during the study. MAP increased significantly during incision (event 3) in the control group compared with the group receiving 0.25% bupivacaine. Although the average mean blood pressure remained higher in the control group during scalp reflection (event 4) and craniotomy (event 5) than either marcaine group the difference was not significant. Sustained hypertension (> 20%) requiring treatment occurred in 50, 33 and 26% of the control, 0.125 and 0.25% bupivacaine groups, respectively. Peak measured bupivacaine concentrations occurred 5 and 10 minutes after infiltration. The highest blood level measured was 1.06 µg/ml. Mean peak bupivacaine levels were 0.36 ± 0.32 µg/ml and 0.4 ± 0.32 µg/ml in the 0.125% and 0.25% groups, respectively. No adverse reactions to infiltration were noted.

Discussion: Preliminary results suggest that scalp infiltration with marcaine is a useful and safe addition to general anaesthesia in paediatric brain surgery. The blood pressure response to scalp incision was significantly blunted by its use and fewer patients required treatment for sustained blood pressure. The seizure threshold of bupivacaine in children is not known. The adult value is thought to be 4 µg/ml.[3] Levels measured in this study were well below this.

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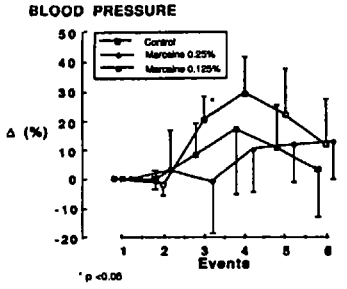
TABLE

| | CONTROL (saline + 1:400,000 EPINEPHRINE) | 0.125% BUPIVACAINE + 1:400,000 EPINEPHRINE | 0.25% BUPIVACAINE + 1:400,000 EPINEPHRINE) |
|---|---|---|---|
| # of Patients | 4 | 6 | 7 |
| Male:Female | 4:0 | 1:3 | 4:3 |
| Age (yrs)* | 11.2±6.1 | 9.5±4.7 | 6.5±3.6 |
| Weight (kg)* | 43.0±11.6 | 34.8±14.1 | 25.0±15.0 |
| Volume Injected (ml/kg)* | 0.5±0.31 | 0.6±0.26 | 0.8±0.35 |

*Data means ± SD

FIGURE



## CORTICOSTEROIDS DO NOT INHIBIT ACUTE PULMONARY RESPONSE TO FAT EMBOLISM

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INTRODUCTION:

High dose corticosteroid therapy has been advocated in the therapy of post-traumatic fat embolism[1]. Particulate fat and marrow microembolism of the lung has been demonstrated during cemented arthroplasty (CA) at the time of cement and prosthesis insertion. The resulting pulmonary dysfunction is characterized by elevated pulmonary artery pressure (PAP), increased intrapulmonary shunt fraction ($\dot{Q}_s/\dot{Q}_t$) associated with hypoxemia, and increased levels of arachidonic acid metabolites (6-keto prostaglandin $F_{1\alpha}$ and thromboxane $B_2$). The purpose of this study was to determine if pre-operative corticosteroid therapy attenuates the acute pulmonary response to fat embolism after CA.

METHODS:

Twelve anaesthetized mongrel dogs were studied before and after bilateral CA[2]. Arterial (BP), right atrial (RA), left atrial (LA), and pulmonary artery (PA) pressures were continuously recorded. Arterial and mixed venous blood samples were obtained and $PO_2$ was measured after reaming of the intramedullary canals and at 1, 5, 15, 30 and 60 minutes after CA. The levels of 6 keto-prostaglandin $F_{1\alpha}$ (6-keto $PGF_{1\alpha}$) and thromboxane $B_2$ ($TxB_2$) were determined by radio-immunoassay in arterial and mixed venous blood samples after reaming and at 1, 5, 15, and 30 minutes after CA. Cardiac output was also measured 5, 15, 30, and 60 minutes. Pulmonary vascular resistance (PVR) was then calculated.

One hour after CA the animals were killed by injecting KCl intravenously. The lungs were excised and the fat-containing emboli in the lungs were assessed using quantitative morphometry. This technique permits an objective assessment of the degree of fat embolism occurring in each animal and between groups.

Six animals served as controls and six dogs were pre-treated with methylprednisolone sodium succinate (30 mg/kg) before CA. Data are presented as mean values ± one standard deviation. Differences from baseline values within groups were analyzed with a repeated measures analysis of variance. When a significant F ratio was found Dunnett's test was used to detect changes from control and Tukey's test was used to evaluate other differences. Differences between groups were compared using analysis of variance.

RESULTS:

There was no significant difference between control and steroid pre-treated groups in the number of fat emboli found in the lungs on quantitative morphometry.

The increase in PAP in the control group one minute after cemented arthroplasty (18.4 ± 13.9 mm Hg) was not significantly different from that in the steroid-treated group (17.8 ± 7.3 mm Hg). Within 5 minutes of CA the PVR increased from 257 ± 93 to 715 ± 340 dyne·sec·cm$^{-5}$ ($p < 0.001$) in the control group. In the steroid pre-treated group, PVR increased from 297 ± 112 to 616 ± 138 dyne·sec·cm$^{-5}$ ($p < 0.001$). There were no significant differences between groups in the changes of hemodynamic or gas exchange measurements from baseline ($P_aO_2$ or $\dot{Q}_s/\dot{Q}_t$) at any time period.

The plasma level of 6-keto $PGF_{1\alpha}$ and $TxB_2$ increased significantly in both groups within 5 minutes of CA but no difference was noted between groups at any time. The increase in transpulmonary 6-keto $PGF_{1\alpha}$ (0.39 ± 0.24 ng/ml in controls and 0.38 ± 0.31 ng/ml in steroid-treated dogs) were both significant ($p < 0.0001$) one minute after CA. However, no significant difference in the transpulmonary gradient of 6-keto $PGF_{1\alpha}$ was detected between groups. Although the arterial $TxB_2$ level was significantly increased one minute after CA in both groups, no significant increase in the transpulmonary thromboxane $B_2$ gradient was found at any measurement time in either group.

DISCUSSION:

Methylprednisolone (30 mg/kg) given prior to CA did not prevent or attenuate the acute cardiopulmonary changes after fat and marrow embolism following CA in this animal model. There was no evidence of a steroid-mediated reduction of pulmonary endothelial cell injury which would have been reflected by an attenuated increase of 6-keto $PGF_{1\alpha}$ in the steroid treated dogs. In particular, the increased transpulmonary gradient of 6-keto $PGF_{1\alpha}$, reflected the acute endothelial cell injury. This was unaltered by steroid prophylaxis. Although steroids may alter the lungs' response to fat-induced embolic injury after 24-48 hours[1], these data suggest that the immediate hemodynamic and gas exchange abnormalities within 60 minutes of the injury are not altered by steroid pre-treatment in this model.

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## INTRAOPERATIVE ANAPHYLAXIS TO LATEX: AN IDENTIFIABLE POPULATION AT RISK

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Introduction: Latex has recently been incriminated as the etiologic agent in a spectrum of IgE-mediated allergic reactions ranging from urticaria and rhinitis to asthma and anaphylaxis.[1-3] Latex-mediated intraoperative anaphylaxis may represent a new or previously unrecognized phenomenon.[4,5] Individuals with a history of occupational exposure to latex products (physicians, nurses) appear to be at increased risk when compared to the general population.[6] We believe that certain patients exposed to latex products as part of their routine daily care represent another population at increased risk for life-threatening latex-mediated intraoperative allergic reactions.

Methods: All patients who experienced perioperative allergic reactions at this institution during the period July 1987 to September 1989 were evaluated prospectively. The hospital records from July 1985 to July 1987 were also reviewed and one additional patient was identified who had experienced an intraoperative anaphylactic reaction. This patient was subsequently investigated as described below. The nature and onset of all allergic reactions were documented. The medical and atopic histories of all patients were reviewed as well as any history of sensitivity to various materials including latex. Six to eight weeks after the intraoperative allergic reaction skin prick testing (SPT) and intradermal testing were performed to anaesthetic agents and antibiotics as indicated, and SPT was performed to common inhalant allergens and latex antigen. The control group for latex SPT consisted of 12 healthy non-atopic adults and 12 children with an atopic history. Serologic tests included measurement of total IgE levels and radioallergosorbent (RAST) testing for latex sensitivity. The control group for RAST testing consisted of 12 ragweed-sensitive patients.

Statistical analysis of the RAST test results was performed with the unpaired t-test and $p < 0.05$ was considered significant.

Results: Fifteen patients experienced 19 episodes of perioperative allergic reactions. All patients (6 females and 9 males ranging in age from 2 to 15 years) had a diagnosis of either spina bifida with neurogenic bladder and bowel or multiple congenital urologic abnormalities. All patients had a history of daily catheterizations of the bladder using rubber catheters and/or regular faecal disimpaction with latex surgical gloves. An atopic history was not a significant feature of the group (4/15), however 7 patients were found to have a local contact sensitivity to latex products as manifested by eczema, urticaria or angioedema on contact with rubber gloves or toy balloons. All patients had undergone from 2 to 26 previous uneventful operative procedures prior to their first allergic reaction. Eleven of the nineteen reactions were anaphylactic and life-threatening in nature. Eight reactions were not life-threatening although bronchospasm or hypotension with or without erythema and urticaria were present. All reactions were delayed in onset occurring from 40 to 290 minutes after induction of anaesthesia. There was no obvious temporal relationship between the allergic event and drug administration. There were no deaths in our series.

All patients had negative SPT and intradermal tests to anaesthetic agents and antibiotics. Of the four atopic patients in the series, 3 had positive SPT to the common inhalant allergens. SPT to latex antigen were positive in all patients in this series and were negative in all members of the SPT control group. Total IgE levels were elevated in two atopic patients and five non-atopic patients in this series. Results of the RAST test for latex sensitization in our patient population ($29.9 \pm 14.6\%$, range 8.85 - 59%) were significantly greater than the RAST control group ($4.11 \pm 1.95\%$, range 2.3 - 9.4%) with $p < 0.001$.

Discussion: This study identifies a group of paediatric patients who appear to be at high risk for the development of intraoperative allergic reactions to latex including anaphylaxis. All patients had a history of exposure to latex during their routine dysfunctional bladder and/or bowel care. The allergic reaction is characterized by delayed onset after induction of anaesthesia with a high frequency of life-threatening anaphylaxis. We recommend a high index of suspicion for latex sensitivity in this group of patients with implications for appropriate perioperative prophylaxis as well as early recognition and management of allergic sequelae intraoperatively.

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# UNRESTRICTED ORAL FLUID UNTIL THREE HOURS PREOPERATIVELY: EFFECT ON GASTRIC FLUID VOLUME AND PH.

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Elective patients commonly fast from midnight, irrespective of their scheduled time of surgery. This applies to liquids as well as solids, although the former normally pass through the stomach within two hours.[1] Patients may fast for 15 hr or more for no benefit, because their gastric fluid volume and pH are not significantly different from those in patients who drink 150 ml 2-3 hr preoperatively.[2,3] On the basis of these findings our department's fasting guidelines for elective inpatients were modified. No solid food is allowed on the day of surgery but unrestricted clear oral fluid is permitted until three hours before the scheduled time of surgery. This follow-up study was undertaken to determine whether the new guidelines affected gastric fluid volume or pH at the time of surgery.

## Methods

One hundred and one elective inpatients aged 18-65 yr, ASA physical status I or II with no upper gastrointestinal disorder, were studied. Their age, sex, weight, smoking habit, and time and volume of last fluid ingestion were recorded. Clear fluids included water, apple juice, tea or coffee with cream and sugar according to taste, and jello. Patients received either no premedication, or oral diazepam 10-15 mg one hour preoperatively. Within five minutes following induction of anaesthesia an 18 Salem sump tube was passed into the stomach and all available fluid aspirated into a 60 ml syringe while an assistant massaged the patient's epigastrium. Volume was recorded and pH was measured using a Corning 150 meter calibrated at pH 4 and 7. Patients were retrospectively assigned to one of three groups according to duration of fluid fast: less than 5 hr; 5-8 hr; NPO from midnight. Results were analysed using analysis of variance, and values of $p < 0.05$ were considered statistically significant.

## Results

The groups were comparable with respect to age, weight, and other demographic data. There were no statistically significant differences between groups for either volume or pH (Table), nor was there a correlation within groups between volume of fluid ingested and gastric fluid volume at the time of sampling. The majority of patients in the NPO group were either scheduled for surgery before 1030 h or they did not wish to drink.

TABLE: Gastric fluid volume and pH.

| group | n | volume | pH |
|---|---|---|---|
| <5 hr | 38 | 27 (0-75) | 1.6 (0.9-7.0) |
| 5-8 hr | 21 | 32 (2-72) | 1.5 (1.1-2.8) |
| NPO | 42 | 24 (0-70) | 1.7 (0.9-4.9) |

Values are given as mean (range)

## Discussion

There is a wide range of gastric fluid volumes and pH in healthy elective patients. These appear to be independent of volume of fluid ingested and of duration of fluid fast, provided this exceeds two hours. Because gastric emptying times vary for different types of solid food we recommend that no solids should be ingested on the day of surgery. However, unrestricted clear fluids may be permitted until three hours before the scheduled time of surgery.

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DAY CARE TONSILLECTOMY: A STUDY. G. O'Connor, FRCPC, K. Riding, FRCSC, B. Laird, RN, S. Riou, RN, D.J. Steward, FRCPC, Departments of Anaesthesia, Otolaryngology and Nursing, British Columbia's Children's Hospital and the University of British Columbia.

INTRODUCTION

Day Care surgery has become widely accepted as a safe alternative to inpatient care in up to 70% of cases at a Children's Hospital. It has the advantage of minimizing the psychological trauma of hospitalization, decreasing noscomial infection, is cost effective and frees up hospital beds.

After carrying out a retrospective review of T's and T's & A's between April 1986 to March 1987 to assess the incidence of primary and secondary post-operative haemorrhage. A prospective study was initiated together with the introduction of a protocol for Day Care T&A surgery.

METHOD

50 patients (21 female and 29 male) were scheduled and two certified E.N.T. surgeons performed the operations. The following criteria were adhered to:

Criteria For Selection of Suitable Candidates:

1. The patient must have adequate accommodation less than 50 km from the Hospital and arrange for suitable transportation.
2. There should be no history of central sleep apnea.
3. There should be no bleeding tendency.
4. There should be no major or chronic medical problem (i.e. diabetes, uncontrolled seizure disorder, severe asthmatics).
5. Surgery should be not less than four (4) weeks after an attack of tonsillitis or upper respiratory infection.
6. there should be no aspirin containing medication taken for two (2) weeks prior to surgery.
7. Children with seasonal allergies are unsuitable Day Care candidates during their susceptible periods.[1]
8. there must be a positive parental attitude toward assuming responsibilities for caring for their child. Parents speak English or have translator present throughout the stay in the Day Care Unit.
9. There should be no evidence of severe respiratory infection in the family.
10. Smokers are not suitable Day Care candidates.

Anaesthetic Protocol For Day Care Tonsillectomy/ Adenoidectomy

1. No premedication
2. Avoidance of long acting agents: - Diazepam - Droperidol (exception: may be given as an anti-emetic dose not more than 70 mc/kg)
3. Demerol IM (1.0 - 1.5 mgm/kg) to be given in the Operating Room near the end of the procedure.
4. I.V. regime for Tonsils - Ringers Lactate calculated 5 hour deficit + 3 hour maintenance to be given over 3 hours.
5. An initial dose of Tylenol given in the Recovery room.

Criteria for Discharge of Patients for Day Care Tonsillectomy/Adenoidectomy

1. The patient has spent a minimum of three (3) hours for adenoidectomy and six (6) hours for tonsillectomy in hospital since arrival in Recovery Room.
2. The patient's condition has been assessed and patient discharged by an anaesthetist from Recovery room.
3. The patient's throat has been checked for post-operative bleeding by the E.N.T. staff or resident.
4. The patient is awake and alert.
5. The patient's vital signs, temperature, pulse, respiration are within normal range for age and emotional status.
6. The patient is mobile within normal range for that individual.
7. The patient is drinking and tolerating fluids.
8. The patient's pain is relieved by oral medication.
9. The parents have received written instructions and the nurse is satisfied they understand and are able to carry out instructions.

Two follow-up telephone calls were to be made by the Day Care staff. The first call one day post-op and the second 10-14 days post-op. Follow-up questionaires were to be completed and data collected to evaluate the care.

RESULTS

- 47 patients were discharged the same day - 1 admitted for vomiting, 1 admitted for bleeding, 1 admitted for poor hydration (Downs Syndrome)
- 1st day post-op telephone follow-up - 46 out of 47 contacted. Dizziness (24%), Drowsiness (41%), Vomiting (23%), Pain in throat (95%), Pain relieved by oral medication (100%), Ability to drink - good (65%), fair (30%), poor (5%), Bleeding from Mouth (Blood tinged mucus) 9%.
- 10th day post-op follow-up, 46 out of 47 contacted. Parents felt comfortable caring for child at home (100%), Cases returned to Hospital (0%), Parents called for Advice (24%), Minor bleeding after 1st day - minimal.

In the group of patients discharged the same day there was no major problem with bleeding or vomiting and no patients returned to the hospital. All the patients admitted overnight were discharged the following day and Downs Syndrome was added to the list for non-eligibility.

CONCLUSIONS

1. Day Care T&A surgery is acceptable and safe.
2. I.V. fluid loading may be advantageous in minimizing immediate post-operative minor morbidity.
3. A preplanned detailed protocol for introduction of new procedures to a Day Care Unit is very advantageous.

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# Gastric Emptying After Clear Fluids

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INTRODUCTION: Outpatient anesthesia is becoming increasingly important in clinical practice in response to recent DRG and cost containment pressures. When these patients do not comply with the specific instructions regarding fasting and ingest fluids pre-operatively, the anesthesiologist is put in dilemma to decide on a safe time for induction of general anesthesia. Whereas the guidelines for fasting after solid food are 8 hours, it is not clear what a safe fasting period is after fluid ingestion. We therefore conducted a prospective randomized study on volunteers to assess gastric emptying time following ingestion of water, black coffee and orange juice.

METHODS: After institutional approval and informed consent, 30 healthy volunteers (ASA I) were included in the study. Volunteers with gastric problems, history of alcoholism or smoking were not included in the study. Following overnight fasting, a 18F Salem sump (Argyle) naso-gastric (NG) tube was inserted through the nostril after application of 2% lidocaine viscus. The position of the NG tube in the stomach was confirmed by auscultation over the stomach while air was inserted through the tube with a syringe. Using a 60cc Toumy syringe, gastric contents were aspirated and measured for pH (with an Ohio PHH-44 meter) and volume (base value). The gastric contents were reinserted through NG tube into the stomach. Volunteers were randomly divided into 3 groups. Group I received 240cc of water, group II received 240cc of black coffee and group III received 240cc of orange juice orally. Following this, the gastric contents were aspirated, the volume and pH were measured and the contents were reinserted into the stomach through the NG tube at 30 minute intervals until gastric volume returned to base volume or less than 25cc. Statistical anlysis was performed with ANOVA test and p value less than 0.05 was considered statistically significant.

RESULTS: The groups did not differ significantly with respect to age, height, weight or duration of fasting (see table 1). After overnight fasting mean gastric volumes and pH were not significantly different in the 3 groups (table 2, figure 1). Following oral intake, all patients had gastric volumes less than baseline or 25cc in less than 2 hours (figure 1).

DISCUSSION: Pulmonary aspiration of gastric contents during anesthesia is a significant cause of morbidity and mortality (1). The severity of the pulmonary damage is related to the volume (>25cc) and the pH (<2.5) of gastric contents aspirated (2). With an increasing number of outpatient procedures, it is not uncommon to find non-compliant patients to fasting. After carefully assessing the time it takes to empty the stomach of water, black coffee and orange juice by estimation of gastric volume and pH every 30 minutes in healthy volunteers, we determined that all of the 30 volunteers studied had empty stomach (Vol. < 25cc) within 2 hours. It would therefore seem appropriate that in cases where patients have ingested a moderate amount of fluids, it would be safe to conduct general anesthesia after 2 hours in otherwise healthy ambulatory surgical patients. This will allow greater flexibility in the management of ambulatory patients who have ingested commonly utilized morning drinks. We would caution that coffee with milk was not included in the study because milk can solidify in the stomach. The post-ingestion pH was lower than base value but since both were below 2.5, we believe this would not pose added risk.

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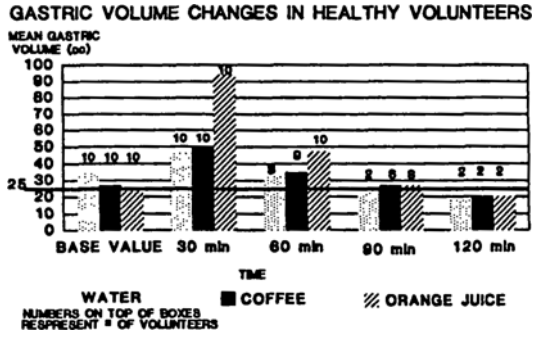
Table I: Comparison of Age, Weight, Height and Duration of Fasting

| | Group I Water | Group II Coffee | Group III Orange Juice | Statistical Significance |
|---|---|---|---|---|
| 1 Age (yrs) | 30.7 ± 9.9 | 30.4 ± 9.9 | 41.5 ± 14.4 | N.S. |
| 2 Height (inch) | 67.8 ± 4.3 | 66.7 ± 2.2 | 67.6 ± 2.4 | N.S. |
| 3 Weight (lb) | 161.6 ± 36.4 | 151 ± 30.2 | 160.5 ± 24.9 | N.S. |
| 4 Sex Male | 7 | 6 | 6 | |
| Female | 3 | 4 | 4 | |
| 5 Fasting time (hrs.) | 11.7 ± 1.1 | 12.3 ± 1.8 | 11.7 ± 1.6 | N.S. |

Table 2: Comparison of Mean Gastric pH

| Time Interval | Group I: Water | Group II: Coffee | Group III:OrangeJuice |
|---|---|---|---|
| Base Value | 2.45±1.7 | 2.07±1.0 | 2.13±1.2 |
| 30 min. | 2.05±1.5 | 1.87±0.9 | 2.49±0.8 |
| 60 min. | 1.58±0.2 | 2.03±1.7 | 1.69±0.6 |
| 90 min. | 1.45±0.2 | 1.34±0.1 | 1.51±0.4 |
| 120 min. | 1.31±0.2 | 1.25±0.2 | 1.34±0.5 |

Figure 1



# HYPOXEMIA ON DISCHARGE FROM THE POST ANAESTHETIC RECOVERY ROOM.

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Introduction: Since the introduction of pulse oximetry, studies have shown that a significant number of patients have decreased arterial oxygen saturation ($S_aO_2$ less than 90%) during transport from the Operating Room to the Post Anaesthetic Recovery Room (PARR)[1] and during their stay in the PARR.[2] Recently, the Post Anaesthetic Recovery Score was found to correlate poorly with hypoxemic episodes in the PARR.[3] To determine the incidence of decreased $S_aO_2$ and the possible related risk factors, we studied 262 patients at the time of discharge from the PARR.

