Haemodynamic Effect of a New Vasodilator, Nicergoline,* During Sternotomy in Open Heart Surgery. F. Prigent, C. Hubscher, G. Oksenhendler, R. Soyer and C. Winkler.

Avoidance of increasing afterload is important during anaesthesia for cardiac surgery. We studied the haemodynamic consequence of deliberate vasodilation during sternotomy in nine patients (mean age 57 ± 12 years, mean left ventricular ejection fraction 0.51 ± 0.09) undergoing valvular replacement. Nicergoline, a new ergol derivative, produces vasodilation (alpha blocking effect), bradycardia (central effect) and has no effect on myocardial metabolism. It was given as a continuous infusion, started after induction, at a rate of 0.8 mg·kg⁻¹/hour.

This group was compared to a control group of 12 patients (mean age 60 ± 13 years; mean left ventricular ejection fraction 0.51 ± 0.1) undergoing valvular replacement (seven patients), coronary artery bypass graft (four patients) or aneurysmectomy (one patient). Premedication was pentobarbitone sodium 60-120 mg PR., with intramuscular promethazine 1 mg·kg⁻¹ and meperidine 1 mg·kg⁻¹. Anaesthesia was neurolepanalgesia with droperidol 100 mg and fentanyl 2 mg·kg⁻¹/hr during induction at 5 mg·kg⁻¹/hr and then maintained at 2 mg·kg⁻¹/hr during sternotomy. Flunitrazepam 0.25 to 0.5 mg and pancuronium bromide 0.08 mg·kg⁻¹ were given at induction. Measurements were made before and after sternotomy in the two groups of patients.

In the control group, sternotomy did result in an increased rate-pressure product (p < 0.01), while cardiac index and systemic vascular resistance remained unchanged. In the nicergoline group, increase in rate pressure product was not significant. Cardiac index increased significantly (p < 0.05) as systemic vascular resistance decreased; volume needed to maintain adequate filling pressure was higher in this group (p < 0.05) as was the weight gain during operation (p < 0.05) and postoperative bleeding. This may be related to nicergoline platelet anti-aggregation properties.

Our study suggests that deliberate vasodilation such as produced with nicergoline may yield to increased vasoplegia, bleeding and weight gain during operation despite decrease in MVO₂ and afterload.

REFERENCE


Intravenous nitroglycerin (NG) is used in coronary patients during anaesthesia to reduce blood pressure (BP) and rate-pressure-product (RPP). It is given orally or intravenously to awake patients for angina. Does the awake patient with cerebration and an active autonomic system react to NG differently than an anesthetized patient?

We studied seven patients having coronary grafts, both awake, sedated and, later, after sternotomy with hypertension. With a radial needle and two thermodilution catheters (pulmonary artery and coronary sinus) we determined total coronary sinus flow (CSF), cardiac index (CI), vascular resistance (SVR), total coronary sinus flow (CSF), myocardial oxygen consumption (MVO₂) and lactate extraction. Studies were done before and after NG 100 µg/min with mean doses of 1.04 mg given in 10.6 minutes awake and 1.2 mg given in 8.2 minutes after sternotomy.

These male patients had a mean age of 57.4 years and mean surface area of 1.95 m². Mean ejection fraction was 70 ± 10 percent. They were sedated with secobarbital (214 mg) and morphine 0.25 mg·kg⁻¹. Five were anesthetized with halothane and two with morphine 1.0 mg·kg⁻¹, with oxygen.

Table I gives mean and standard errors for 12
circulatory and metabolic variables determined both awake and after sternotomy. The changes after NG given awake were compared statistically to those when NG was given during anaesthesia. NG in awake patients increased heart rate, decreased CI and wedge pressure but not BP. SVR, RPP, CSF. Coronary sinus oxygen content and MVO2 were unchanged. During anaesthesia, decreases were seen in BP, wedge pressure, SVR, work index, RPP and MVO2. Coronary sinus oxygen content increased as less oxygen was taken up. Lactate extraction remained normal in both situations, so myocardial oxygen supply was not grossly deficient. Stroke work index decreased in both situations but the changes were similar. Stroke volume index decreased in the awake state but not under anaesthesia.

We conclude that the same dose of nitroglycerin is more effective in treating a hyperdynamic circulation in patients with coronary artery disease when given during anaesthesia than when awake. In both instances we found that myocardial oxygenation is well maintained.

**ABSTRACTS OF PAPERS PRESENTED AT THE ANNUAL MEETING**

**TABLE 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>PreNG</th>
<th>PostNG</th>
<th>p**</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mm Hg)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Awake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP mm Hg</td>
<td>108 ± 3*</td>
<td>100 ± 6</td>
<td></td>
</tr>
<tr>
<td>H. R.</td>
<td>67 ± 7</td>
<td>75 ± 5</td>
<td></td>
</tr>
<tr>
<td>CI.</td>
<td>3.80 ± 0.14</td>
<td>2.85 ± 0.15</td>
<td></td>
</tr>
<tr>
<td>SWI</td>
<td>76.5 ± 2.5</td>
<td>54.7 ± 4.5</td>
<td></td>
</tr>
<tr>
<td>SVI</td>
<td>43.2 ± 2.4</td>
<td>33 ± 2.3</td>
<td></td>
</tr>
<tr>
<td>Wedge mm Hg</td>
<td>14 ± 0.7</td>
<td>10 ± 1.1</td>
<td></td>
</tr>
<tr>
<td>SVR</td>
<td>1451 ± 112</td>
<td>1013 ± 147</td>
<td></td>
</tr>
<tr>
<td>RPP</td>
<td>10983 ± 920</td>
<td>11236 ± 147</td>
<td></td>
</tr>
<tr>
<td>CSF ml/min</td>
<td>92.9 ± 15.1</td>
<td>82.1 ± 13.2</td>
<td></td>
</tr>
<tr>
<td>CI.</td>
<td>67.7 ± 0.3</td>
<td>64.4 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>MVO2 ml/min</td>
<td>10.3 ± 1.2</td>
<td>10.3 ± 0.8</td>
<td></td>
</tr>
<tr>
<td>Lact. Ext. %</td>
<td>24.9 ± 6.2</td>
<td>24.9 ± 4.7</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Poststernotomy</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP mm Hg</td>
<td>106 ± 6</td>
<td>72 ± 5.3</td>
<td>0.03</td>
</tr>
<tr>
<td>H. R.</td>
<td>65 ± 4.9</td>
<td>64 ± 5.0</td>
<td>0.04</td>
</tr>
<tr>
<td>CI.</td>
<td>2.22 