Methods: After obtaining institutional approval, a non-randomized, prospective, observational study involving patients undergoing a variety of surgical procedures was performed. $S_aO_2$ was measured non-invasively with a Nellcor 100 pulse oximeter and a standard adult finger probe in the holding area outside the PARR after the patient was discharged from the PARR. The $S_aO_2$ reading was considered valid if the pulse was within 5 beats per minute of a simultaneously obtained manual pulse. The anaesthetist was notified of any patients with $S_aO_2$ less than 90% and treatment initiated.

The demographic data collected included age, weight, height and smoking habit. Other information included ASA status, type of anaesthesia, use of endotracheal tube (ETT) during anaesthesia, premedication, intra-operative medications (narcotics, Benodiazapines, neuromuscular blocking agnets) and narcotics received in the PARR. Type and length of surgery, patient position during surgery, length of PARR stay and the highest post anaesthetic recovery score were also recorded.

Statistical analysis was performed using CHI-SQUARE statistics to analyze the potential risk factors associated with hypoxemia at the time of discharge from the Recovery Room, using contingency tables. Because multiple statistical testing was required the Alpha level (P) for each test was necessarily decreased ($P < 0.001$). In order to control for different variables, cross-tabulation was carried out to analyze associations between the different variables

Results: Of the 262 patients followed out of the Recovery Room, 11 patients had incomplete data collected regarding either height, weight or smoking habit and were, therefore, excluded. The incidence of hypoxemia in the 11 patients excluded was 9.09% (1 out of 11) which was comparable to the overall incidence of hypoxemia of 9.98% (25 out of 251). All patients had post-anaesthetic scores of 7 or greater (maximum 8). Factors found to be significantly associated with hypoxemia at the time of leaving the Recovery Room were increased body mass index (B.M.I. greater than 28), use of an ETT during anaesthesia and ASA status greater than or equal to 3 ($P < 0.001$ for all three). During cross-tabulation significant association was found between general anaesthesia and the use of an ETT ($P < 0.001$), between the use of an ETT and age greater than 70, ($P < 0.001$) and ASA status and increased body mass index ($P < 0.001$). A trend of association between ASA status and age was also noted (P equalled 0.0012).

**Table 1**

**FACTORS ASSOCIATED WITH HYPOXEMIA ON DISCHARGE FROM PARR**

i) **Obesity - BMI $>28$ ($P < 0.001$)**
ii) **ETT Anaesthesia ($P < 0.001$)**
iii) **ASA $\geq 3$ ($P < 0.001$)**

**NOT ASSOCIATED**

i) **Age**
ii) **Gender**
iii) **Site of surgery**
iv) **Smoking**

Discussion: The incidence of decreased $S_aO_2$ at the time of discharge from the PARR is nearly 10%. These patients had no clinical symptoms and had normal post-anaesthetic recovery scores. The patients at high risk for developing hypoxemia at the time of discharge from the PARR include the patients who, have a body mass index greater than 28, require endotracheal intubation during anaesthesia, and those with an ASA status greater than or equal to 3.

We recommend, therefore, that pulse oximetry be used as an adjunct in patient assessment prior to discharge from the PARR.

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# NITROGEN INSUFFLATION DECREASES PVC ENDOTRACHEAL TUBE CUFF FLAMMABILITY DURING $CO_2$ LASER SURGERY

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Introduction: The precision, intrinsic hemostatic properties and power of the laser have led to its wide use in surgery. Its employment during airway surgery, however, has been associated with catastrophic fires. In fact, in a survey of complications of laser airway surgery, tracheal tube fires have been shown to be the most common serious complication.[1] The shafts of combustible endotracheal tubes can be protected from the laser by techniques such as foil wrapping,[2] however the cuffs remain at risk for combustion since they cannot be protected with foil. We evaluated the use of nitrogen insufflation to protect tracheal tube cuffs from the $CO_2$ laser.

Methods: A LaserSonics (Santa Clara, CA, USA) model LS880 $CO_2$ laser and Zeiss (W. Germany) operating microscope with a "joy stick" micromanipulator and 400 mm lens were used. The laser was set to 3 watts in the continuous mode of operation with a beam diameter of 0.68 mm. Mallinckrodt (Glens Falls, NY, USA) size 7.5 ID polyvinylchloride "Hi-Lo" endotracheal tubes were studied. A 20 inch Abbott (North Chicago, IL, USA) no. 4429 intravenous extension set was used as a source of tubing which was placed alongside the endotracheal tube down to a level just above the endotracheal tube cuff. The tubing had an ID of 2 mm. Venture (Rockland, MA, USA) 1 mil copper foil tape was used to wrap the intravenous tubing to the endotracheal tube in an overlapping spiral manner using a single piece of tape. Care was taken so that there were no gaps in the taping. This tape has previously been shown to provide excellent protection of polyvinylchloride endotracheal tubes from the $CO_2$ laser.[2] The wrapped tracheal tube was placed in a 100 cc Pyrex (Corning, NY, USA) graduated cylinder with a 25 mm ID which served as a "mock trachea." In each case, 2 L/min of oxygen were delivered to the endotracheal tube via a circle airway system and anesthesia machine with a closed pop off valve. The cuff was then inflated with 20 cc of air and the pop off valve of tth anesthesia machine was adjusted to maintain a system pressure of 15 cm $H_2O$. The laser was carefully aimed down the "mock trachea' at the cuff. Two groups of five such tubes were studied by activating the laser until a fire was noted or 1 min of laser fire had elapsed. In group 1, five of the modified tracheal tubes were studied by flowing 10 L/min of nitrogen through the intravenous tubing taped to the tracheal tube. Using the mass spectrometer, the concentration of oxygen was noted to be $<3\%$ just above the endotracheal tube cuffs prior to firing the laser. In group II, the modified tubes had no gases delivered via the intravenous tubing. The incidence of combustion of the two groups was compared using the Mann-Whitney U-test.

Results: All the endotracheal tube cuffs in both groups of tracheal tubes were perforated after $\leq 0.5$ sec of laser fire. In group I, combustion was observed in only one out of the five endotracheal tubes studied. It occurred after 5.56 sec of laser fire. In group II, combustion was noted in all five of the modified endotracheal tubes studied. The time to combustion was $6.68 \pm 3.65$ (Mean$\pm$S.D.) sec in group II. The incidence of tracheal tube fires was significantly different when the two groups were compared ($P<0.05$). In group I, the concentration of oxygen noted at the cuff after its puncture by the laser was approximately 16% as measured with a mass spectrometer.

Discussion: The laser has become an important surgical tool because of its precision and power. In addition, laser surgery is usually associated with reduced postoperative pain and edema and has an intrinsic hemostatic effect. The high energy density of the laser and its proximity to combustible tracheal tubes during airway surgery have resulted in serious airway fires. These fires have been reported to cause extensive burns. The shafts of combustible tracheal tubes can be protected from the $CO_2$ laser operating at high power by techniques such as wrapping them with the Venture copper or 3M no. 425 aluminum foil tapes.[2] The cuff, however, remains unprotected.

Undersized tracheal tubes are usually employed during airway surgery to improve the surgeon's exposure. This requires the use of a large cuff to make an adequate seal with the trachea. The cuff presents a large target to the laser. Furthermore, the alignment of the laser with the operating laryngoscope predisposes to its being aimed down the trachea at the tracheal tube cuff especially during laryngeal procedures.

LeJeune et. have suggested that tracheal tube cuffs can be protected from the $CO_2$ laser by filling them with saline.[3] This has been confirmed experimentally.[4] The saline acts as a "built-in fire" extinguisher. A small amount of dye such as methylene blue should be added to the saline so that cuff perforation will signal the surgeon to stop the laser. Tracheal tube cuffs can also be protected by packing them off with wet pledgets. The insertion of the pledgets is however, time consuming and they may be difficult to retrieve. Furthermore, they must be kept wet or they will be combustible.

The present study shows that nitrogen insufflation via a catheter aligned next to the tracheal tube significantly decreases the incidence of $CO_2$ laser induced tracheal tube cuff fires as compared to identical modified tracheal tubes without nitrogen insufflation. This technique, when combined with a smoke evacuator will keep the surgical field and operating room free of the products of combustion. The nitrogen insufflation catheter is easily attached to the tracheal tube with the same foil wrap as is used for protection of the tracheal tube's shaft from the $CO_2$ laser. This technique reduced the concentration of oxygen at the trachea tube cuff to <3% as determined by mass spectrometry and prevented laser induced combustion in 4 out of the 5 trachea tubes studied.

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## SUPPLEMENTAL OXYGEN DURING CAESAREAN SECTION UNDER EPIDURAL ANAESTHESIA: NASAL PRONGS VS FACE MASK

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INTRODUCTION It is current practice during epidural anaesthesia (EA) for caesarean section (C/S) to provide the mother with a source of supplemental oxygen ($O_2$) until delivery in order to provide more $O_2$ to the baby (1). This is done either with nasal prongs (NP) or by face mask (FM). The purpose of this study is to determine whether there is any difference between the two methods when fetal oxygenation is examined. In addition, we wished to determine which method is more comfortable for the mother.

METHODS Informed consent was obtained from forty healthy (ASA 1 or 2) patients presenting for elective C/S under EA. Patients were randomly assigned to one of 2 groups: Patients in Group I received NP with 4 litres/minute of $O_2$ and those in group II received FM with 8 litres/minute of $O_2$. Oxygen therapy was initiated after the test dose and continued until after delivery. All patients received EA using incremental doses of carbonated lidocaine with 5 ug/ml epinephrine to a T4 level of analgesia. All patients were supine with the uterus tilted to the left. Parturients were monitored continuously with an ECG and pulse oximeter. Maternal blood pressure was taken every 2 minutes prior to delivery with an automatic blood pressure cuff.

The following data were collected: Maternal height, weight, and gestational age, Fetal presentation, Maternal $O_2$ saturation before $O_2$ therapy, maternal $O_2$ saturation at delivery with $O_2$ therapy, uterine incision-delivery time, umbilical vein (UV) and artery $O_2$ saturation, pH, and $pCO_2$ and Apgar scores. Maternal hypotension was considered to be present if a blood pressure of 100 systolic or a drop in BP of more than 20% occurred. At the end of the procedure, the mother was asked, in a standard fashion, whether or not the $O_2$ device was comfortable.

The primary outcome measurement compared between the two groups was the UV $O_2$ saturation since this is a measure of $O_2$ delivery to the fetus. The sample size was chosen on the basis of previously published data (1), the assumption that a UV saturation difference between groups of 5% was clinically significant and an acceptance of a power of 0.8. Data were analyzed using chi- square, Fishers exact test and paired and unpaired Student's t- tests. A p value of $< 0.05$ was considered statistically significant.

RESULTS There were no differences between the groups in maternal demographic data. There were 2 primary C/S for breech in Group I and 7 in Group II. Maternal $O_2$ saturation was significantly increased in both groups by $O_2$ therapy ( $P<0.01$) but there was no difference in maternal $O_2$ saturation between the two groups at the time of delivery. The difference in UV $O_2$ saturations between the groups was not statistically significant nor was $O_2$ utilization as reflected by UA values (Table). There was no difference between the UA or UV cord pH or $PCO_2$ between the groups. Two women in each group found the $O_2$ delivery device uncomfortable.

DISCUSSION $O_2$ transfer from mother to fetus is affected by many factors. The most important of these are uterine intervillous blood flow and fetal placental blood flow. In addition, $O_2$ transfer is directly proportional to the difference between maternal arterial and fetal UV $O_2$ saturations. This is clinically important when maternal $O_2$ saturation is abnormally low (2). When preoperative maternal $O_2$ saturation is normal, $O_2$ delivery to the fetus is improved at C/S under EA when 100% $O_2$ is delivered to the mother compared to when the mother is breathing room air (1). However, this concentration of oxygen is not readily achieved using routine clinical delivery systems. Since supplemental $O_2$ through either NP or FM significantly increases maternal $O_2$ saturation to the same degree and there is no difference in the $O_2$ delivery to the fetus, both devices are suitable for this purpose. We suggest that patient preference could be accommodated in this matter during elective C/S.

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TABLE

| DEVICE | NP | FM | P |
|---|---|---|---|
| N | 20 | 20 | NS |
| GESTATION | 39 (1) | 39 (1) | NS |
| BREECH (N) | 2 | 7 | 0.06 |
| MAT O SAT (PRE EPI) | 98 (1.2) | 98 (1.0) | NS |
| MAT O SAT (DELIVERY) | 99 (1) | 99 (0.7) | NS |
| HYPOTENSION (%) | 25 | 25 | NS |
| UT INCISION-DEL(SEC) | 118 (58) | 134 (64) | NS |
| UV $O_2$ SAT | 46 (18) | 54 (17) | 0.08 |
| UA $O_2$ SAT | 18 (10) | 15 (8) | NS |
| APGAR<8 1 MIN(%) | 15 | 15 | NS |
| APGAR<8 5 MIN(%) | 0 | 0 | NS (SD) |

# INTUBATING CONDITIONS WITH A MEGADOSE OF VECURONIUM, WITH OR WITHOUT PRIMING

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INTRODUCTION: In order to check whether a large dose of vecuronium (V) of 300 $\mu g.kg^{-1}$ administered as a single bolus (group I) could provide as good intubating conditions at 60 seconds as the same total dosage of V (300 $\mu g.kg^{-1}$) but divided in a priming dose of 10 $\mu g.kg^{-1}$ followed by an intubating dose of 290 $\mu g.kg^{-1}$ (group II) without its risks, a prospective randomized single blind study was done. This dose of V has been chosen because it provides the same duration of action as pancuronium (P) 100 $\mu g.kg^{-1}$ with a much shorter onset[1]. A control group receiving d-tubocurarine (DTC) 50 $\mu g.kg^{-1}$ followed by succinylcholine 1.5 $mg.kg^{-1}$ (group III) was included in the study.

METHODS: 151 patients conform with our inclusion criteria are enrolled in the study. Possibility of early muscle paralysis is observed with questions and a head lift manoeuvre. Neuromuscular function is monitored with an evoked electromyogram (EEMG) from the start of induction of anesthesia and at the moment of intubation (60 seconds later). Intubating conditions is observed by a blind anesthesiologist and graded by a scale from Lund and Stovner [2]: grade 0: excellent: no movement; grade 1: good: small cords movement, little diaphragmatic motion; grade 2: fair: intubating still possible with less favorable conditions; grade 3: intubating impossible. Patients were all administered 2-3 $\mu g.kg^{-1}$ of fentanyl prior to EMG calibration. Then the priming dose of myorelaxant (or saline in group I) is given. Three and a half minutes later, possible early paralysis is ruled out with standard questions and a 5 seconds head lift. The patient was then put to sleep with thiopental 4-7 $mg.kg^{-1}$ and the intubating dose of myorelaxant is injected (time 0). Sixty seconds later the patient is intubated and conditions recorded. Data are expressed as mean ± SD, and statistical analysis is done with ANOVA and a chi-square when appropriated.

RESULTS: The 3 groups are comparable in age, sex, weight and ASA class distribution. Their relative number varies: group I: 45 patients; group II: 58 patients; group III: 48 patients.

TABLE I: preinduction period problems (% patients)

| Group | I | II | III |
|---|---|---|---|
| Double vision | 4.4 | 82.8* | 79.2* |
| Problem breathing | 2.2 | 8.6 | 0 |
| Problem swallowing | 0 | 19.0* | 6.3* |
| Inability to maintain head lift for 5 seconds | 2.2 | 20.7* | 10.4* |

* $p < 0,05$

TABLE II: neuromuscular function with EMG: $T_1$ and $T_4/T_1$ (% mean ± SD) * $p < 0,05$

| Group | I | II | III |
|---|---|---|---|
| $T_1$ ($t_0$) | 99.2 ± 4.6 | 96.5 ± 13.2* | 96.9 ± 5.1* |
| $T_4/T_1$ ($t_0$) | 100.3 ± 1.8 | 99.3 ± 8.8 | 100.0 ± 2.7 |
| $T_1$ ($t_{60}$) | 31.8 ± 22.7 | 25.6 ± 23.8 | 4.4 ± 6.7* |
| $T_4/T_1$ ($t_{60}$) | 60.8 ± 29.4 | 48.6 ± 35.5 | 11.6 ± 28.4* |

TABLE III: intubating conditions (from Lund and Stovner [2] (%)

| Group | I | II | III |
|---|---|---|---|
| Grade 0 | 75.6 | 91.4 | 89.6 |
| Grade 1 | 20.0 | 6.9 | 10.4 |
| Grade 2 | 4.4 | 1.7 | 0 |
| Grade 3 | 0 | 0 | 0 |

N.B. 4 out of 58 (6.9%) in group II had to be induced earlier because of great discomfort.

DISCUSSION: As thought, V 300 $\mu g.kg^{-1}$ in single bolus dose provides little discomfort. The only patients in group I who had any problem has experienced thoracic rigidity secondary to fentanyl sedation. On the contrary patients in group II and III show frequent signs of muscle paralysis and discomfort (group II > group III). $T_1$ and $T_4/T_1$ evaluation indicates more rapid depression in group III patient. Part of this can be explained by the fact that EMG monitoring underestimates neuromuscular function with depolarazing neuromuscular blocking drug (NMBD) compared to non-depolarizing NMBD. Intubating conditions are less frequently excellent in group I patients. But if we combine grade 0 and grade 1 patients, meaning intubating conditions good or excellent, then in group I, II and III respectively, we find 95.6%, 98.3% and 100% of patients. None of the groups had 100% grade 0 patients.

In conclusion, administrating V in single bolus dose of 300 $\mu g.kg^{-1}$ provides satisfactory intubating conditions at 60 seconds. However, a few patients (4.4%) will experience only fair intubating conditions with this regimen.

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# LOSS OF THE ANTIEMETIC EFFECT OF DROPERIDOL IN MENSTRUATING WOMEN

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Introduction:

Post-operative nausea and vomiting is common in women. The incidence seems to be increased in women undergoing laparoscopic tubal ligations and the incidence of nausea and vomiting may be increased in menstruating women.[1] Droperidol has been found to be effective in reducing post-operative nausea and vomiting in some studies.

The purpose of this study was to evaluate dose response for droperidol between women menstruating and women who were more than nine days past their menstrual period.

Method:

Women coming for elective laparoscopic tubal ligations, A.S.A. I and II, were randomly entered into this trial after informed consent. All patients had a standard anaesthetic consisting of pretreatment with fentanyl ≤2 µg/kg and 3 mg d-tubocurarine. Anaesthesia was induced with sodium thiopental 1 - 5 mg/kg and succinylcholine 1 - 2 mg/kg. Patients were maintained on isoflurane as required. All patients were intubated. The incidence of nausea and vomiting was determined in the recovery room both before the patients had received any narcotics for pain control and after receiving narcotics for pain control. In the Short Stay Unit they were again monitored for nausea and vomiting before and after narcotics and a follow-up telephone interview was conducted 48 hours after the anaesthetic.

Both the evaluator and the patient were blinded as to the dose. Prior to administration of any other medications, patients received either saline placebo, or droperidol in a dose of 10, 20, or 30 µg/kg.

Results:

The results of the study are summarized in Table 1 and represent an interim analysis of our on-going trial. Women who are >9 days after their menstrual period have a step-wise reduction in the incidence of nausea and vomiting such that there is no nausea and vomiting at a dose of 30 µg/kg of droperidol. There was some evidence that the effect was short-lived and they did have nausea at home at the higher doses in menstruating women. All women who received less than 30 µg/kg of droperidol displayed nausea.

Discussion:

Results of this study indicate that droperidol is an effective antiemetic in women after they have finished menstruating, however, early in their period droperidol may have lost its potential as an antiemetic drug.

INCIDENCE OF NAUSEA & VOMITING %

| DOSE | MENSTRUAL | POST MENSTRUAL |
|---|---|---|
| Placebo | 50 | 33 |
| 10 µg/kg | 60 | 33 |
| 20 µg/kg | 60 | 20 |
| 30 µg/kg | 100 | 0 |

Reference:

1. Can J Anaesth 1989;36:S78-9.

# ATRACURIUM AND D-TUBOCURARINE PRETREATMENT IN THE PREVENTION OF SUCCINYLCHOLINE MYALGIAS: A STUDY IN VAGINAL HYSTERECTOMIES.

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## INTRODUCTION

The effectiveness of a small dose of a non depolarizing muscle relaxant prior to the administration of succinylcholine, in the prevention of post operative myalgias, has been clearly established in outpatient surgery (1). In studies in patients having major abdominal surgery, the incidence of post succinylcholine myalgias has been small and not prevented by defasiculating doses of a non depolarizing relaxant prior to succinylcholine(2). We sought to study the incidence of post succinylcholine myalgias (PSM) in inpatients having surgery of a less traumatic nature (ie vaginal hysterectomies without bladder repair), and compare the results with patients having more major surgery(vaginal hysterectomies with repair).

## METHODS

Institutional approval was obtained, as was informed consent from each subject. Patients with significant cardiorespiratory or neuromuscular diseases, drug allergies, or anatomic features which might preclude easy endotracheal intubation were excluded. 60 patients having vaginal hysterectomy with or without bladder repair were randomized to one of three groups: pretreatment with atracurium $0.05 mg \cdot kg^{-1}$, d-tubocurarine $0.05 mg \cdot kg^{-1}$, or placebo. After standard anæsthetic induction with thiopentone and fentanyl, patients received the pretreatment in double blind fashion. 3 minutes later, succinylcholine $1.5 mg \cdot kg^{-1}$ was administered, and the patients were intubated when a nerve stimulator revealed no twitches in response to a supramaximal stimulus. Fasiculations and intubating conditions were graded according to published scales (3). Surgery was completed without the further use of muscle relaxants. An investigator unaware of events in the operating room visited the patient for the first three postoperative days. Subjects were questioned about myalgias and graded according to a published scale(2). Activity was quantified as follows: 0-unable to get out of bed, 1-up in the chair, the number of times limited by patient discomfort, 2-unlimited activity in the patient's room, able to walk in the hall with activity limited by patient discomfort, 3-unrestricted activity.

Hysterectomy patients and those having hysterectomies with repair were analyzed separately. Demographics were compared with a one way analysis of variance. Measured variables were compared using a Kruskal-Wallis one way analysis of variance followed by Dunn's approximation. A p value<0.05 was considered significant.

## RESULTS

There was no difference in groups with respect to age or weight. No patient suffered severe PSM. Intubating conditions were equivalent in all patient groups. Fasiculations were significantly reduced in the atracurium and d-tubocurarine groups when compared to placebo ($p<0.025$).

Hysterectomy group n=43: On the second postoperative day, there were significantly fewer myalgias in the patients pretreated with atracurium ($p<0.025$, graph); no other significant differences in muscle pains were seen. Patients were significantly more active on the second postoperative day ($p<0.025$).

Hysterectomy/repair group n=17: No significant differences between groups were observed. Mild myalgias were reported by one patient on the first and second postoperative days. Patients were similarly inactive on all postoperative days.

When activity levels were compared between the hysterectomy and hysterectomy/repair groups, there was no difference seen on the first post operative day; however patients having hysterectomies alone were significantly more active on the second post operative day ($p<0.05$).

## DISCUSSION

We have demonstrated a decreased incidence of PSM in vaginal hysterectomy patients pretreated with atracurium as compared to placebo; this difference was only significant on the second post operative day. Our patients undergoing hysterectomy and repair were significantly less active than their hysterectomy counterparts, required more postoperative analgesics, and not surprisingly had a very low incidence of PSM. It is hypothesized that the increased activity in the hysterectomy patients on the second postoperative day led to an increased incidence of PSM, and that this was effectively mitigated by atracurium, though not by DTC, pretreatment. With outpatient surgery, individuals are generally mobile by the first postoperative day, and this corresponds to the peak level of PSM in that population (1).

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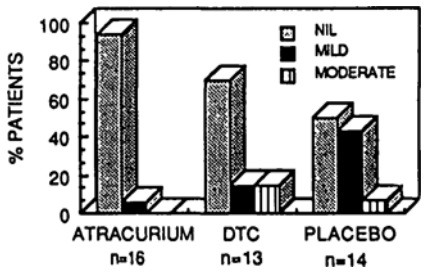
MYALGIAS-DAY2



# PROPOFOL FOR INDUCTION AND MAINTENANCE OF ANAESTHESIA: A COMPARISON WITH THIOPENTAL - ISOFLURANE

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## INTRODUCTION

Propofol is an intravenous anaesthetic agent with a very short half-life[1]. Induction characteristics of propofol are well-described. Its use as a maintenance agent, administered over a relatively short period by repeated boluses[2] or by infusion[3] is also established. Recovery characteristics of propofol when used for induction and maintenance of anaesthesia of 1 to 2 hours' duration, and how these compare to other anaesthetics currently in use are less well known.

## METHODS

With institutional approval and informed consent, 60 adult ASA I-II patients scheduled to undergo surgery of an expected duration of 1-2 hours, were randomized into 2 groups. One group received 2 mg/kg of propofol for induction, followed by an infusion of 0.2 mg/kg/min, decreased to 0.1 mg/kg/min after $^1/_2$ hour. The other received 4 mg/kg of thiopental for induction, followed by isoflurane, with inspired concentration as needed. 60-67% $N_2O$ in oxygen was administered to both groups. All subjects received 1.5 µg/kg of fentanyl prior to induction, but no further narcotic was administered until emergence. Succinylcholine and vecuronium were used as necessary.

Recovery assessments included measurements of times to eye-opening, ability to obey simple commands, and achievement of full orientation. In the recovery room, quality of recovery was assessed, and presence of untoward side-effects noted. Patients' Aldrete recovery scores were recorded every 15 minutes until discharge. Baseline tests of psychomotor function, including a Trieger dot test and Deletion of P test were applied prior to induction of anaesthesia, and again in the recovery room prior to discharge.

## RESULTS

Both drug groups were similar with respect to sex distribution, age, weight, A.S.A. class, and types of surgical procedures undergone. Anaesthetic durations were 80.3±49.7 mins for the isoflurane group, and 58.3±30.2 mins for the propofol group ($p$ =NS). Although not statistically significant, propofol more often required additional doses before intubation was possible; this was accordingly associated with a longer interval before intubation occurred, i.e. 137±29 secs for propofol as compared to 116±29 secs for thiopental ($p$ =0.03). There was no significant difference between groups in incidence of pain on injection of the induction agent, nor was there a strong correlation between the site of injection and degree of pain. The average infusion dose of propofol was 0.164±0.024 mg/kg/min; the maximum end tidal concentration of isoflurane was 1.16±0.44%, and the end tidal concentration at discontinuation of isoflurane administration was 0.6±0.4%. Recovery times for both groups after discontinuation of $N_2O$ and the major maintenance agent are shown below (mean±S.D.). There was no statistical difference between the groups.

| | *RECOVERY TIMES* *PROPOFOL* | *ISOFLURANE* |
|---|---|---|
| **AFTER $N_2O$ DISCONTINUED** | | |
| Time to extubation | 8.59±5.57 min | 8.16±6.84min |
| Time to open eyes | 10.29±6.69 min | 10.83±7.72min |
| Time to follow commands | 12.29±13.68 min | 11.23±7.91min |
| Time to full orientation | 13.39±16.58 min | 13.03±10.23min |
| **AFTER MAJOR AGENT DISCONTINUED** | | |
| Time to extubation | 12.07±4.73 min | 11.40±5.31min |
| Time to open eyes | 13.89±6.42 min | 14.43±7.05min |
| Time to follow commands | 15.89±13.46 min | 14.83±7.25min |
| Time to full orientation | 16.99±15.88 min | 16.63±9.93min |

In the recovery room, despite favourable trends for the propofol group in times to ability to sit unaided and to achieve their maximum Aldrete score, differences did not achieve statistical significance, and times to recovery room discharge were almost identical. The subjective assessment of quality of recovery of the propofol group was significantly better ($p$ <0.04). There was no difference in the incidence of nausea in the recovery room.

Insignificant differences in performance occurred between drug groups in the Trieger and Deletion of P tests, both at baseline and in the recovery room, although there were significant differences between the baseline and postoperative results, particularly with respect to speed and fine control of hand movements ($p$ <0.005).

Hemodynamic stability was seen throughout anaesthesia in both groups; however, systolic, diastolic and mean blood pressures, and heart rates were significantly higher on extubation in patients receiving isoflurane ($p$ <0.05).

## DISCUSSION

Propofol has been shown in this study to compare very favourably to isoflurane when used for maintenance over a 1 to 2 hour period. Although measured recovery times were not significantly different between drug groups, the subjective impression of awakening was frequently that of a clearer-headed recovery in patients receiving propofol. In addition, patients who had on former occasions received other anaesthetics, often preferred propofol here. Side-effects were infrequent for both drug groups. Propofol thus is a very satisfactory induction and maintenance agent, and might be used in situations when inhalational anaesthetics are not feasible.

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# A COMPARISON OF THE HEMODYNAMIC EFFECTS OF ATRACURIUM AND VECURONIUM DURING ANAESTHETIC INDUCTION

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INTRODUCTION: The sequence of anaesthetic induction and intubation is frequently associated with significant hemodynamic changes[1]. Nondepolarizing muscle relaxants, given to facilitate endotracheal intubation, may possibly attenuate or exaggerate such hemodynamic responses. A prospective, randomized double-blind study was designed to compare the hemodynamic responses and the effects on ventricular function of either atracurium (ATR) or vecuronium (VEC) during induction of anaesthesia and endotracheal intubation.

METHODS: Eighty ASA I and II non-premedicated day care surgical patients under 70 years of age, entered this study after giving a written informed consent to the protocol approved by the Hospital Human Experimental Procedures Committee. Patients were ramdomly assigned to one of four study groups:

Group A: Atracurium and Alfentanil (ATR-ALF)
Group B: Vecuronium and Alfentanil (VEC-ALF)
Group C: Atracurium and Fentanyl (ATR-FEN)
Group D: Vecuronium and Fentanyl (VEC-FEN)

Prior to induction (IND), patients received curare 0.04 mg/kg IV, and either ALF 20 mcg/kg or FEN 4 mcg/kg IV from a coded syringe. Two minutes later, anaesthesia was induced with sodium thiopenthal 5 mg/kg IV immediately followed by either ATR 0.5 mg/kg or VEC 0.08 mg/kg administered from another coded syringe over 30 seconds. Endotracheal intubation was performed two minutes following induction. Non-invasive measurements of heart rate (HR) and mean arterial pressure (MAP) were determined using a Critikon Dinamap 1846P monitor. Cardiac index (CI) and ejection fraction (EF) were measured non-invasively by transthoracic bioimpedance cardiography (BoMed NCCOM3). Measurements were recorded at baseline (BL), one minute post-induction (IND) and every minute for 5 minutes following intubation (INT+1...INT+5). Data were analyzed using repeated measures analysis of variance, and statistical significance was assumed when $p<0.05$.

RESULTS: Heart rate (Fig.1) did not change significantly in any group in response to IND, but increased significantly at INT+1 in group D ($p<0.05$). Mean HR values were stable and similar in groups A, B and C. After induction, there was a significant decrease in MAP in all 4 groups (Fig.2). The absolute MAP change ($-7\pm8$ mmHg) was minimal in group D ($p<0.05$), but this group had a significant increase in MAP to $108\pm15$ mmHg following INT ($p<0.05$). By the second minute following intubation, mean HR and MAP values were no longer different from BL in any group. CI and EF decreased slighty over time, but there were no significant differences in either of these parameters between groups at any corresponding time during the study period. The intubating conditions were good to excellent in all groups.

DISCUSSION: VEC has been shown to have no effect on the cardiovascular system whereas ATR may cause slight hypotension when given in doses of ED95X3. Our data shows that after induction, the response of HR and MAP is similar to that reported in other studies[2,3]. We also studied the hemodynamic effects of ATR and VEC following endotracheal intubation and found a significant increase in HR and MAP in the VEC-FEN group. We conclude that the cardiovascular profile of ATR compares very favourably with VEC when used in a surgical day care population.

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Fig. 1 HEART RATE
Mean ± SD

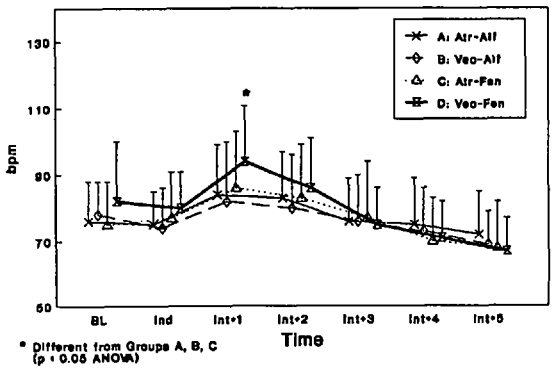
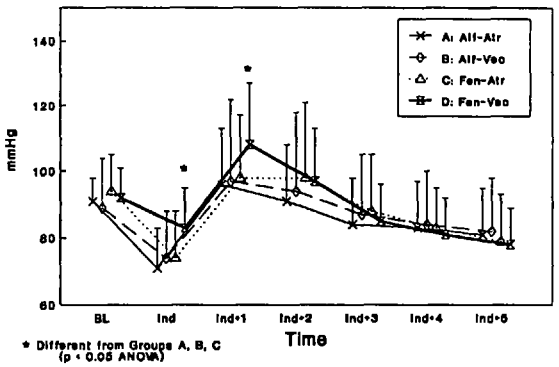



Fig. 2 MEAN ARTERIAL PRESSURE
Mean ± SD



# NARCOTIC ANALGESIC, ITS ANTAGONISTS AND COMMON BILE DUCT PRESSURE

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Introduction. By using biliary tract pressure measurement technique, the effects of narcotic analgesic and its antagonists on common bile duct pressure (CBDP) were measured in 27 patients during selective cholecystectomy.

Methods. 27 ASA class I patients age 22-75 years, no history of jaundice, absence of CBD or intrahepatic biliary tract stons and ampullary abnormality were received elective cholecystectomy. All of cases were divided into 4 groups randomly (patient number 7,6,8,6).Group I: Fentanyl 1ug/kg + Naloxone 0.4mg. II:Fentanyl 1ug/kg + Atropine 0.5 mg. III: Fentanyl 1ug/kg + Aminophylline 2mg/kg. IV: Fentanyl 1ug/kg + Normal Saline 2 ml . The day before operation, all the drugs which would influnce the biliary pressure were stoped. Continuous epidural anesthesia with a mixture of 1.6 % X and 0.2 % D were adnisted prior to the completion of the pressure mesurements. After removal of the gallbladder, a cannula (a low conformability polyethylene tube of 100 cm long, i.d 1 mm, o.d 1.8 mm)filled with normal saline at body temperature was inserted through the cystic duct remnent into the CBD deeply. The other end of the cannula was connected to the MPU-0.5 A pressure sensor, then the latter was connected with a 4-channel physiological recorder of model RM 6100. The operation came to a pause during the pressure measurment. First,we measured the base pressure of CBD for one minute, then gave an intravenous injection of fentanyl 1ug/kg. After continuous recording of intraductal pressure for 10 minutes. we injected intravenously the respective antagonist and observed pressure fluctuation for another 7 minutes. The data obtaind were processed by the t-test.

Results: The results were shown in the table and figure attached. After injection of fentanyl the CBDP increased 26.0 - 56.6 % (mean 37.4 %) in the 4 groups, $P < 0.05$-$0.01$. When naloxone and aminophylline were administered, CBDP decreased significantly from 16.43 ± 3.98, 16.44 ± 4.18 to 13.59 ± 3.63, 11.50 ± 5.50 mmHg respectively, all returned nearly to the base values, $P < 0.05$. Similar to the control group, the CBDP after giveing atropine did not decreased but even had a tendancy of slight increase. Contrasted with the basic values, a significant difference was noted, $P < 0.01$.

Discussion. Narcotic analgesics used in patients with biliary tract disease in the perioperative period may be harmful(1,2), because they are able to cause spasm of the spincter of Oddi, resulting in increasing CBDP sharply. Spasm of the spincter of Oddi caused by fentanyl, induced prompt elevation of CBDP,which was a temporary and reversible phenomenon(3), but the reaction was violent, especially for the patients suffering from biliary inflammation, accompanied with biliary hypertension. Spasm of the spincter may give rise to cholangiographic findings indistinguishable CBD. It may thus cause unnecessary surgical exploration of the CBD and increased surgical morbidity(4). Fentanyl-induced spasm may be relieved by antagonists and the possible complications during or after operation are then to be avoided. Artropine could not reverse biliary hypertension induced by fentanyl. Naloxone however had a marked reversing effect, but it antagonizes the antagesic effect and influences the hemodynamics such as the elevation of blood pressure. Aminophylline in small dose had same effect of reversing the biliary hypertension as that of the naloxone. Because of the small dose requised, there is few side effect and absence of reversing a analgesic action. Aminophylline is therefore a kind of reasonable antagonist, due to not only its efficacy but also its safty.

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Changes of CBDP after fentanyl & antagonists

| Group | Baseline (mmHg) | 10 min.CBDP Fentanyl | 7 min.CBDP Antagonist |
|---|---|---|---|
| I n=7 | 13.04±3.17 | 16.43±3.98** | 13.59±3.63# |
| II n=6 | 10.67±2.99 | 14.17±5.03* | 15.30±6.19## |
| III n=8 | 10.58±2.96 | 16.44±4.18** | 11.50±5.50# |
| IV n=6 | 11.25±3.28 | 15.17±4.08** | 16.08±4.09## |

*P < 0.05 Postfentanyl versus baseline
**P < 0.01 Postfentanyl versus baseline
#P < 0.05 Postdurg versus 10 min.CBDP
##P < 0.01 Postdurg versus baseline

# INTRANASAL NIFEDIPINE FOR POST-BYPASS HYPERTENSION - HEMODYNAMICS AND PHARMACOKINETICS

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**Introduction:**

The optimal treatment of hypertension (HT) after coronary artery bypass graft (CABG) surgery is unresolved. Nifedipine (NIF) possesses certain advantages, having both coronary and peripheral vasodilator effects. Sublingual NIF's effectiveness in acute control of HT is due to absorption of swallowed drug[1]. Intranasal (IN) NIF is effective in anaesthetized intubated patients[2]. We studied the clinical effects and absorption of IN NIF at three dosages.

**Patients and Methods:**

With institutional approval and individual consent, 23 patients with mean arterial pressure (MAP) > 95mmHg after elective CABG were randomized to receive a single dose of 10, 20 or 30 mg IN NIF. The contents of one to three 10mg capsules were aspirated into a 1ml saline-alcohol (1:1) mixture and instilled into one nostril which was covered with foil to prevent photodegradation[2]. Haemodynamic data were recorded and arterial blood samples for plasma levels ($C_{NIF}$) using gas chromatography[3] were obtained at 0,2,4,6,8,10,20,30 and 45 minutes and 1,2,4,6,8,10 and 12 hours after IN NIF administration. Haemodynamics were evaluated using analysis of variance for repeated measures. The relationships between peak $C_{NIF}$ ($C_{max}$) or area under the curve ($AUC_{\infty}$) and NIF dosage were assessed using least-squares regression.

**Results:**

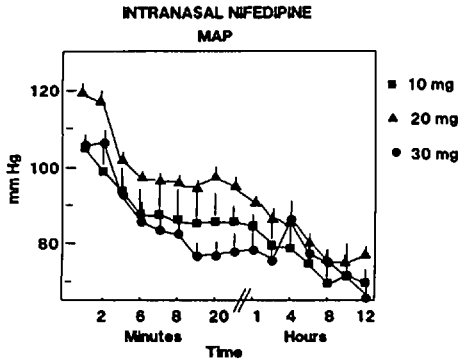
There were no demographic differences. Significant decreases in MAP occurred with each dosage. MAP $\leq$95 mmHg was achieved by 20 minutes in all but one patient, who had received 10mg IN NIF. There were no significant differences in mean MAP between dosages (Figure 1). However, additional vasodilator therapy was required at 1.5 to 4 hours in 5 patients given 10 or 20mg, but none in patients given 30mg. Pressor agents to restore MAP >80mmHg were required in one patient given 20mg and three patients given 30mg. Heart rate and pulmonary artery pressure were unchanged.

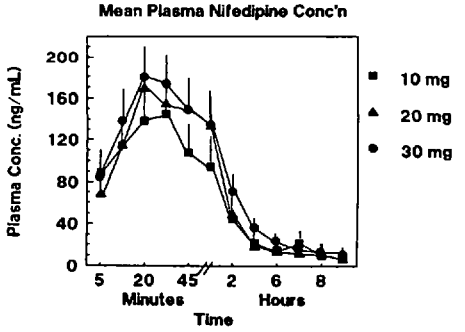
Mean $C_{NIF}$ did not differ significantly between groups (Figure 2). Large variability was observed in $AUC_{\infty}$ at each dose (coefficient of variation 40-60%). There was no apparent correlation between dose and $AUC_{\infty}$ or Cmax. Median time to Cmax was 20 minutes. Mean elimination half life was 5.8 $\pm$ 2.7 hours. MAP was inversely related to the natural logarithm of $C_{NIF}$ for the first 20 minutes.

**Discussion:**

All three doses of IN NIF produced a sustained reduction in MAP. There was a trend towards hypotension at higher doses. Mean $C_{NIF}$s were similar but extremely variable for all doses. The similar haemodynamics in the three groups, consistent with $C_{NIF}$, appeared to be attributable to variation in drug levels achieved by IN delivery.

10mg IN NIF is safe and effective as a primary agent in short term control of post-CABG HT. Variable absorption limits the usefulness of higher bolus doses. Repeat 10mg boluses may be the method of choice in the management of recurrent episodes of HT.

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# ESMOLOL VERSUS FENTANYL FOR PREVENTING HAEMODYNAMIC RESPONSE TO INTUBATION IN CARDIOVASCULAR DISEASE.

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Introduction:

Narcotics (eg Fentanyl up to 8µg/kg) as an adjunct to Thiopental (STP) induction is a popular method to prevent postintubation hypertension and tachycardia[1]. Esmolol, a new short-acting cardioselective beta blocker given as a 100 or 200 mg bolus prior to intubation blunts the haemodynamic response[2]. To date these methods have not been compared. We designed a double-blind randomized controlled study in a population with cardiovascular disease (CVD) to compare these two methods for control of blood pressure (BP), heart rate (HR) and incidence of ischaemia/arrhythmias.

Methods:

With Ethics Committee approval and informed consent, 66 ASA II-IV patients with chronic stable hypertension or angina scheduled for non-cardiac surgery were included. Exclusion criteria were contraindications to beta blockers. Patients were randomized in a double-blind and double-dummy fashion into 3 groups: Fentanyl 500 µg (F500) and 2 Esmolol groups, 100 (E100) and 200 (E200) mg. Diazepam 5-10 mg was given 90 mins preoperatively. After 3 baseline HR and BP values, a defasciculation dose of dTC was given. At 4 mins prior to intubation, Fentanyl 500 µg or placebo was given over 60 secs. At 2 mins prior to intubation, Esmolol or placebo followed by 3-5 mg/kg of STP and 1.5 mg/kg of succinylcholine was given over 60 secs. Postintubation, the patients were ventilated with 50% $N_2O/O_2$, and after 5 mins the study was concluded. BP and HR were measured at one minute intervals and a 2-channel ECG Holter monitor recording was taken throughout the procedure. Data was assessed by covariance analysis.

Results:

Demographically, the 3 groups E100 (n=24), E200 (n=21) and F500 (n=21) were comparable for age, weight, ASA, sex, ward HR/BP and STP dose. The HR, compared to baseline (BL), was well controlled postintubation in all three groups with no statistical differences. Following intubation, mean arterial pressure (Figure 1), diastolic BP (Figure 2) and systolic BP, as compared to BL were stable in the E200 group, increased in the E100 group and decreased in the F500 group. Hypotension occurred in 3/E200 and 7/F500 patients ($p<0,01$); 5 F500 patients required Ephedrine. There were no ischaemic episodes and no statistical difference between the 3 groups for arrhythmias.

Discussion:

Esmolol 200 mg 90 secs prior to intubation effectively blunts HR and BP response. The 100 mg Esmolol bolus was not effective for control of BP. Fentanyl 500 µg controls HR, but is associated with a significant drop in BP. The diastolic BP, essential to coronary perfusion, appears better preserved with Esmolol. This technique may offer advantageous haemodynamics in patients with CVD.

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Figure1

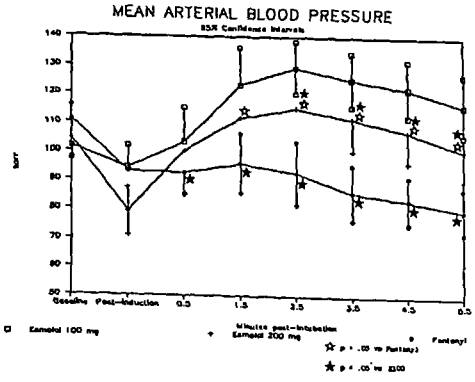
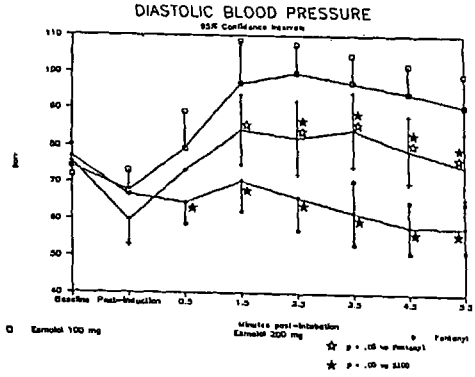



Figure 2



# ISOFLURANE DOES NOT INHIBIT PLATELET-INDUCED VASOCONSTRICTION IN THE CANINE CORONARY ARTERIES

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**INTRODUCTION:** Platelets play a major role in the physiology of vascular and coronary smooth muscles. Platelet adhesion and aggregation on coronary arteriosclerotic lesion release several vasoconstrictors. Vasoconstricting agents which increase coronary tone are responsible for myocardial ischemia. The endothelium cells protect against platelet-induced reduction in coronary flow. EDRF and prostacyclin produced by the endothelium are not only potent inhibitors of platelets aggregation but also break down vasoconstriction induced by the vasospastic agents. Coronary artery disease alters the endothelium in its structure and function, leading to an increased risk of platelets aggregation and vasospasm. We have previously shown that halothane attenuates the response of isolated canine coronary rings to platelet aggregation in vitro.[1] In this research project we studied the effect of isoflurane on the same response of isolated canine rings to platelet activation in vitro.

**METHODS:** Canine coronary arteries were dissected, cleaned, cut into 5 mm rings and suspended on a pair of stirrups. The endothelium was mechanically removed in some rings. Each ring was then placed in the organ chamber, immersed in Krebs-Ringer solution with 95% $O_2$ / 5% $CO_2$ and maintained at 37°C. The upper stirrup was attached to an isometric force transducer sending signals to a recorder. After stretching each ring to its optimal passive tension, KCl 40 mM was added to the bath producing a standard reference contraction for every ring. Relaxation by acetylcholine $10^{-6}$M was then used to check for the presence of end othelium. The rings were then washed with Krebs and allowed to relax for a few minutes. Isoflurane, 1.5 MAC, was added to the gas mixture in half the chambers. After reaching a steady concentration, we proceed with the dose response to human platelet in concentrations of 20, 50 and 70 x $10^{-9}$/liter.

30 ml of blood were obtained from healthy human donors drawn the morning of the experiment. It was anticoagulated with 10% vol. citrate solution and centrifuged to obtain platelet rich plasma (PRP). Anticoagulation and centrifugation were repeated, separating the PRP to platelets and plasma. The isolated platelets were diluted in the citrate anticoagulant to achieve the concentrations needed for the the experiment.[2] Statistical analysis is done using the Student paired t-test to compare areas under the dose response curves.

**RESULTS:** Human platelets induced a dose dependant increase in coronary rings tension. Isoflurane does not attenuate this response in rings either with or without endothelium. (Fig. 1 and 2)

**DISCUSSION:** We have previously shown that isoflurane can only attenuate the response of isolated canine coronary arteries to 5-HT in the presence of endothelium.[3] The data presented here show that isoflurane does not attenuate the response of vessels with and without endothelium to platelets aggregation. Platelets release several vasoconstrictors and the response is the result of the action from the different agonists (5HT, $TBA_2$,PGF2-alpha, ADP, ATP). These data suggest that contrary to halothane, isoflurane does not interfere with canine coronary smooth muscle response to activation of human platelets in vitro. It also suggests that isoflurane does not have a beneficial effect on the vasoconstrictor response to aggregating platelets in humans.

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Fig. 1

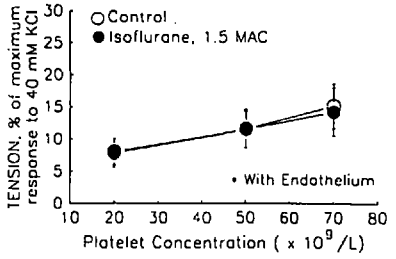
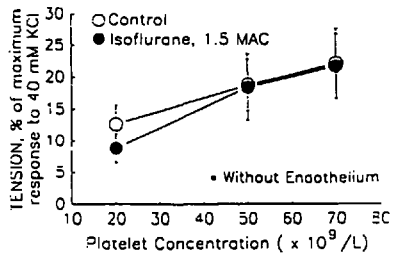



Fig. 2



# HALOTHANE AND ISOFLURANE PREVENT FREE RADICAL INDUCED REDUCTION IN THE CORONARY FLOW AND CONTRACTILITY OF THE ISOLATED RABBIT HEART

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INTRODUCTION: The mechanism of the injury that occurs at the time of reperfusion of a previously ischemic tissue is still not completely understood. However, the hypothesis that oxygen-derived free radicals (ODFR) contribute to myocardial reperfusion injury has received a lot of support. These radicals can induce marked increases in coronary vascular resistance and a decrease in myocardial contractility leading to myocardial ischemia, cardiac failure and severe arrhythmia. It has been shown, in vivo, that halothane and isoflurane can improve myocardial recovery after temporary suppression of coronary flow.(1) Nevertheless, the mechanism of the beneficial effects of these anesthetics on the reperfusion injury has not been studied. In this research project, we measured the effects of volatile agents on the changes induced by ODFR on the coronary flow and ventricular pressure of an isolated rabbit heart.

METHODS: Isolated rabbit hearts were perfused in a Langendorff apparatus with an oxygenated (95% $O_2$, 5% $CO_2$) Krebs-Ringer solution. The perfusion pressure was kept constant at 85 cm of water. The coronary flow was measured by an ultrasonic flow meter probe placed in the perfusion line. A preformed latex balloon was introduced in the left ventricle through the left atrium and connected to a pressure transducer; the systolic and diastolic ventricular pressure were measured and recorded. The balloon was filled with saline solution until the ventricular diastolic pressure reached 14 mmHg. The ODFR were produced by the electrolysis of the physiologic buffer (DC current 0.6mA). A calibrated vaporizer was used to add the volatile agents to the perfusion solution. The effects of free radicals on the intraventricular pressure and coronary flow were measured in the presence and absence of each anesthetics. One way ANOVA was used to analyse the data.

RESULTS: In the isolated perfused rabbit heart ODFR induced a significant stable reduction in coronary flow and a decrease in systolic ventricular pression. Pretreatment of the heart with halothane 1.0 % or isoflurane 0.7 attenuates the diminution in systolic pressure induced by the free radicals produced (Fig). In the presence of the volatile agents, the effect of free radicals on coronary flow is biphasic. The initial vasoconstriction is followed by a transient return of coronary resistance toward the basal level obtained before the generation of free radicals. This inhibition of the ODFR-induced coronary vasoconstriction was still significant after 10 min of ODFR exposure for isoflurane 0.7% and halothane 1.0% (Fig. 2). ($p<0.01$ ANOVA compared to the flow in hearts not treated by the volatile agents)

DISCUSSION: These data confirm the effects of ODFR on contractility and coronary flow.(2) In the presence of the volatile agents studied, the negative inotropic effect of ODFR is prevented and their coronary effect is partially antagonized by isoflurane 0.7% and halothane 1.0%. These data suggest that the volatile agents interfere with the ODFR cells damage pathway. However, it has yet to be determined if these volatiles are scavengers of ODFR or cellular protector. The negative inotropic action of volatile agents could be beneficial as demonstrated in previous studies, where a better functional recovery from a hypoxic episode was obtained in presence of volatile anesthetics agents.(3) These mechanisms of action could explain the beneficial effect of these anesthetics on the recovery of reperfused myocardium.

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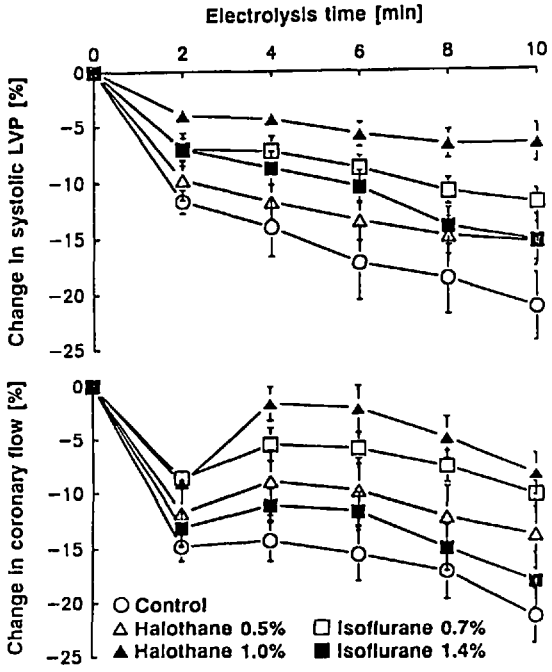

# SYSTEMIC COMPARED WITH CORONARY INFUSION OF ADENOSINE DURING ACUTE CORONARY HYPOPERFUSION IN DOGS

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Introduction. Adenosine has been used for controlled hypotension (1). Primarily an arterial and coronary vasodilator and a sinus node inhibitor, adenosine may counter haemodynamic and metabolic impairment (2) during myocardial ischaemia. However, adenosine may produce intramyocardial redistribution and "steal" (3). We compared the effects of adenosine-controlled hypotension and intracoronary administration of adenosine during complete or partial left anterior descending artery (LADa) constriction.

Methods. In 25 dogs anaesthetized with a barbiturate infusion and ventilated, the pulmonary artery (PA), aorta (Ao), left ventricle (LV), LADa and vein (v), and circumflex vein were cannulated. LADa flow was measured (flow meter) and the LADa constricted by a micrometer to create 50%, 75%, and 100% of resting flow for 15 min each, with 1 hr of normal flow before each constriction. Adenosine was infused systemically (n = 9) to keep mean Ao pressure at 50-60 mmHg or into the LADa (n = 7) (distal to the constriction) at a rate that created maximal coronary hyperperfusion and no change in baseline systemic pressures. Heart rate (HR); electrocardiogram; LADa flow; Ao, PA, LADa, and LV pressures; and LV first derivative (dP/dt) were recorded continuously. Cardiac output (thermodilution) and regional myocardial blood flow (RMBF) (microspheres) were measured and blood sampled before and after constriction for analysis of glucose, lactate, sodium, potassium, and blood gases.

Results (Table). Haemodynamic and metabolic data were similar for all dogs before tests. Systemic adenosine (SA) decreased Ao, PA, and systolic LV (SLVP) pressures; LV dp/dt; systemic and pulmonary resistances; and HR during each constriction period. Coronary adenosine (CA) decreased HR and LV dP/dt but did not affect other haemodynamic variables before or during ischaemia. Stroke volume was significantly higher with SA during constriction than before it. RMBF increased and remained high with SA in the nonischaemic area, while the increase in the ischaemic area was not significant; with CA, ischaemic zone RMBF did not decrease during ischaemia compared with RMBF in nontreated dogs. Arteriovenous oxygen content difference, oxygen consumption, lactate extraction (LE), and lactate flux (LF) in the ischaemic area were less negative (negative = net production) during ischaemia only with SA. RMBF, endocardial-to-epicardial ratio, electrolytes, and glucose extraction in the nonischaemic and ischaemic areas during constriction were affected similarly in all groups.

Discussion. These data suggest that systemic adenosine decreased oxygen demand (by decreasing myocardial rate, contractility, and pressures), induced redistribution of blood flow but not "steal," which reduced myocardial oxygen consumption and lactate formation. Coronary infusion of adenosine, however, had minimal haemodynamic effects, did not create "steal," but did not minimize metabolic and haemodynamic impairment during coronary hypoperfusion.

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TABLE. Affect of Adenosine Infused Systemically (n = 9) or Into LADa (n = 7) During Coronary Constriction in Dogs

| | Adenosine Group | Baseline | 50% Constriction | 75% Constriction | 100% Constriction |
|---|---|---|---|---|---|
| Heart rate (beats/min) | Control | 150 ± 12 | 151 ± 12 | 150 ± 12 | 155 ± 13 |
| | Systemic | 170 ± 14 | 105 ± 12*† | 105 ± 7*† | 110 ± 12*† |
| | Coronary | 128 ± 8 | 112 ± 8 | 99 ± 8* | 91 ± 8* |
| SLVP (mm Hg) | Control | 149 ± 9 | 151 ± 10 | 141 ± 8 | 139 ± 10 |
| | Systemic | 164 ± 8 | 88 ± 5*†‡ | 88 ± 9*† | 82 ± 6*† |
| | Coronary | 159 ± 7 | 124 ± 9 | 106 ± 11 | 96 ± 13 |
| Stroke volume (ml/beats) | Control | 28 ± 3 | 25 ± 2 | 22 ± 1 | 20 ± 2 |
| | Systemic | 33 ± 3 | 35 ± 3 | 37 ± 4* | 38 ± 6* |
| | Coronary | 29 ± 4 | 29 ± 4 | 30 ± 4 | 24 ± 4 |
| RMBF--nonischaemic (ml/min/100 g) | Control | 137 ± 27 | 108 ± 21 | 102 ± 13 | 90 ± 8 |
| | Systemic | 280 ± 90 | 365 ± 58* | 361 ± 88* | 290 ± 24*‡ |
| | Coronary | 122 ± 25 | 285 ± 60 | 159 ± 47 | 68 ± 16 |
| RMBF--ischaemic (ml/min/100 g) | Control | 153 ± 34 | 71 ± 12 | 25 ± 3 | 11 ± 2 |
| | Systemic | 227 ± 86 | 107 ± 25 | 81 ± 42 | 16 ± 11 |
| | Coronary | 144 ± 35 | 155 ± 32* | 97 ± 22* | 20 ± 5 |
| LV dP/dt (mm Hg/sec) | Control | 2317 ± 75 | 2200 ± 63 | 2080 ± 97 | 1920 ± 146 |
| | Systemic | 1900 ± 71 | 1280 ± 66*† | 1160 ± 133*† | 1140 ± 186*† |
| | Coronary | 1800 ± 90 | 1314 ± 91* | 1186 ± 94*† | 1000 ± 143*† |
| LE LAD (%) (LE = [a-v]a x 100) | Control | 22 ± 11 | -68 ± 14† | -227 ± 86† | -231 ± 48† |
| | Systemic | 22 ± 7 | 9 ± 9 | -15 ± 8* | -30 ± 11* |
| | Coronary | 10 ± 32 | -9 ± 17 | -60 ± 40 | -80 ± 31 |
| LF LAD (mg/min/100 g/$10^2$) | Control | 43 ± 24 | -47 ± 27† | -53 ± 11† | -27 ± 7† |
| | Systemic | 101 ± 35 | 73 ± 43* | 7 ± 33 | -4 ± 2* |
| | Coronary | 53 ± 50 | -21 ± 40 | -30 ± 56 | -41 ± 11† |

Values are means; abbreviations defined in the text.
*P < 0.05 vs Control (no adenosine) at same time.
†P < 0.05 vs with Baseline in same group.
‡P < 0.05 vs Coronary Adenosine at same time.

# COMPARISON OF THE HAEMODYNAMIC EFFECTS OF SNP AND AMP FOLLOWING ACUTE MICROSPHERE INDUCED ISCHAEMIC VENTRICULAR DYSFUNCTION

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Acute ischaemic ventricular dysfunction occurs following acute myocardial infarction or following cardiopulmonary bypass procedures. It is characterized by elevated ventricular filling pressures and low cardiac output. Management includes the use of catecholamines to enhance contractility and vasodilators to reduce afterload. Adenosine, a vasoactive nucleoside, may be a useful alternative to sodium nitroprusside (SNP) in the reduction of afterload. Adenosine receptor stimulation results in relaxation of vascular smooth muscle, inhibition of atrial and ventricular automaticity, increases in coronary blood flow and inhibition of the renin secretion.[1] The objective of this study was to compare the haemodynamic effects of adenosine monophosphate (AMP), a soluble adenosine prodrug, in a canine model of acute ischaemic ventricular dysfunction.

**METHODS**

This study was approved by the Animal Care Committee of the University of Alberta. Following induction of anaesthesia with pentobarbital (30 mg/kg I.V.) dogs (n=14) were intubated and ventilated to maintain normoxia and nomocapnia by a Harvard respirator. Anaesthesia was maintained by a constant infusion of pentobarbital (3 mg/kg/hr). ECG, pulmonary artery, systemic arterial and central venous pressures and cardiac output were measured. Left ventricular pressure was measured by a Konigsberg pressure transducer placed in the apex of the left ventricle and the signal differentiated to yield dP/dt. A left coronary artery catheter (8F; 3.5 cm) was positioned under fluoroscopic guidance in the left coronary ostium. After 60 min of stabilization baseline measurements were obtained. Glass microbeads (47-53 um) were then injected into the left coronary artery until dP/dt was decreased by 25% from baseline and LVEDP increased to 12-16 mmHg. Following 30 minutes of stabilization each animal received graded doses of AMP and SNP (randomized order) and dose response curves were constructed.

**RESULTS**

AMP and SNP decreased systemic arterial pressure by a similar extent and in a dose-dependent manner. Heart rate was not significantly altered by either drug. Stroke index was unchanged during SNP administration whereas significant increases were induced by AMP. PCWP and LVEDP were unaltered by AMP whereas SNP significantly reduced both these parameters. No evidence of myocardial depression, as assessed by dP/dt, was observed with either drug.

**DISCUSSION**

AMP induced significantly greater increases in cardiac and stroke indices compared to SNP in this model of acute failure. AMP appeared to act as a selective arterial vasodilator as it did not alter PCWP or LVEDP.

Adenosine receptor stimulation is associated with delayed AV nodal conduction and with depression of cardiac contractility. Nevertheless, no depressant effects were demonstrable with AMP in this study. The absence of these effects probably reflects pronounced sympatho-adrenal stimulation secondary to cardiac failure.

Further investigations are warranted to evaluate the benefits of AMP relative to SNP during acute failure particularly in respect to regional organ blood flow and energy consumption.

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# CRITERIA FOR THE DIAGNOSIS OF PERIOPERATIVE MYOCARDIAL INFARCTION IN PATIENTS UNDERGOING CABG SURGERY.

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Introduction. Perioperative mycardial infarction (PMI) is a major complication following coronary artery bypass grafting (CABG). The incidence varies between 2 and 35% and can be attributed to several factors including patient population, variations in myocardial protection, and criteria used to define PMI.[1] The purpose of this study was to determine if we could detect PMI by monitoring serum "cardiac" enzymes in CABG patients post bypass and define a "gold" standard to accurately determine PMI utilizing serial ECG's, echocardiograms and technetium pyrophosphate scans.

Methods. With approval from our human experimentation ethics committee and patient consent, 100 consecutive patients undergoing CABG surgery were prospectively studied. All patients underwent narcotic induction and maintenance after appropriate monitors were established. Surgery was performed utilizing standard hypothermic (25-27°C) cardiopulmonary bypass techniques and cold potassium cardioplegic solution (4°C). The average duration of aortic cross clamping was 64 mins. Internal mammary and saphenous vein grafts were used in all patients (average 3.4±1.0).

CRITERIA FOR PMI DETECTION:

ECG. A standard 12 lead ECG was recorded preoperatively and repeated on each of the first three postoperative (P.O) days. Interpretations for transmural PMI was according to definite and probable criteria for infarction utilizing the Minnesota code.[2]

Echocardiogram. Standard parasternal, apical and subcostal scans were recorded from all patients pre and post surgery and was stored on video tape. A new akinetic segment appearing P.O. was considerated indicative of a PMI.

Pyrophosphate Scan. Technetium pyrophosphate scans (T.P.S.) were obtained preoperatively and 2-4 days P.O. in all patients. Scans were defined abnormal if discrete focal myocardial uptake was identified with intensity equal to or greater than rib.

TABLE 1

CLASSIFICATION OF PATIENTS BY VARIOUS CRITERIA

| GROUP | n | ECG | Echo | Pyrophosphate | CKMB(16hr) |
|---|---|---|---|---|---|
| A. Non-MI | 68 | - | - | - | - |
| B. Indeterminate | 10 | ± | - | - | - |
| | 1 | - | ± | - | - |
| | 14 | - | + | - | - |
| | 1 | + | - | - | - |
| | 2 | ± | + | - | - |
| | 1 | - | - | ± | - |
| Subtotal: | 29 | | | | |
| C. MI | 1 | + | + | + | + |
| | 1 | - | + | + | + |
| | 1 | + | - | + | + |
| Subtotal: | 3 | | | | |
| TOTAL: | 100 | | | | |

Cardiac Enzymes. Blood samples were drawn, two days preoperatively and P.O. at time zero (admission to S.I.C.U.), and at 8, 16, 24, 48 hours. Total CK, andAST was measured at 37°C using a Dupont aca analyzer.Serum CKMB was determined using a Dupont analyzer with a reference range of 0-7 u/l. CKMB was also measured by agarose gel electrophoresis.

Results. According to their ECG, echocardiogram and T.P.S. results, the patients were divided into 3 groups. Group A: negative for MI (n=68), Group B: intermediate (positive (+) or borderline (±)) for MI by one or more of the criteria (n=29), Group C: positive for MI by 2 or all 3 of the techniques (n=3). Table 1 shows the classification of patients groups. Group A and C were easily defined. Group B patients were in a "gray" zone. This included patients where the interpretation was borderline or where there was some difficulty in interpretation (ie. ECG conduction disturbances). Table 2 shows CKMB enzymatic results for the 3 groups. The highest enzyme results in each group at the designated sampling time are shown. The enzyme results for all 3 patients in Group C show that there was a clear separation of the 3 Group C patients vs Group A and B at 16 and 24 hours postoperatively by CKMB (aca). The same clear separation was shown to be similar at 16 hours for the CKMB (electrophoresis) and at 16, 24, 48 hours for AST.

Discussion. The criteria selected to define PMI are arbitrary. In our study, 3 patients were positive for PMI by T.P.S. plus at least one or other criteria - ECG or echocardiogram. Examination of the enzyme data revealed that the 3 M.I. patients can be clearly separated from all other patients by results of serum CKMB and AST at 16 hours P.O. From this data all CKMB results greater than 21 u/l by the Dupont aca method and/or 54 u/l by the electrophoretic method are considered "positive" for P.M.I.

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TABLE 2

SERUM CKMB BY DUPONT aca

| GROUP | NUMBER OF POSITIVE CRITERIA | NO. OF PATIENTS n | HIGHEST ENZYME VALUE AT TIME (HOUR) POSTOPERATIVELY | | | | |
|---|---|---|---|---|---|---|---|
| | | | 0 | 8 | 16 | 24 | 48 |
| A | 0 | 68 | 44 | 18 | 21 | 18 | 18 |
| B | ±1 | 11 | 47 | 22 | 12 | 8 | 7 |
| | ±2 | 1 | | 2 | 2 | 1 | 0 |
| | 1 | 15 | 42 | 22 | 11 | 8 | 5 |
| | ±1, 1 | 2 | 35 | 13 | 9 | 15 | 6 |
| C | 2 | 2 | 9 | 12 | 75 | >125 | 30 |
| | | | 22 | 43 | 55 | 46 | 10 |
| | 3 | 1 | 5 | 29 | 102 | 83 | 36 |

## INOTROPIC EFFECT OF CALCIUM ON STUNNED MYOCARDIUM

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**INTRODUCTION:**
Controversy exists regarding the use of calcium as an inotrope in patients with coronary artery disease. Calcium has been shown clinically and experimentally improve cardiac function[1,2]. However, concern exists regarding its potential to aggravate ischemic injury[3]. Despite this controversy, the effect of calcium on the function of post-ischemic or stunned myocardium, at normothermia, has not previously been studied. We therefore measured systolic shortening in normal and stunned myocardium before and after calcium administration in a canine model of ischemia and reperfusion.

**METHODS:**
Eight mongrel dogs (28 ± 5.5 kg) were anaesthetized with nembutal (25 mg/kg bolus + 2 mg/kg/hr), fentanyl (23 ug/kg + 0.8 ug/kg/hr), pancuronium (5 mg bolus), and mechanically ventilated. The heart was exposed via a left thoracotomy. A hydraulic occluder placed on the left anterior descending (LAD) artery just distal to the first diagonal branch. To create post ischemic or 'stunned' myocardium the LAD was occluded for fifteen minutes then reperfused. The percent systolic shortening (%SS) was measured using pairs of piezoelectric crystals implanted in the LAD and circumflex (CX) myocardium prior to ischemia. The %SS was calculated as:

$$((EDL-ESL)/EDL)\cdot 100$$

where EDL is end-diastolic length and ESL is end-systolic length. A positive value denotes systolic shortening whereas a negative value denotes systolic lengthening. The %SS was measured prior to and for 15 minutes after calcium chloride (10 mg/kg IV bolus). Heart rate was controlled throughout the experiment with atrial pacing. In order to distinguish the direct effect of calcium on %SS from any indirect effect mediated through increased blood pressure, %SS 30 seconds after calcium administration was compared to 2 values : (1) the pre calcium control and (2) a pre calcium value during transient partial aortic occlusion at a peak LV pressure similar to that 30 sec post calcium. Results are expressed as mean ± SD. Data was analyzed by t tests or repeated measures ANOVA with Dunnett's test where appropriate; $p<0.05$ was considered significant.

**RESULTS:**
LAD occlusion and reperfusion resulted in a significant decrease in systolic shortening. Four dogs required defibrillation by DC countershock upon reperfusion. They were given calcium 15 minutes later. The remaining dogs were given calcium at 3 hours reperfusion. Data was pooled as there was no statistically significant difference between groups. Heart rate did not change significantly during the study period. Calcium chloride caused a statistically significant increase in %SS for 30 seconds in post-ischemic (LAD) myocardium and for 5 minutes in non-ischemic (CX) myocardium (Table). A transient increase in blood pressure accompanied the increase in systolic function. The %SS was significantly greater 30 seconds post calcium than during aortic occlusion prior to calcium, though the blood pressure was similar.

**TABLE:**

| | LVP-S | %SS-LAD | %SS-CX |
|---|---|---|---|
| PRE CaCl | 141±14 | -1.8±6.7 | 11.2±2.8 |
| 30 sec. | 152±18* | 2.0±5.7* | 14.2±3.3* |
| 1 min. | 156±23* | 0.5±6.6 | 13.9±3.3* |
| 5 min. | 152±18* | -0.7±6.9 | 12.8±3.2* |
| 10 min. | 145±22 | -0.5±5.9 | 12.3±2.4 |
| 15 min. | 138±24 | 0.2±6.0 | 12.0±2.5 |
| AoOCC | 150±22 | -2.7±6.1♦ | 9.7±3.3♦ |

LVP-S = peak LV systolic pressure
mean ± S.D. N=8 (except for 5, 10, 15 min. N=7)
* $p < 0.05$ compared to PRE CaCl
♦ $p < 0.005$ compared to 30 sec. post Calcium

**CONCLUSIONS:**
Intravenous calcium chloride (10 mg/kg bolus) increases blood pressure and systolic shortening in both post-ischemic and normal myocardium. The improvement in systolic shortening is not a result of an increase in blood pressure, since systolic shortening at similar blood pressures is higher post-calcium. Although the effect of calcium appears more transient in stunned than normal myocardium, there is a positive inotropic effect in both. Longer term effects of calcium on post-ischemic myocardium are yet to be determined.

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# PERIPHERAL NERVE INJURIES IN CARDIAC ANAESTHESIA

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Injuries to peripheral nerves during cardiac surgery are common[1]. In a recent report of closed-claim malpractice suits from the United States[2], these injuries were the second most common type of anaesthesia-related complication to give rise to a lawsuit . The present study was designed to investigate the frequency of injury to the ulnar nerve, and to identify patient and procedural factors associated with the development of such injuries, in patients undergoing coronary artery bypass (CABG) surgery.

**Methods:** Twenty patients undergoing CABG involving one to four vein and/or left internal mammary artery grafts gave informed consent and were studied prospectively. Patients with clinical evidence of a peripheral neuropathy or with diabetes mellitus were excluded.

Electrophysiological testing of the ulnar nerve bilaterally included motor studies to determine motor conduction velocity across the various regions of the arm, and if necessary multiple point stimulation across the elbow to determine the exact site of slowest conduction velocity. Sensory pathways were assessed using ulnar nerve stimulation at the wrist.

All patients had high dose narcotic anaesthetics using fentanyl or sufentanil, administered by one of nine anaesthetists. Patients were positioned with their arms tucked at their sides in all cases, with the elbows and hands padded with absorbent cotton pads, and the position of the elbow (supinated, pronated, or mid-positioned) was noted. All patients underwent non-pulsatile cardiopulmonary bypass using alpha-stat ph management protocols. The "Favaloror" sternal retractor was used to facilitate dissection of the internal mammary artery in 12 cases.

Demographic and other data about the patient and the case was collected as noted in the table. Statistical analysis of associated variables used Student's T-test and Chi squared analysis as appropriate.

Table: Patient and Procedural factors assessed

Patient factors:
age, height, weight, BSA, BMI, chest size (CXR dimensions). Subjective assessment of patients size.

Procedural factors:
number of grafts; use of IMA retractor; anaesthesia, surgery, cardiopulmonary bypass or aortic x-clamp duration; anaesthesia, pump, or total intraoperative fluids; attempts at internal jugular vein catheterization. Position of arms. Intensive care unit sedation; duration of unconsciousness postop, ICU stay, and hospital stay.

**Results:** All patients had baseline nerve conduction studies performed within 48 hours preoperatively. An initial postoperative assessment was carried out at 24-48 hours in 14 patients, and within 3-6 days in the other 6 patients. Fourteen patients had studies a second time at 4-6 weeks, and 2 patients a third time at 6-12 months. Clinical examination was often not possible at the first post-operative examination, but was completed subsequently.

All patients were clinically normal preoperatively. One third (11 of 20 patients, 13 of 40 limbs studied) showed subclinical ulnar neuropathies preoperatively on electrophysiologic examination.

One patient developed symptoms and signs of ulnar nerve injury immediately postoperatively, and one patient had signs of right brachial plexus injury, although he had no complaints. At the first postoperative examination, 8 of 20 patients developed from 10-40% slowing in nerve conduction velocity across the elbow (3 at the cubital tunnel and 5 in the post-condylar segment, 6 left-sided, 2 right- sided). Six of these patients had normal conduction preop, and two developed significant worsening of abnormalities present preop. Nine of the 11 patients with preop abnormalities were unchanged postop.

At 4-6 weeks, a second patient had developed signs of ulnar neuropathy, despite being clinically and electrophysiologically normal at the first post-operative examination. Electrophysiologically, 4 of 6 patients with abnormalities immediately postop had returned to normal, 2 patients had the same abnormality, and 2 patients had developed new conduction abnormalities, one of which was clinically apparent and had developed denervation potentials in addition to conduction slowing.

Statistical analysis of associated factors identified significant factors as follows: age (with lesion 63±8 years vs 56±6 years without, $p < .05$), sedation during the first ICU day (morphine, 8.3±7 mg vs 2.5±2 mg, $p < .05$), and the anaesthetist's assessment of the patient's body size on the OR table (large/medium/small: 6 of 8 injured patients were 'large' vs 1 of 12 not injured, $p < .05$). No specific measurement of body size reached statistical significance, although the trend in each measurement was for injured patients to be larger. Total fluids administered by the anaesthetist intraoperatively (2.2±.6 l vs 3.1±.9 l) was just short of statistical significance ($p = 0.053$).

Left first rib fractures were noted on routine chest radiograph in two patients, one of whom had a subclinical left ulnar neuropathy early postop, while the other was normal. The single patient with brachial plexus abnormality had no bony injury on rib radiograph and CT scan.

**Summary:** Clinical nerve damage in patients undergoing CABG is frequent (15% of patients), while subclinical changes in ulnar nerve function are more common (40% here). Not all injuries develop in the early perioperative period. Most injuries are located at the elbow, and most recover without sequelae. Larger patients appear to be at most risk, but this study does not identify specific interventions which might decrease the risk of injury.

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## CEREBRAL HAEMODYNAMICS IN INFANTS DURING CARDIOPULMONARY BYPASS

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### INTRODUCTION:

Recent reports using reflectance spectroscopy[1], Xenon microspheres[2], and transcranial doppler (TCD)[3] suggest that cerebral autoregulation is not preserved in infants, during non-pulsatile cardiopulmonary bypass (CPB), regardless of the method of acid-base management. Others, using measurements of cerebral metabolic rate for oxygen ($CMRO_2$), with alpha-stat (not temperature corrected) acid-base management, found definite cerebral autoregulation during profound hypothermic, non-pulsatile CPB (PHCPB) in dogs and reported an abrupt decline in $CMRO_2$ when perfusion fell below 30 mmHg[4]. The role of blood gas management during CPB and its effect on cerebral haemodynamics remains controversial[5].

### METHODS:

With institutional approval, cerebral haemodynamics were investigated in 6 infants, during normothermic CPB (35-37°C)(NCPB), moderate hypothermic (<26°C) (MoHCPB) and PHCPB (<20°C), using alpha-stat methods of acid-base CPB management. A range-gated, pulsed wave, TCD was used, (Medasonics, Canada) with the transducer probe placed over the temporal region, to display middle cerebral artery (MCA) flow with some anterior cerebral artery flow, seen as retrograde flow, to ensure a reproducible window. Mean systemic blood pressure (MAP) was measured using a radial or femoral arterial catheter. Anterior fontanelle pressure (AFP), using a Ladd transducer, nasopharyngeal temperature (NPT), carbon dioxide tension ($PaCO_2$), and haematocrit (Hct) were also recorded. Cerebral perfusion pressure (CPP) was calculated as the difference between MAP and AFP. Cerebral blood flow velocity (CBFV) was plotted against CPP for the three temperatures. Linear regression analysis and coefficient of determination ($r^2$) was used to compare plots of CBFV versus CPP during NCPB, MoHCPB and PHCPB.

### RESULTS:

Six infants (9.2 ± 11.2) weeks of age, had CBFV measurements over a range of CPP from 10-80 mmHg during NCPB (n=5)(fig 1) and MoHCPB (n=5)(fig 2). PHCPB measurements were only possible in 1 infant for a range of CPP (fig 3). $PaCO_2$ (36±7 Torr) and Hct (0.26 ± 0.01) were maintained in a narrow range during the study period (mean±SD). Autoregulation appeared to be intact during normothermic CPB ($r^2$=-0.017), ie no relationship between CPP and CBFV. However, during MoHCPB (fig 2) there was a relationship between CBFV and CPP ($r^2$=0.544), indicating that cerebral blood flow is pressure-passive. This relationship was more pronounced during PHCPB (n=1) (fig 3).

### DISCUSSION:

Cerebral autoregulation is preserved in infants, during NCPB, but at <26°C CBF becomes pressure-passive (ie. MoCPB and PHCPB). This is in agreement with previous reports some of which used invasive methods for investigation of cerebral haemodynamics[1,2,4]. Our results indicate how non-invasive methods may be used to investigate cerebral haemodynamics during CPB. AFP measurement, during CPB, may offer advantages to CVP to determine CPP .

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Fig 1.

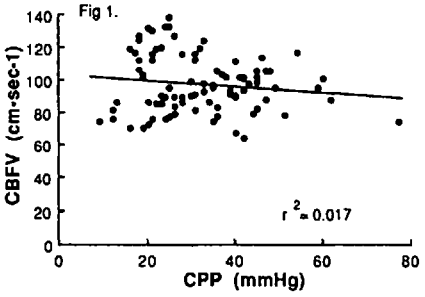



Fig 2.

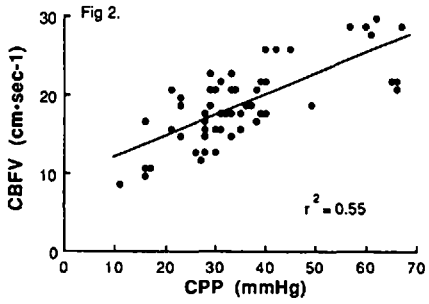
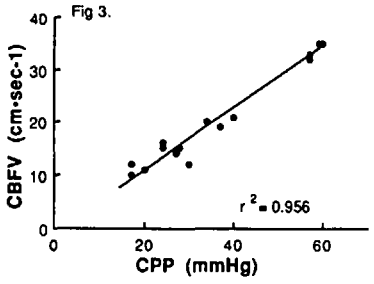



Fig 3.



# CENTRAL VENOUS HEMOGLOBIN SATURATION INACCURATELY ESTIMATES $S\bar{v}O_2$.

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Introduction. Several studies have assumed central venous oxygen saturation accurately reflects the truly mixed oxygen saturation of the pulmonary artery ($SvO_2$).[1,2] These studies have tended to be correlational in analysis rather than focusing on quantitative differences between saturations acquired from anatomically different sites.

The present study evaluates two aspects of venous saturation monitoring in a porcine model: 1) Can venous saturation outside the pulmonary artery (PA), i.e. right ventricle, right atrium and inferior and superior caval veins, replace mixed venous saturation? 2) Do fiberoptic venous catheters accurately measure saturation outside the PA?

Methods. Nine Yorkshire swine (35-40 kg) were induced with ketamine (18 mg $kg^{-1}$) and tracheostomized. Each was ventilated with 15 ml $kg^{-1}$ and an $FIO_2$ of 0.30. Maintenance anesthesia consisted of fentanyl (40 µg $kg^{-1}$ $hr^{-1}$) and ketamine (5 mg $kg^{-1}$ $hr^{-1}$) and muscular relaxation with succinylcholine (9 mg $kg^{-1}$ $hr^{-1}$). Two identical fiberoptic pulmonary artery catheters were placed in the PA as verified by pressure tracings. One was inserted via the right internal jugular vein and the other via the right femoral vein such that the light signal and balloon inflation of one catheter did not interfere with the other. After both catheters were placed an *in vivo* calibration was performed and the oximeters standardized to a conventional bench oximeter. The saturations were recorded from both blood samples and both oximeters. Two trials followed: While one catheter remained stationary in the PA, the other was retracted into the right ventricle (RV), 1(RA1), 3, 5 and 8 cm out of the ventricle(positions 3, 5, and 8). After 10 min of stable saturations at each position fiberoptic saturations were recorded concurrently with blood samples collected from each catheter. These samples were immediately analyzed by bench oximetry. After saturations were recorded at position 8 the mobile catheter was placed back into the PA (PA2) and saturations recorded. Trial 2 consisted of the same procedure as trial 1 with the exception that the other PA catheter became mobile. The order of catheter retraction (i.e. IVC or SVC) was randomized between animals. Saturation data was expressed as mean±SEM for each of two groups (IVC=9, SVC=9). Analyses of variance were used to compare: 1) bench oximetry saturations between samples taken at the PA and samples taken at subsequent experimental positions; 2) bench oximetry and fiberoptic saturations of mobile catheters.

Results. Table 1 shows saturation data (mean±SEM) measured by bench oximetry from the stationary catheters ($COOX_{PA}$) and mobile catheters ($COOX_{MOB}$) for both IVC and SVC retraction trials. Significant divergence ($p<.05$) is symbolized (*) at positions where the difference between values is statistically different from the difference at $PA_1$. There was no difference at $PA_1$. This divergence occurs in the IVC retraction at position 1($RA_1$) and remains until the mobile catheter is reinserted into the PA ($PA_2$). Divergence in the SVC does not occur until position 3 but also remains until $PA_2$. Table 2 compares fiberoptic and bench oximeter saturations for the mobile catheters in both IVC and SVC retraction trials. Divergence and significance are expressed as in Table 1. In the IVC retraction the catheters become divergent at position 1 and remain so until $PA_2$. Divergence does not occur at any position in the SVC trials.

Table 1.

| | Position of mobile catheter | | | | | | |
|---|---|---|---|---|---|---|---|
| IVC | $PA_1$ | RV | $RA_1$ | 3 | 5 | 8 | $PA_2$ |
| $COOX_{PA}$ | 44±2 | 44±2 | 45±2* | 49±3* | 50±3* | 49±4* | 48±4 |
| $COOX_{MOB}$ | 44±2 | 47±2 | 41±2 | 43±34 | 45±3 | 40±3 | 48±3 |
| SVC | | | | | | | |
| $COOX_{PA}$ | 48±3 | 47±3 | 47±3 | 46±3* | 47±3* | 48±3* | 48±3 |
| $COOX_{MOB}$ | 48±3 | 47±3 | 48±4 | 50±4 | 53±4 | 55±4 | 48±3 |

Table 2.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| IVC | $PA_1$ | RV | 1 | 3 | 5 | 8 | $PA_2$ |
| $COOX_{MOB}$ | 44±2 | 47±2 | 41±2* | 43±3* | 45±3* | 40±3* | 48±3 |
| $FIB_{MOB}$ | 44±2 | 49±2 | 48±2 | 48±2 | 51±3 | 45±4 | 49±3 |
| SVC | | | | | | | |
| $COOX_{MOB}$ | 48±3 | 47±3 | 48±4 | 50±4 | 53±4 | 55±4 | 48±3 |
| $FIB_{MOB}$ | 47±3 | 51±3 | 48±3 | 51±3 | 54±3 | 59±4 | 47±2 |

Discussion. Although correlational studies have found central venous saturations to be an adequate estimate of $SvO_2$,[3,4] the results of this study suggest caution must be exercised in regard to where the sample is acquired. Using statistical criteria it was found that the only locations in this study yielding saturations not different from PA was the RV and retracting through the SVC one cm into the right atrium. In general, the farther away from the PA saturations were measured, there was an increase in the divergence between PA and central venous saturations. In addition, it was found that fiberoptically measured saturation was most effective for central venous oxygen saturation measurement in the SVC retracted catheters. We conclude that when it is essential to acquire accurate saturation data that it can only be obtained from the PA with good reliability.

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# TRANSFUSION USING A CELL SAVER APPARATUS DURING SURGERY FOR CORONARY ARTERY DISEASE: IS IT BENEFICIAL?

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**INTRODUCTION:** Anesthesiologists frequently initiate transfusion therapy during surgery and should be aware of alternatives to transfusion of homologous blood products. Employment of devices, such as the Hemonetics® Cell Saver apparatus (CSA), which reduce homologous transfusion requirements is increasing but concern that utilisation will result in increased bleeding due to removal of platelets and plasma persists.[1,2] The enhanced concern about blood borne illnesses has also led to an increased willingness to accept lower hemoglobin and hematocrit levels during surgery and previous transfusion studies may be invalid due to these changes in transfusion practices. This retrospective study of patients having uncomplicated coronary artery bypass graft surgery (CABG) sought to determine: 1) whether utilisation of the CSA device reduced or increased exposure to homologous blood products; 2) whether such use increased the risk of post surgical bleeding.

**METHODS:** The medical records of all CABG patients for the months of February/March 1987 were reviewed. Hematocrit (HCT) was recorded prior to induction of anesthesia, before CPB, just after initiation of CPB, during the phase of maximum hypothermia (25-28°C), prior to discontinuing CPB, and prior to transfer to the ICU. Homologous transfusion requirements were determined by examining the anesthetic record and the laboratory record of blood products issued for the patient. Donor exposure was defined as transfusion of 1 unit of packed red blood cells, plasma, platelets, or cryoprecipitate. The number of autologous units (1=250 ml) transfused was determined by reviewing the CSA transfusion record. Excessive bleeding was defined as a requirement for >10 component blood products in the first 24 hr following initiation of surgery. Patients who had surgery other than first time non-emergent CABG, whose hospital stay extended beyond 15 days or died were excluded. Statistical analysis was by ANOVA or Chi-square analysis as appropriate with $p<0.05$ taken as a significant difference.

**RESULTS:** Of the 134 patients who met the criteria for inclusion, 3 distinct groups were identified based on their transfusion requirements. Group 1 (No Hemonetics®-NH; n=54) received no autologous transfusions during surgery. Group 2 (Hemonetics®; n=47) received only autologous transfusions during surgery. Group 3 (PC+Hemonetics-PCH; n=33) received both homologous and autologous transfusions. Demographics and donor exposure history are shown in Table 1.

**TABLE. DEMOGRAPHICS AND HOMOLOGOUS BLOOD PRODUCT DONOR EXPOSURE IN THREE GROUPS OF PATIENTS HAVING CABG SURGERY.**

| | NH (n=54)[1] | H (n=47)[2] | PCH (n=33)[3] |
|---|---|---|---|
| Age(yr) | 61±9 | 59±10 | 64±8 ** |
| Sex(M/F) | 41/13 | 44/3 * | 17/16 ** |
| BSA($m^2$) | 2.0±.2 | 2.0±.2 | 1.8±0.2 ** |
| Initial HCT(%) | 39±4 | 41±5 ** | 37±3 ** |
| CPB Time(min) | 82±18 | 98±33 ** | 103±26 ** |
| No. Grafts | 3.6±1.3 | 3.1±1.1 ** | 3.2±1.0 |
| Donor Exposure (Units) O.R. | 1.2±1.4 | 0±0 ** | 2.5±3.0 |
| TOTAL DONOR EXPOSURE | 3.7±8.3 | 0.6±1.8 * | 3.7±3.5 |
| CSA(Units) | 0 | 3.6±1.2 ** | 3.8±1.4 ** |

[1]Patients in this group received no autologous blood intraoperatively.
[2]Patients in this group received no homologous blood intraoperatively.
[3]Patients in this group received both autologous and homologous blood intraoperatively.
*p<0.05 vs PCH
**p<0.05 vs NH

**DISCUSSION:** Use of the CSA significantly reduced the requirement for homologous transfusions by 4-6 fold. Increased transfusion requirements were required for women or patients with a small BSA suggesting that use of the CSA alone is insufficient in meeting transfusion requirements in this sub-group of patients. There was no excessive post-op bleeding attributable to use of the CSA. We conclude that, despite current changes in transfusion practices, in patients having uncomplicated CABG use of the CSA is safe and reduces requirements for homologous blood products.

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# A COMPARISON OF DILTIAZEM, ESMOLOL, NIFEDIPINE AND NITROPRUSSIDE THERAPY OF POST-CABG HYPERTENSION.

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## Introduction

The treatment of post ACB hypertension (HT) by sodium nitroprusside (SNP) has been shown to result in ischaemic metabolism without a reduction in coronary sinus blood flow, suggesting intracoronary steal.[1,2] The calcium antagonists diltiazem (DTZ) and nifedipine (NIF) used intra-venously to treat HT may increase collateral coronary perfusion. Esmolol (ESM), an ultra fast-acting beta blocker administered for HT, may have beneficial effects on myocardial metabolic demand.

## Methods

After institutional approval and individual informed consent, 77 patients who developed post ACB HT (MAP>95mmHg) were studied in a prospective randomized trial. All drugs were administered intravenously by preset protocols and titrated to maintain the MAP at 85mmHg.

Haemodynamic data were recorded throughout. Left ventricular (LV) pressures (by intraventricular Millar manometer catheters) and volumes (by nuclear ventriculography) were assessed before and after therapy in response to volume loading (VL) (2 mmHg increase in PCWP) and atrial pacing (AP) (110 beats /min). The effects on systolic function were estimated by examining the end-systolic pressure (SBP) vs volume (ESVI) relationship; myocardial performance was evaluated by comparing LV stroke work index (SWI) at given end diastolic volumes (EDVI). Arterial and coronary sinus blood samples were collected to determine myocardial lactate production and oxygen extraction.

Haemodynamics were evaluated using one-way and two-way analysis of variance, Duncan's multiple range test and paired t tests. Ventricular function was assessed by analysis of covariance.

## Results

All four patient groups were demographically similar. All agents effectively reduced MAP. One patient developed sinus arrest with DTZ therapy and required AV pacing.HR decreased with ESM and DTZ. CI decreased with ESM alone. SNP enhanced systolic function (lower ESVI at higher SBP) and myocardial performance (higher SWI at lower EDVI) while ESM depressed both systolic function and myocardial performance. NIF and DTZ were intermediate in effect on heart function. With AP,DTZ enhanced $O_2$ and lactate extraction significantly better than other therapies.

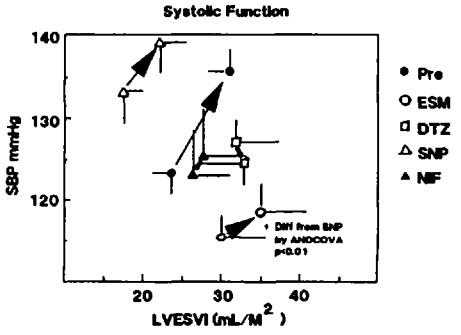
## Conclusions

All four agents effectively treat post-ACB HT.

DTZ results in lower HR, intermediate depression of ventricular function and improved oxygen/lactate metabolism. However, its slow onset, longer duration of action and effects on A-V conduction make it more difficult to titrate safely.

SNP enhances ventricular function while ESM depresses it. NIF has intermediate effects.

Pharmacologic reduction of post-operative HT-induced anaerobic metabolism is optimally achieved with agents which depress systolic function. Combinations of such agents with vasodilators may be the technique of choice.

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Supported by HSFO

## THE CONTRIBUTION OF PHARYNGEAL SUCTION DEVICES TO SORE THROAT AFTER ENDOTRACHEAL ANAESTHESIA

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**INTRODUCTION**:
Sore throat after endotracheal intubation occurs in approximately 40% of patients (1). The commonly used Yankauer rigid suction device can induce pharyngeal mucosal damage as evidenced by blood on the tip following suctioning. We believe that the routinely used rigid Yankauer pharyngeal suctioning device may be responsible for a significant portion of post-operative sore throats.

Our hypothesis was that pharyngeal suctioning with a softer, less traumatic device would decrease the incidence of postoperative sore throat.

**METHODS**:
In a randomized, blind, prospective study approved by our institutional ethics committee, 100 patients were either assigned to the hard suction (HS) or soft suction (SS) groups. Inclusion criteria were consenting ASA I or II volunteers ages 18-65 booked for elective surgery under general endotracheal intubation lasting under 2 hours in the supine position. Exclusions were those with pre-op sore throats, gastroesophageal reflux, difficult or traumatic intubation, intra-abdominal, thoracic or head and neck surgery.

At the end of a standardized general anaesthetic, the HS group had the pharynx cleared with the Yankauer device. The SS group had pharyngeal suctioning with a soft 18Fr endotracheal tube control suction catheter.

Sore throat and difficulty swallowing were assessed by visual analogue scale (VAS) preop, and at two and 24 hours postop.. The patient and the investigator administering the VAS were blinded to the type of suction device used.

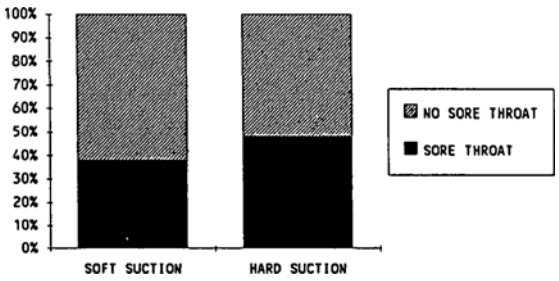
Data were expressed as mean +/- standard deviation. Comparisons were performed using an unpaired Student's t-test for age, weight, intubation time, Wilcoxon for VAS, and ANOVA with Sheffe's correction for VAS over time.

**RESULTS**:
There were no significant differences in age, sex, weight, smoking, or intubation time between groups. Also there was no difference in the amount of coughing or blood present in the suctioning device between groups. There was a significant increase in the incidence in sore throats 2 hours post-op as compared to pre-op within both groups ($p<0.05$). However there was no difference in the incidence of sore throat pre-op, at 2 or 24 hours post-op between groups. Similarly, there was no difference in the incidence of nausea or difficulty swallowing between groups at any time.

**DISCUSSION**:
In this study the occurrence of postoperative sore throat was not affected by the type of pharyngeal suction device used.

This may indicate that pharyngeal irritation caused by pre-extubation pharyngeal suctioning is not an etiologic factor in postoperative sore throat.

**INCIDENCE OF SORE THROAT 2 HR POST-OP**

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# PULMONARY PRESSURES AT HIGH FLOWS IN THE INTACT PULSATILE FLOW PERFUSED LUNG

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Introduction: It is well known that pulmonary blood flow can increase to quite a large degree with only a small increase in pulmonary artery pressure. Modern textbooks still attribute this phenomenon to recruitment and distension of the pulmonary circulation. If this is the case one would not expect the relationship between pressure and flow to be linear. Work using in-situ roller perfused lungs has found that the pulmonary pressure flow relationship (PPFR) is linear in the physiologic range and up to flows 500% of normal[1,2]. The only work analysing the PPFR in intact animals over a comparable range was done by Lategola[3]. His work suggested that at flow increases of greater than 250% there was a marked change in the pressure flow relationship. The reason for this discrepancy is not immediately clear.

Using a combination of arteriovenous (a-v) fistulas and inferior vena cava (IVC) occlusion, pulmonary pressure flow curves can be easily generated in the intact animal[4]. By modifying this technique we are able to generate pulmonary pressure flow curves over a broader range of flows and pressures than has been previously done in the intact, resting animal using pulsatile flow. The purpose of this study was to see if indeed there is a break from linearity at higher pressure and flows in the intact resting lung.

Methods: Five Mongrel dogs (20-28kg) were anesthetized using pentobarbital 25 mg/kg. Anesthesia was maintained using a pentobarbital drip and pavulon. The animals were ventilated with 100% oxygen at a rate and volume sufficient to maintain normo-carbia throughout. An arterial line and swan ganz catheter were placed to facilitate measurement of arterial blood gases and standard hemodynamic variables. Two a-v fistulas were created and a fogarty occlusion catheter was placed in the inferior vena cava. The animal was placed in the left lateral decubitus position and a left thoracotomy was performed. The right pulmonary artery was identified, dissected free and a adjustable ligature placed around it. Hemostasis was achieved and the chest loosely closed with the ligature coming out through the wound. The animal was placed in the supine position and heparinized. The transducers were zeroed to the mid axillary line.

Pressure flow curves were generated by varying flow through opening and closing of the a-v fistulas in conjunction with inflating and deflating the IVC balloon. All hemodynamic measurements and cardiac output CO determinations were done during an expiratory pause. The pressure flow curves were done under two conditions; 1) with both lungs perfused; 2) with the right lung excluded from the circulation. Arterial blood gases were obtained prior to and after each curve was generated.

Data Analysis: The slope and pressure axis intercept for each animal in each condition were derived using linear regression. Flow was assumed to be the independent variable and pressure the dependent variable. The slopes, intercepts and alveolar arterial (A-a) oxygen gradient under the two conditions were compared using paired T-tests. Composite pressure flow curves using the data from both conditions were generated for each animal. The CO for one lung was scaled using a factor of 2.32 to allow for the greater cardiac output to the right lung[5]. The $r^2$ values for the scaled and unscaled data were compared using a repeated measures analysis of variance. All values are reported as mean +/- standard error of the mean.

Results: PA occlusion resulted in no change in (A-a) oxygen gradient. The pressure flow relationship for one lung and two lungs were well described by linear equations ($r^2$ = .83+/-.03 and .82+/-.04 respectively). The slope of the equations increased with PA occlusion (3.6+/.4 to 5.9+/-.9). There was no change in the pressure axis intercept with PA occlusion (8.34+/-.8 pre occlusion and 8.9+/-1.3 post occlusion).

When the data was scaled the relationship between pressure and flow remained linear. Flows ranged from 1-2 l/min (50-75% of normal) up to scaled values of 8-9 l/min (370% of normal). The mean $r^2$ value for the scaled pressure flow curves was .78+/-.05 which was not significantly different from the values seen with the unscaled data.

Discussion: Scaling the data requires the assumption that the vascular tone of the right and left lung were equivalent. The lack of change in the pressure axis intercept and the A-a gradient with right PA occlusion support this assumption.

This study confirms what has been found in the isolated roller pump perfused lung. The pressure flow relationships of the lung are essentially linear in the physiologic range and there is no break from linearity at higher flows. There is good evidence that recruitment and distension do occur with higher pressures and flows[6]. The linear nature of these curves suggests however that recruitment and distension are not resulting in large decreases in resistance. Thus the small rise in PA pressure seen with large increases in flow are due to the large cross-sectional area of the pulmonary bed rather than any large change in the vascular cross-sectional area due to recruitment and distension.

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# OXYGEN DELIVERY BY THE PERITONEAL ROUTE

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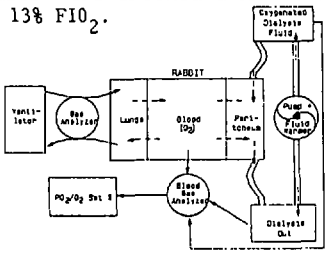
INTRODUCTION: The gas exchange in the alveolar capillary membrane depends on surface area, thickness of the membrane, the diffusion coefficient, and the partial pressure differences. This Fick's laws can be applied to any membrane.

The peritoneum has a large surface area and is permeable to solutes of molecular weight up to 30,000 Daltons. Splanchnic blood flow to the peritoneum is approximately 70 mls/minute and 25% of the blood volume in man is stored in the splanchnic circulation. During peritoneal dialysis the surface of the peritoneal capillary bed is more important than the total surface of the peritoneal membrane, yet these two parameters are thought to be closely related.[2]

In acute parenchymal lung diseases like ARDS and hyaline membrane disease; Infants born with a massive shunt needing correction; or any acute respiratory failure where lung recovery is possible, maintaining the oxygenation of tissues is vitally important. There are several methods which can be used for this purpose like different methods of artificial ventilation including high frequency ventilation and negative pressure ventilation; cardiopulmonary bypass (bubble & membrane oxygenators); extracorporeal membrane oxygenation, use of intravenacaval blood gas exchange devices; and increase oxygen carrying capacity by efficient $0_2$ carriers like flurocarbons and stroma free haemoglobin.

The object of this study is to determine the efficacy of oxygen tranfer through the peritoneum using well oxygenated dialysate fluid (Plasmalyte) in rabbits.

METHOD. With the IRBAR approval, we studied six healthy New Zealand white female rabbits. Anesthesia was induced with Ketamine 50 $mg.kg^{-1}$ IM and Xylazine 2 $mg.kg^{-1}$ IM. Tracheostomy was performed and subject was intubated and then ventilated with $N_20$ 66%, $0_2$ 33% and Isoflurane (0.75%-1.5%). IV cathetre was inserted in the ear and carotid artery cannulation done under direct vision. Subjects were paralised with Vecuronium 100 $mcg.kg^{-1}$. Two peritoneal cannulae (about 0.5 and 1 cm in diameter) were inserted and sutured carefully to prevent any leaking during dialysis. Baseline blood gas was sampled with $FIO_2$ of 21% $0_2$. Then the $FIO_2$ was reduced to 12 to 13% (checked with Datex gas analyses). Ventilation adjusted for the same blood gases were checked after 10 minutes of stabilization on 13% $FIO_2$.




Meanwhile dialysis fluid (Plasmalyte) was bubbled with 100% $0_2$ and checked the dissolved $0_2$ concentration.

Then continuous peritoneal dialysis (saturated with $0_2$) commenced. Arterial blood gases were analysed at 10, 20, 30 minutes.

Then rabbits were ventilated with no inspired $0_2$ (100% $N_20$) but maintaining the peritoneal oxygenation. Time taken to get $ETC0_2$ 0 was noted.

| Rabbit # | | $FIO_2$ 21% baseline | $FIO_2$ 12% baseline | $FIO_2$ 12% after treatment time 10min | 20min | 30min |
|---|---|---|---|---|---|---|
| 1 | $PaO_2$ | 86 | 38.8 | 62.5 | 75.2 | 86.8 |
| | $PaCO_2$ | 31.7 | 29.5 | 30.5 | 29.3 | 26.8 |
| | %Sat $O_2$ | 95.5 | 81.3 | 94 | 96.3 | 99.7 |
| 2 | $PaO_2$ | 127.8 | 34.4 | 74.7 | 56.1 | 111.2 |
| | $PaCO_2$ | 30.8 | 39.8 | 41.2 | 41 | 35.2 |
| | %Sat $O_2$ | 98.8 | 62.2 | 93.1 | 83.7 | 97.6 |
| 3 | $PaO_2$ | 61.1 | 29 | 30.4 | 44.7 | 62.1 |
| | $PaCO_2$ | 56.4 | 45.1 | 42.6 | 31.7 | 34.9 |
| | %Sat $O_2$ | 90 | 56 | 58.1 | 82.2 | 92.2 |
| 4 | $PaO_2$ | 138.7 | 78.4 | 132 | 143.2 | 150.2 |
| | $PaCO_2$ | 30.6 | 34.1 | 29 | 31.3 | 29 |
| | %Sat $O_2$ | 98.5 | 93.5 | 98.3 | 98.7 | 98.9 |
| 5 | $PaO_2$ | 84.5 | 45.5 | 70.1 | 62.3 | 73.6 |
| | $PaCO_2$ | 24.8 | 32.2 | 26.1 | 23.6 | 23.2 |
| | %Sat $O_2$ | 96.8 | 81 | 94.5 | 96.8 | 95.9 |
| 6 | $PaO_2$ | 110.9 | 43.1 | 64.8 | 109.14 | 81.8 |
| | $PaCO_2$ | 43.3 | 42 | 39.7 | 39.9 | 34.5 |
| | %Sat $O_2$ | 98.3 | 71.8 | 85.8 | 98.4 | 93.3 |

RESULTS. Results show augmentation of oxygenation by the peritoneal route is very satisfactory but as expected total oxygenation was not possible. No excessive fluid retension was noted and no gas trapping or surgical emphysema occurred.

DISCUSSION. In these hypoxic rabbit models we were able to augment the oxygenation by peritoneal route satisfactorily. The ability to remove $C0_2$ was remarkable. As the solubility of $0_2$ in $H_20$ at room temperature is 3.3 vol./100 vol., to supply the total $0_2$ demand, we need very high flows of the dialysis. The gas transfer depend on the splanchnic blood flow and the exposed surface area to the dialysate, any fault in the delivery system will markedly reduce the adequacy of the oxygenation. We conclude that with proper usage of this technique, one would be able to augment the adequate oxygenation and removal of $C0_2$ in a critically ill patient with acute respiratory failure.

The $0_2$ carrying capacity of the dialysate could be improved by using dialysates containing flurocarbons, or stromafree haemoglobin. Further studies using human subjects is needed. This is a simple technique with very few complications. This method shows promise of providing an artificial lung capability with substantial advantages over existing methods.

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# OXYGEN DESATURATION AND BREATHING PATTERNS IN PRE-OPERATIVE THORACIC PATIENTS

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INTRODUCTION: Many studies have shown that sedated and post-operative patients are susceptible to hypoxaemia and apneas[1,2]. It is also known that normal patients and those with COPD may exhibit disordered breathing and desaturation during normal sleep[3]. The current study was undertaken to determine the frequency of oxygen desaturation and disordered breathing pre-operatively in a typical thoracic surgical population.

METHODS: Data from 27 (18M,9F), ASA 1-2 thoracic surgery patients were reviewed. They had previously been included in epidural narcotic studies done by our group (with institutional approval). Patients with sleep apnea syndrome or severe COPD were excluded. All patients were studied the night prior to planned lung resection (24) or trans-thoracic hiatus hernia repair (3) using continuous respiratory inductive plethysmography (RIP). Continuous pulse oximetry was obtained on 23 of the patients. All patients had arterial blood gases taken prior to the monitoring period and 17 had in-dwelling arterial lines through which intermittent blood gas analysis was performed every two hours.

Pre-operative demographic data and pulmonary function tests were available for all patients. RIP data were analyzed for respiratory rates (RR), slow respiratory rates (SRR $\leq$10 breaths per minute), apneas (AP$\geq$15 seconds of Vt<100ml). Pulse oxygen saturation ($SpO_2$) average and minimum was determined. Arterial blood gases were analyzed for $pO_2$ and $pCO_2$.

Data are expressed as mean $\pm$ standard deviation. The Mann-Whitney U test was used where appropriate. A $p\leq.05$ was considered statistically significant.

RESULTS: Patient data are shown in TABLE 1. Of the 27 patients, 21 had more than one apnea, 13 had more than one apnea per hour and 4 met criteria for sleep apnea syndrome with 5 or more apneas per hour. SRR's were present in 9 with a lowest RR of 6/min. The lowest $SpO_2$ was 68%, the lowest $pO_2$ was 47mmHg. The maximum decrease in $SpO_2$ was 16 from the preceding 5 minute baseline. The lowest $pO_2$, $SpO_2$ or maximum decrease in $SpO_2$ did not significantly correlate with an AP or SRR. The highest $pCO_2$ was 53mmHg. Blood gas, RR, and oximetry data during the study are summarized in TABLE 2.

There was no difference in minimum $SpO_2$, SRR, or number of apneas between subgroups divided on the basis of sex, smoking, planned operation, clinical COPD, FEV1/FVC%, or pre-operative blood gases.

DISCUSSION: This study demonstrates that "normal" thoracic surgery patients have episodes of apneas, slow respiratory rates and desaturation during the night prior to surgery. None of the usual clinical criteria allow prediction of these patients. Any study that concludes that a certain treatment predisposes patients to intra- or post-operative breathing abnormalities or oxygen desaturation without monitoring the same patients pre-operatively may be in error.

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TABLE 1
PATIENT and STUDY DATA

| AGE years | %IBW Kg | FEV1/FVC % | SMOKE pack/yr | APNEAS /hour | $SpO_2$ drop | SRR %time |
|---|---|---|---|---|---|---|
| 60±10 | 111±18 | 63±10 | 28±28 | 3±5 | 5±3 | 3±9 |

*$SpO_2$ drop* is decrease from the preceding 5-minute baseline during a desaturation.

TABLE 2
VARIABLES versus TIME OF STUDY

| | awake | 2hrs | 4hrs | 6hrs | 8hrs | mean+SD |
|---|---|---|---|---|---|---|
| $pCo_2$ | 39±5 | 40±6 | 40±3 | 41±3 | 40±6 | 39±.6 |
| $pO_2$ | 82±8 | 82±12 | 79±9 | 81±10 | 75±15 | 80±3 |
| low $pO_2$ | 70 | 47 | 65 | 63 | 47 | ##### |
| $SpO_2$ | 97±2 | 96±1 | 96±1 | 96±2 | 97±2 | 96±1 |
| RR avg | 16±3 | 16±2 | 16±3 | 16±3 | 16±3 | 16±2 |

-all data pooled except *low $pO_2$* is the lowest measured for any patient.
-*$SpO_2$* is the average of the 5 minute averages for that hour in all patients

# EFFECTS OF SEVOFLURANE AND ENFLURANE ON CONTRACTILITY OF CANINE DIAPHRAGM

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## Introduction

Volatile anaesthetics have been known to interfere with the contractility of striated muscle in vitro[1], but data are not available regarding the effect of sevoflurane, a new inhalational agent, on diaphragmatic function in vivo. Therefore, the purpose of this study is to compare the effect of sevoflurane and enflurane on diaphragmatic contractility in vivo.

## Methods

Twelve healthy mongrel dogs weighing between 8 to 15 kg were anaesthetized with thiopental(25mg/kg iv), tracheostomized and mechanically ventilated throughout the experiment. Rectal temperature was monitored continuously with a thermistor and was maintained at a constant. All dogs were studied in the supine position. They were divided into two groups of six animals each, namely sevoflurane and enflurane groups. The strength of the diaphragm was quantified by measuring the trans diaphragmatic pressure (Pdi) which was generated by bilateral supramaximal phrenic nerve stimulations. Each phrenic nerve was hooked by the stimulation electrodes at the neck. To ensure same diaphragmatic lengths during the stimulation, the airway was occluded at functional residual capacity, and a closely fitted plaster cast was placed around the abdomen up to the lower part of the rib cage. Measurements were performed at the anaesthetic levels of 1, 1.5 and 2 MAC after 1 hour of exposure. The sequence of changing anaesthetic depths was altered in random fashion between animals.

## Results

The effects of sevoflurane and enflurane on Pdi at three different concentrations are summarized in the table. In the sevoflurane group, the amplitude of Pdi was significantly reduced only at 2 MAC during 100Hz stimulation. By contrast, increasing enflurane concentration significantly reduced the amplitude of Pdi at 50 and 100 Hz. Additionally, a significant decrease in Pdi at 20 Hz was observed at 2 MAC of enflurane.

Table Values of Pdi at different stimulation frequencies of phrenic nerve under three depths of sevoflurane and enflurane anaesthesia.

Sevoflurane group

| | 10Hz | 20Hz | 50Hz | 100Hz |
|---|---|---|---|---|
| 1 MAC | 12.0±1.8 | 28.6±2.8 | 37.3±3.5 | 35.5±3.7 |
| 1.5MAC | 11.8±1.9 | 27.9±3.6 | 32.8±4.2 | 31.5±4.3 |
| 2 MAC | 11.4±1.5 | 29.6±4.1 | 35.2±5.0 | 28.1±5.0※ |

※ $p<0.05$ vs 1 MAC, 1.5 MAC

Enflurane group

| | 10Hz | 20Hz | 50Hz | 100Hz |
|---|---|---|---|---|
| 1 MAC | 12.5±2.5 | 27.3±3.0 | 37.4±4.7 | 34.0±4.4 |
| 1.5MAC | 12.7±2.5 | 28.6±3.0 | 32.7±3.3 | 21.0±5.0* |
| 2 MAC | 11.0±2.1 | 22.8±3.3# | 25.3±4.1*# | 14.1±3.8*# |

* $p<0.01$ vs 1MAC, # $p<0.05$ vs 1.5 MAC
Mean±SE($cmH_2O$)

## Discussion

We found that the two inhalational anaesthetics impair the contractility of the canine diaphragm, and that such depressant effect was more marked in enflurane than in sevoflurane at 1.5 and 2 MAC. The changes in Pdi during high frequency stimulation (50-100Hz) are related to alterations in neuromuscular transmission and/or membrane excitability[2], whereas changes during low frequency stimulation (20Hz) are attributed to alterations in the excitation-contruction coupling process. Thus the results showing the decrease in Pdi at high frequency stimulation during sevoflurane and enflurane indicate impaired neuromuscular transmission and/or membrane excitability, presumably. The exact mechanisms underlying the different effects of sevoflurane and enflurane on diaphragmatic function in vivo remain unclear. Further studies are needed to determine the clinical importance of this phenomenon in man.

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# PHRENIC ARTERY BLOOD FLOW PATTERNS DURING AND AFTER TOF STIMULATION OF THE DOG DIAPHRAGM

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Introduction. Monitoring of neuromuscular blockade (NMB) has been standardized with respect to preventing fatigue of the neuromuscular junction,[1] but not with respect to its potential effects on muscle blood flow. A graded increase in blood flow has been shown to proportionally accelerate the onset of NMB in a perfused isolated preparation of dog gastrocnemius.[2] Recently in vivo studies have shown that train-of-four (TOF) stimulation of the dog diaphragm prior to muscle relaxant administration reduced the onset time and increased the degree of NMB for both succinylcholine and vecuronium.[3,4] The potentiation of NMB with TOF stimulation was associated with an increase in phrenic artery blood flow ($\dot{Q}_{ph}$) to the diaphragm. Since monitoring of NMB using TOF stimulation increases the effects of neuromuscular blockers probably through an increase in blood flow, it is important to determine how quickly after initiation of TOF stimulation muscle blood flow increases and to what degree. Furthermore what is even more relevant in setting up protocols studying NMB is how long after cessation of TOF stimulation does muscle blood flow return to control. Thus, we studied phrenic a. blood flow before, during, and after a predetermined period of diaphragmatic TOF stimulation.

Methods. This study was approved by our institutional animal care committee. Seven mongrel dogs (weight: 30-40 kg) were anesthetized with pentothal 10 mg/kg at induction and halothane 1% during maintenance. All animals were supine, intubated, and mechanically ventilated. $PO_2$ and $PaCO_2$ were maintained at $>$ 60 mmHg and between 35-40 mmHg, respectively. TOF stimulation of the diaphragm was achieved using a transvenous pacing catheter connected to a Grass S48 stimulator using supramaximal voltages at a frequency of 2 Hz for 2 sec every 10 sec. The evoked response of the diaphragm was measured using transdiaphragmatic pressure (Pdi) which is the difference between abdominal pressure and pleural pressure. Isometric contraction of the diaphragm was assured by binding the lower chest and abdomen with a cast. Blood flow to the diaphragm was estimated using a Doppler flow probe of appropriate size around the left phrenic artery.[5]

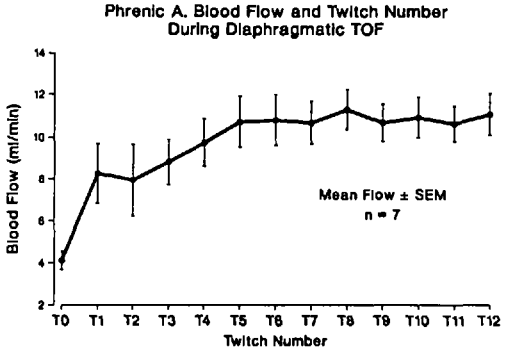
We measured CO, ABG's, and temp before stimulation; mean blood pressure, heart rate, $\dot{Q}_{ph}$ and Pdi were continuously recorded. After control measurements were taken at rest, we studied the change in $\dot{Q}_{ph}$ with each consecutive TOF (every 10 sec) during 3 min. Recovery of $\dot{Q}_{ph}$ after cessation of stimulation was measured also, every 10 sec for 180 sec. $\dot{Q}_{ph}$ was measured for another 3 min period after cessation of TOF. Data are presented as mean and standard error of the mean.

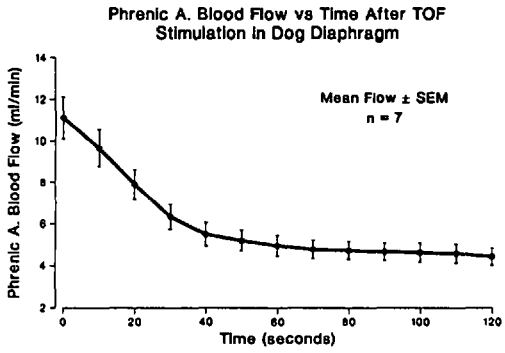
Results. Heart rate, blood pressure, acid-base status, temp and Pdi were constant throughout the experimental period. The graphs depict the mean $\dot{Q}_{ph}$ during and after TOF stimulation.

Discussion. TOF stimulation of the diaphragm increases $\dot{Q}_{ph}$ on the average 2-1/2 fold. This increase occurred consistently as early as the first twitch and was already twice control at that point, although a sustained plateau was not reached until the sixth twitch. From that point on blood flow was constant for the duration of stimulation. After cessation of stimulation, $\dot{Q}_{ph}$ had returned to control level by 120 sec in all animals. $\dot{Q}_{ph}$ had dropped by half at 40 sec after stimulation. In conclusion, in the dog diaphragm:

- a single TOF stimulation doubles $\dot{Q}_{ph}$.
- maximal increases in muslce blood flow are attained after 6 TOF's at 10 sec intervals.
- after 3 min of TOF stimulation muscle blood flow does not return to control levels until 2 min after cessation of stimulation.

If peripheral muscles have a similar degree of change in blood flow as does the diaphragm and these changes are similar in dog as in man then the implications are the following: (1) as little as one TOF immediately prior to NMB administration can alter the pharmacodynamics of the drug; (2) no stimulation should be performed for at least 2 min prior to muscle relaxant administration in order to measure the intrinsic properties of a muscle relaxant independently of the changes in blood associated with TOF monitoring.

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# COMPLICATIONS FOLLOWING TOTAL KNEE ARTHROPLASTY - DOES THE ANAESTHETIC TECHNIQUE MAKE A DIFFERENCE?

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**INTRODUCTION:** Complications following regional (RA) or general (GA) anaesthesia for total hip arthroplasty (THR) have been described.[1] Reduction of blood loss and thromboembolic events have been reported with the use of RA.[2-4] No comparison of complications following either RA or GA for total knee arthroplasty (TKR) is available.

This retrospective review compares the outcome of 165 TKR's using RA or GA.

**METHODS:** The charts for patients having first time TKR at one institution during 1987 were examined (n=165). From each chart demographic data, the surgical indication and the present and past disease profile were noted including history of remote myocardial infarction (MI), controlled congestive heart failure (CHF), stable angina, controlled hypertension, smoking, previous deep venous thrombosis (DVT) or pulmonary embolism (PE) and presence of respiratory disease, diabetes or antiinflammatory drug usage. Operative information included the anaesthetic technique, the identity of surgeon and anaesthetist, the duration of surgery, tourniquet application and anaesthesia (time between entrance to and exit from operating room of anaesthetist and patient), use of bone cement, crystalloid transfused and hemodynamic variability requiring pharmacotherapy.

Variables recorded for the postoperative period included length of stay and transfusion requirement in the recovery room (PAR), the duration of hospitalization and range of motion of the knee at discharge. Complications as recorded in the chart were arbitrarily classified as major or minor by system (Table). An early hemarthrosis was noted if greater than 500 ml blood was drained from the knee prior to discharge from the PAR.

Statistical differences ($p<0.05$) were determined using chi squared analysis, paired t-tests with Bonferroni correction, or a one-way analysis of variance.

**RESULTS:** There were 37 patients who received RA (36 spinal and 1 epidural block) and 128 patients who received GA. There were two patient deaths, one from each group. The groups were comparable for demographic data, surgical indication, present and past disease profile except for a higher incidence of remote MI in the RA group (RA: 8/37 vs GA: 7/128; $p<.05$). Duration of surgery and tourniquet application, cement use and crystalloid transfusion were comparable but duration of anaesthesia (RA:118±29.8 vs GA:106±19.6 min; $p<.05$) (all results mean ± SD) and PAR detention time (RA:319±152 vs GA:248±104 min; $p<.05$) were longer in the RA group. Transfusion of red cells before PAR discharge was greater in the RA group (RA:0.7±1.0 vs GA:0.4±0.8 units; $p<0.05$).

Hospital stay and range of motion of the operated knee at discharge were comparable.

The incidence of major (RA: 7 vs GA: 20) and minor (RA: 29 vs GA: 116) complications did not differ (Table). Patients with a history of previous MI were separately compared and no significant differences were noted.

**TABLE: NUMBER OF PERIOPERATIVE COMPLICATIONS IN A GROUP OF PATIENTS RECEIVING GA (n=128) OR RA (n=37) FOR TKR.**

| COMPLICATION | GROUP | | | |
|---|---|---|---|---|
| | GA | | RA | |
| | Major | Minor | Major | Minor |
| CARDIOVASCULAR | 3 | 37 | 2 | 6 |
| HEMATOLOGICAL | 2 | 0 | 1 | 1 |
| HEMARTHROSIS | 0 | 51 | 0 | 18 |
| INFECTIOUS | 6 | 7 | 0 | 2 |
| SKIN | 1 | 8 | 0 | 0 |
| GENITOURINARY | 2 | 7 | 2 | 4 |
| ANAESTHETIC | 4 | 4 | 0 | 0 |

**DISCUSSION:** There was no difference in the incidence or degree of complications following RA or GA. The absence of significant blood loss due to thigh tourniquet application, and less manipulation of iliofemoral veins (in a surgical procedure with an incidence of clinically significant thromboembolic complications comparable to general surgical patients[5,6,7]) makes TKR a procedure in which the documented benefits of RA for THR[1] may not be transferable. Conclusions from a retrospective study must be guarded. The possibility that RA offers no advantage over GA for TKR warrants further investigation with a prospective study.

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# DOES ANESTHETIC TECHNIQUE AFFECT THE OXYGENATION DURING ONE LUNG ANESTHESIA ?

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## INTRODUCTION

During thoracic surgery, one lung ventilation has been widely accepted in order to enhance the surgical exposure and to prevent the aspiration of blood and infected material to the dependent lung. One lung ventilation has been known to increase the intrapulmonary shunt and result in severe hypoxia, since the hypoxic pulmonary vasoconstriction is attenuated by general anesthetics and vasodilating agents. Although there have been several reports that the degree of the attenuated hypoxic pulmonary vasoconstriction depends on the choice of anesthetics, intensive study has not been performed. The present study was performed to evaluate whether choice of anesthetic technique, i.e., inhalational anesthesia, intravenous or epidural anesthesia, affects oxygenation differently during one lung ventilation.

## METHODS

Seventy-five patients undergoing thoracic surgery such as esophagectomy, lobectomy or pneumonectomy were involved in the present study with informed consents. Double-lumen endobronchial tube or an endotracheal tube with balloon occlusion catheter (Univent) was intubated, and PaO2, SpO2 by means of a pulseoximeter, and endtidal PCO2 were monitored. The maintenance of anesthesia was either by O2-enflurane (25 patients), fentanyl and diazepam (27 patients) or thoracic epidural block with N2O-O2 (23 patients). Pancuronium was given in all cases to facilitate muscle relaxation. The position of the tube or the balloon was confirmed by a bronchofiberscopy. Arterial blood gas was measured at FiO2 1.0 in lateral decubitus position before one lung ventilation (control). and 5, 10, 20, 30 minutes after the initiation of one lung ventilation. Preoperative pulmonary function, such as %VC and FEV1%, PaO2, chest X-ray, and the degree of obesity and the history of smoking were also evaluated in relation with the intraoperative hypoxia. All data are given as mean ± S.D., and statistical analysis was performed by using Student's paired t-test and least square method, where p value less than 5% was considered as statistically significant.

## RESULTS

PaO2 during one lung ventilation decreased significantly, compared with control values in all groups, but there was no significant difference between the types of anesthesia. PaO2 was less than 100 mmHg in 24 of 75 patients, but no significant difference was found among the three methods. No significant correlation was found between the degree of hypoxia and the preoperative %VC, FEV1%, PaO2,chest x-ray findings,the degree of obesity and the degree of smoking.

## DISCUSSION

One lung ventilation attenuated hypoxic pulmonary vasoconstriction significantly and resulted in the impaired oxygen capability, but the degree of the reduction in PaO2 did not depend on the choice of anesthetic technique. Preoperative patient's condition, which was represented by pulmonary function tests, arterial blood gas, and the history of smoking, did not alter the degree of the reduction in the PaO2. Since no predictive factor was found in the present study, previously proposed mechanism plays little role in the attenuation of hypoxic pulmonary vasoconstriction during one lung anesthesia.

**Table 1. The changes in PaO2 (mmHg) during one lung ventilation and the type of anesthesia**

| | CONTROL | One Lung Ventilation | | | |
|---|---|---|---|---|---|
| | | 5 min | 10min | 20 min | 30 min |
| GOE (n = 25) | 450 ± 18 | 315 ± 30 | 237 ± 28 | 196 ± 24 | 205 ± 22 |
| EDB (n = 27) | 469 ± 15 | 322 ± 26 | 226 ± 26 | 176 ± 21 | 167 ± 16 |
| NLA (n = 23) | 462 ± 16 | 306 ± 27 | 244 ± 31 | 198 ± 22 | 196 ± 23 |

## ACUTE CARDIOPULMONARY EFFECTS OF AN ANTERIOR MEDIASTINAL MASS

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### Introduction

The patient with an anterior mediastinal mass may require general anaesthesia to facilitate tissue biopsy. The use of positive pressure ventilation and muscle relaxants has been anecdotally associated with major morbidity and death. It is not known if these major catastrophies are precipitated by respiratory or cardiac embarrassment. Using a canine model, we wished to compare the acute effects of an anterior mediastinal mass on cardiopulmonary function during spontaneous ventilation (SV) and mechanical ventilation (IPPV).

### Methods

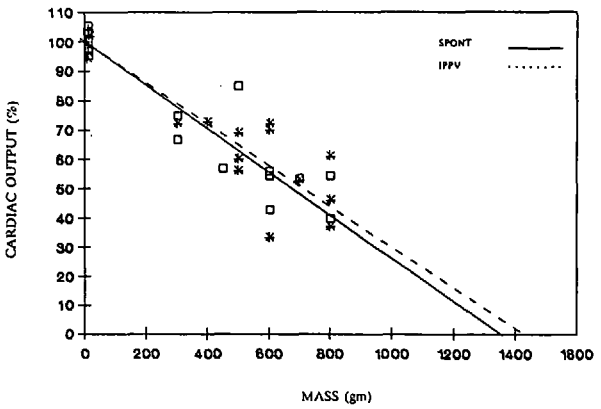
This study followed the guidelines of the Animal Care Committee. Twelve mongrel dogs were anaesthetized and instrumented with pulmonary artery, aortic, left and right atrial catheters. Airway pressures were measured at the mouth and distal bronchus. Expired minute ventilation was measured by spirometry. A 500 ml intravenous bag was placed in the anterior mediastinum through a left thoracotomy and connected to external tubing. After surgery the dogs were allowed to breath spontaneously adjusting inspired halothane to the minimal concentration that ensured tolerance to the tracheal tube (Period SV). The intravenous bag was then inflated with water until cardiac output fell by at least 25% (Period SV + Mass). The mass was deflated, pancuronium (.1 mg/kg) administered and IPPV instituted keeping $P_aCO_2$ constant (Period IPPV). The mass was then reinflated with the identical volume used during the prior spontaneous ventilation (Period IPPV + Mass). Airway pressures, vascular pressures, cardiac output, arterial and mixed venous blood gases were measured during each period. Subsequently, the mass was deflated and each dog randomized to a SV or IPPV group. In each group the mass was inflated in two stages until cardiac output fell by 50%. All respiratory and hemodynamic measurements were repeated at each stage. Data was compared by paired t-test.

### Results

As illustrated in the table, inflation of the anterior mediastinal mass resulted in a significant decrease in cardiac index and mean arterial pressure with both spontaneous ventilation and mechanical ventilation. This decrease in cardiac index was also demonstrated comparing mixed venous and arterial oxygen. During mechanical ventilation and spontaneous ventilation, inflation of the mass resulted in small but significant increase in distal airway pressure but minute volume was similar in all groups. The figure illustrates the relationship between cardiac index and increase in mass volume. Initial cardiac index without the mass was normalized to 100% for each dog. The 95% confidence limits for the regression lines of mass volume plotted against cardiac index during spontaneous ventilation (solid line) and mechanical ventilation (dashed line) were similar.

| | $Pa0_2$ | $Pmv0_2$ | Pinsp | MV | MAP | CI |
|---|---|---|---|---|---|---|
| SV | 230 ±32 | 64 ±2 | -2.2 ±.5 | 2.7 ±.3 | 175 ± 9 | 164 ±13 |
| SV + MASS | 206* ±33 | 54* ±3 | -1 * ±.2 | 2.7 ±.3 | 123* ±10 | 106* ±4 |
| IPPV | 247 ±36 | 62 ±3 | 8 ±.5 | 3.0 ±.2 | 169 ± 9 | 152 ±8 |
| IPPV+MASS | 223! ±36 | 48! ±5 | 11! ±1 | 3.0 ±.2 | 116! ± 9 | 94! ±10 |

$Pa0_2$ = arterial oxygen (mmHg), $Pmv0_2$ = mixed venous oxygen (mmHg), Pinsp = distal inspiratory air pressure (cm $H_20$), MV = minute volume (l/min), CI = cardiac index (ml/kg/min), MAP = mean arterial pressure (cm $H_20$) , * denotes $p<.05$ comparing SV to SV + MASS, ! denotes $p<.05$ comparing IPPV to IPPV + MASS.




### Discussion

An anterior mediastinal mass results in major cardiac impairment with small changes in respiratory mechanics and gas exchange. This pattern of decompensation was similar during both spontaneous or mechanical ventilation and neither ventilatory method afforded any advantage. Funded by the Saskatchewan Heart and Stroke Foundation.

# BRONCHODILATING EFFECT OF INHALED OR ORALY ADMINISTERED CALCIUM CHANNEL BLOCKING AGENTSON METHACHOLINE-INDUCED BRONCHOCONSTRICTION

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Calcium-dependent excitation-contraction and stimulus -secretion coupling mechanisms play central roles in the pathopysiology of airway obstrucion in asthma. Recently interest has been concentrated on the possibility that Ca2+ antagonists might therefore be useful in the treatment of asthma.
The present study was designed to examine the bronchodilating effects of organic calcium channel blocking agents (diltiazem, verapamil and nifedipine) and orciprenaline sulfate on metacholine-induced bronchoconstriction.

## MATERIALS AND METHODS

Eleven stable asthmatics (5 men and 6 women)between 17 and 57 years of age were studied. Bronchial hyper-responsiveness was examined by direct recording of the dose-response curve of respiratory resistance (Rrs) during continuous inhalation with tidal breathing of methacholine hydrochloride solution at stepwise increasing concentrations before and after treatment with saline (for controls), 10mg of inhaled diltiazem, 20mg of inhaled diltiazem, 5mg of inhaled verapamil, 10mg of orally administered nifedipine or 30mg of inhaled orciprenaline sulfate. An'Astograph' (TCK-6100H, Chest Co., Tokyo, Japan) was also used to measure bronchial hyper-responsiveness 15 minutes after inhalation of saline, diltiazem or verapamil or 60 minutes after oral administration of nifedipine. Inhalation of saline, diltiazem, verapamil or orciprenaline sulfate was facilitated by IPPB nebulization. Methacholine hydrochloride solution (Daiichi pure chemicals, Co., Ltd., Tokyo Japan) was diluted with saline to make various solution concentrations, i.e., 25.0, 12.5, 6.25, 3.125, 1.56, 0.78, 0.39, 0.19, 0.098 and 0.049mg/ml. Bronchial hyper-responsiveness was evaluated with control respiratiory resistance just before starting methacholine inhalation (Rrs-control) as well as the threshold dose of methacholine at the beginning of Rrs increase (Dmin) and the curvilinear slope of the dose-response curve (bronchial reactivity). Systolic and diastolic blood pressure and heart rate were measured before and after treatment.

## RESULTS

Relative Rrs-control values after treatment with inhalation of 10mg or 20mg of diltiazem, 5mg verapamil, oral administration of 10mg of nifedipine or inhalation of 30mg of orciprenaline sulfate as compared to control were 68.4%, 65.6%, 55.6%, 57.1%, 83.3%, respectively. Significant decrease of Rrs-control was observed after treatment with inhaled 10 and 20mg of diltiazem, 5mg of verapamil and 30mg of orciprenaine. Dmin values after treatment with 10 and 20mg of diltiazem, 5mg of verapamil, 10mg of nifedipine or 30mg of orciprenaline were 2.7 times, 4.9 times, 4.0 times, 2.5 times, 7.2 times, larger, respectively than the Dmin value before treatment. Significant increase of Dmin was observed after treatment with inhalation of 20mg of diltiazem or 30mg of orciprenaline. Relative bronchial reactivity values after treatment with 10 or 20mg of diltiazem, 5mg of verapamil, 10mg of nifedipine or 30mg of orciprenaline as compared to control were 43.4%, 40.3 %, 37.1%, 62.5%, 19.8%, respectively.
Significant decrease of bronchial reactivity was observed after all treatments except the oral nifedipine treatment. Changes of blood pressure and heart rate after treatment were not significant.

## DISCUSSION AND CONCLUSION

Our data show that inhaled diltiazem and verapamil or orally administered nifedipine may have direct bronchodialating effects, because methacholine is a drug of direct constrictive effects on brochial smooth muscle. It is therfore concluded that diltiazem and verapamil inhalation might be effective treatments for asthma patients.

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## HALOTHANE EFFECTS REGIONAL HYPOXIC PULMONARY VASOCONSTRICTION

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### Introduction

Halothane selectively inhibits hypoxic pulmonary vasoconstriction (HPV) in an isolated canine lobe. We extended these findings to an atelectatic lobe to more closely mimic a clinical setting.

### Methods

This was approved by the University Animal Care Committee. The left lower lobes of 6 mongrel dogs were prepared by canullating the lobar artery, vein and bronchus. The lobes were maintained in situ and perfused through an extracoporeal circuit primed with autologous blood. Lobar flow was set to Zone 3 by adjusting the heights of the inflow and outflow reservoirs which in turn set the inflow and outflow pressures (Pa and Pv). We used a stop flow technique to partition pulmonary vascular resistance (PVR) into total ($R_{TOT}$), inflow (Ra), outflow (Rv) and middle segment (Rm) resistances. We sequentially ventilated each lobe with normoxic (35% $O_2$) and hypoxic (3% $O_2$) gas mixtures. Following these baseline periods (periods 35%$O_2$ and 3%$O_2$), we introduced small steel ball bearings into the lobar bronchus to produce atelectasis. Each lobe was ventilated with 35% $O_2$ and then 3% $O_2$ (periods 35%$O_2$+A and 3%$O_2$+A). Halothane (0.5% and 2.5%) was added and the periods repeated (periods 35%$O_2$+A+0.5H; 3%$O_2$+A+0.5H; 35%$O_2$+A+2.5H; 3%$O_2$+A+2.5H). The lobes were finally ventilated with 35% $O_2$ and then 3% $O_2$ without added halothane (periods 35%$O_2$+$A_2$ and 3%$O_2$+$A_2$). We measured resistances, lobar venous $O_2$ ($PvO_2$) and $CO_2$, inspired gases, perfusate temperature and haematocrit during each period. Periods were compared using analysis of variance and a multiple comparison test when indicated ($p < 0.05$ showing a significant difference).

### Results

Values of temperature, haematocrit, Pa, Pv, pH, and $PCO_2$ were not different between periods. Inspired $O_2$ (35% and 3%) and halothane (0.5% and 2.5%) concentrations were near the preset gas concentrations for each period. Atelectasis caused $PvO_2$ to decrease significantly. Both $R_{TOT}$ and Rm increased significantly during hypoxic periods compared normoxic periods except when 2.5% halothane was added. Compared to periods 35%$O_2$ and 3%$O_2$, $R_{TOT}$ and Rm increased significantly after atelectasis for all periods except when 2.5% halothane was added. Neither Ra nor Rv changed significantly between periods.

| | $R_{TOT}$ | Rm | $PvO_2$ |
|---|---|---|---|
| 35%$O_2$ | .08 ±.01 | .02 ±.01 | 115 ±20 |
| 3%$O_2$ | .13$^{b}$ ±.02 | .06$^{b}$ ±.02 | 28$^{b}$ ±6 |
| 35%$O_2$+A | .12$^{a}$ ±.02 | .05$^{a}$ ±.01 | 77$^{a}$ ±23 |
| 3%$O_2$+A | .18$^{ab}$ ±.04 | .08$^{ab}$ ±.02 | 27$^{b}$ ±7 |
| 35%$O_2$+A +0.5H | .11$^{a}$ ±.01 | .04$^{a}$ ±.01 | 68$^{a}$ ±18 |
| 3%$O_2$+A +0.5H | .17$^{ab}$ ±.03 | .07$^{ab}$ ±.03 | 31$^{b}$ ±7 |
| 35%$O_2$+A +2.5H | .09 ±.02 | .02 ±.01 | 69$^{a}$ 17 |
| 3%$O_2$+A +2.5H | .09 ±.02 | .02 ±.01 | 36$^{b}$ ±10 |
| 35%$O_2$+$A_2$ | .12$^{a}$ ±.02 | .03$^{a}$ ±.01 | 65$^{a}$ ±18 |
| 3%$O_2$+$A_2$ | .20$^{ab}$ ±.04 | .09$^{ab}$ ±.03 | 33$^{b}$ ±10 |

Where "a" represents a difference from control periods 35%$O_2$ and 3%$O_2$; "b" represents a difference between periods of hypoxia (3% $O_2$) compared with normoxia (35% $O_2$). Resistance is shown in units of cm $H_2O$/ml/min x $10^{-2}$.

### Discussion

Sublobar atelectasis acts to increase PVR through hypoxic vasoconstriction. High (2.5%) but not low (0.5%) concentrations of halothane inhibit HPV and selectively decrease middle segment resistance. That $R_{TOT}$ and Rm returned to baseline values with 2.5% halothane implies that mechanical compression of the lobar vasculature is not important in diverting blood away from hypoxic atelectatic regions. Extrapolating to the clinical setting, our data suggest that halothane might worsen gas exchange in atelectatic lungs.

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# EVALUATION OF BREATHING PATTERN FOR SUCCESSFUL WEANING FROM MECHANICAL VENTILATION

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**INTRODUCTION** The assessment of respiratory function of the patient, who is being weaned from mechanical ventilation, is sometimes difficult, since the patient is intubated, and conventional pulmonary function tests are not possible. There have been several weaning criteria proposed: clear consciousness, stable cardiovascular state, adequate respiratory muscle power, and optimal oxygen capability. The unsuccessful weaning, however, has benn reported as more than 20% of the weaning trials. The purpose of the present study is to evaluate the breathing pattern quantitatively by means of respiratory inductive plethysmography (RIP), along with conventional spirometry and blood gas analysis, in order to determine whether breathing pattern is an important factor for successful weaning.

**SUBJECTS AND METHODS**

Thirty-seven weaning trials were evaluated in 28 adults patients, who underwent esophageal cancer operation. All patients were mechanically ventilated over 24 hours postoperatively. Epidural buprenorphine was given for postoperative analgesia. Weaning criteria include stable general condition, clear consciousness, $PaO_2$ > 100 mmHg and $PaCO_2$ < 45 mmHg at CPAP ($F_IO_2 \leq 0.4$). Weaning was considered as unsuccessful, when the reinitiation of mechanical ventilation was needed because of progressive hypoxia and/or hypercapnia, or when the tracheostomy was performed for the maintenance of the airway. Ventilatory performance of vital capacity (VC), minute ventilation ($V_E$), tidal volume ($V_T$), respiratory frequency (f), mean inspiratory flow ($V_T/T_I$), fractional inspiratory time ($T_I/T_{TOT}$), arterial blood gas, and ribcage and abdominal movement by RIP were measured. Statistical analysis was performed by using Chi-square, and Student's t-test, where p less than 5% was considered as statistically significant.

**RESULTS** Of thirty seven weaning trials, 18 trials were successful (group S) and 19 were unsuccessful (group U). There were no significant difference in the age and sex between the 2 groups. There was no significant difference in ventilatory variables such as VC, $V_E$, $V_T$, f, $V_T/T_I$, and $T_I/T_{TOT}$ between the 2 groups. AaDO2 was significantly greater in group U than that in group S ( $p < 0.05$). %RC, which is % contribution of ribcage movement to tidal volume, and ribcage tidal volume, which is the product of VT and %RC, were significantly greater in group U than in group S. %RC was 42 % in group S, whereas 57 % in group U. In group S, 80% of the patients showed %RC less than 50%, on the other hand 12% in group U, which was significantly less. Total compartmental displacement (TCD), which is the parameter to quantitate the paradoxical ventilation, shows no significant difference between the 2 groups.

**DISCUSSION** Inability to tolerate the discontinuation of mechanical ventilation or the need for reintubation has been reported in as much as 20% of mechanically ventilated patients. A number of factors may be responsible for unsuccessful weaning outcome including hypoventilation secondary to decreased respiratory center output, or respiratory muscle fatigue, impaired pulmonary gas exchange, and excessive ventilatory requirements. The relative importance of such factors as breathing pattern and respiratory muscle coordination is poorly understood, as most published data on patients being weaned from mechanical ventilation have been of a descriptive nature. The present study demonstrates that the respiratory muscle coordination is one of the important factors for successful weaning, even when their ventilatory variables and blood gas data are within normal limits. Although we could not elucidate the pathophysiologic mechanism inducing more activation of ribcage movement and impaired oxygen capability, the reduction in the functional residual capacity (FRC) due to micro-atelectasis in the lung or the diaphragmatic fatigue is likely suspected. The reduction in FRC might result in the increased pulmonary shunt, and decreased lung compliance, thus provoked increased activation of the ribcage movement.

**Table Rib Cage and Abdominal Contribution to Tidal Ventilation**

| | successful | unsuccessful | |
|---|---|---|---|
| $V_T$ (ml/kg) | 9.67 ± 2.94 | 10.08 ± 1.97 | |
| %RC (%) | 41.9 ± 10.3 | 56.6 ± 13.9 | *1 |
| $V_T$-RC (ml/kg) | 4.01 ± 1.74 | 5.66 ± 1.61 | *1 |
| $V_T$-AB (ml/kg) *2 | 5.48 ± 1.83 | 4.38 ± 1.57 | |
| TCD / VT *3 | 1.03 ± 0.06 | 1.03 ± 0.08 | |

*1 $p < 0.05$ significant
*2 abdominal tidal volume
*3 total compartmental displacement

# EFFECTS OF SEVOFLURANE AND HALOTHANE ON PATTERN AND MECHANICS OF BREATHING IN MAN

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*Introduction:*

Sevoflurane, a new inhalation anaesthetic, has been shown to depress ventilation more than halothane does[1]. However, its effects on the pattern and mechanics of breathing are not well determined. Therefore, we compared the timing, depth of breathing and respiratory mechanics between the two anaesthetics at equianaesthetic depth of 1 MAC (minimum alveolar concentration).

*Methods:*

The study was approved by the Institutional Ethical Review Committee and informed consent was obtained from all patients.

Fourteen patients scheduled for minor gynecological surgery were randomly allocated between sevoflurane (S) (n=7) and halothane (H) (n=7) groups. No premedication was given prior to the induction of anaesthesia. Anaesthesia was induced with either S- or H- nitrous oxide (66%) / oxygen by mask. Following tracheal intubation (ID 7.5mm) performed without the aid of muscle relaxant, spontaneous breathing was allowed to resume. Tracheal pressure (Ptr), air flow ($\dot{V}$), changes of the lung volume ($\Delta V$), and the fractional concentrations of carbon dioxide and inhalational agent were continuously monitored. Having obtained the steady state condition, defined by the stable breathing pattern and end-tidal carbon dioxide ($F_{ET}CO_2$) level at end-tidal anesthetic concentration of 1 MAC, ventilatory parameters were recorded for two minutes. Then, five end-inspiratory airway occlusions followed by five end-expiratory airway occlusions were performed every ten breaths. From these data inspiratory and expiratory durations (Ti, Te), tidal volume (Vt), mean inspiratory flow rate (Vt/Ti), duty ratio (Ti/Ti+Te), respiratory frequency (f) and minute ventilation ($\dot{V}e$) were determined. Passive respiratory elastance (Ers) and active respiratory elastance (E'rs) and resistance (R'rs) were also calculated according to the method described in the literature[2]. Arterial blood sample was drawn at the end of the experimental procedures and the partial pressure of carbon dioxide ($PaCO_2$) was measured using the blood gas analyzer (ABL2). Results were analyzed using the Student's t test where appropriate. Statistical differences were considered significant at $p<0.05$.

TABLE

| | | *SEVOFLURANE* | *HALOTHANE* | p |
|---|---|---|---|---|
| Ti | (s) | 1.06±0.05 | 0.86±0.02 | <0.01 |
| Te | (s) | 1.91±0.26 | 1.27±0.08 | <0.05 |
| Ti/Ttot | | 0.37±0.02 | 0.41±0.01 | ns |
| f | (bpm) | 21.2±1.7 | 28.5±1.2 | <0.01 |
| Vt | (ml) | 274±41 | 232±31 | <0.05 |
| Vt/Ti | (ml/s) | 259±17 | 268±27 | ns |
| $\dot{V}e$ | (l/min) | 5.72±0.35 | 6.56±0.29 | ns |
| $PaCO_2$ | (mmHg) | 45.5±1.1 | 44.1±2.3 | ns |
| Ers | ($cmH_2O$/l) | 21.8±0.9 | 22.3±2.8 | ns |
| E'rs | ($cmH_2O$/l) | 28.7±1.7 | 28.0±3.0 | ns |
| R'rs | ($cmH_2O$/l/s) | 3.21±0.63 | 2.42±0.64 | ns |
| $P_{0.1}$ | ($cmH_2O$) | 1.21±0.18 | 2.34±0.20 | <0.05 |

(Mean±SEM)

Figure 1.

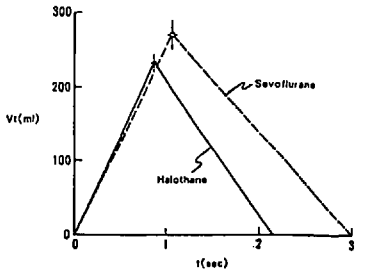
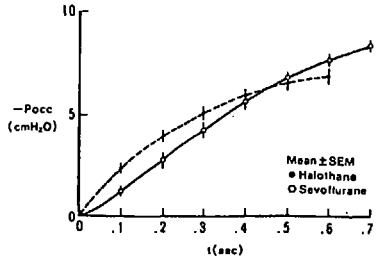



Figure 2.




*Results*

Both Ti and Te were longer and f lower in S group than in H group. By contrast, Vt was greater in S than in H while duty ratio, Vt/Ti, $\dot{V}e$ and $PaCO_2$ were not different between the two groups. Ers, E'rs and R'rs were also identical between S and H. Whereas, occlusion pressure at 0.1s following the inspiratory effort was significantly less in S than in H anaesthesia (Table).

*Discussion*

We found no significant difference of $\dot{V}e$, $PaCO_2$ and mechanical parameters of the respiratory system between S and H at 1 MAC of anaesthesia. However, as illustrated in figure 1, the pattern of breathing determined in terms of Ti, Te and Vt was significantly different between the two anaesthetics. Moreover, occlusion pressure waveform was also markedly different between S and H (figure 2). These differences probably reflect the different patterns of central neural drive between the two anaesthetics. On the other hand, the smaller pressure generation at the beginning of inspiration and the slower respiratory rate of S are similar to the changes induced by the graded incease of muscle relaxation[3]. Thus we speculate that observed differences of the breathing pattern may be accounted for, at least in part, by the greater degree of muscle relaxation by S. In order to test this hypothesis, further study including the measurement of the contractile properties of the respiratory muscles would be needed.

*References*

1 Anesth Analg 66.241.
2 J Appl Physiol 51.109.
3 J Appl Physiol 64.78.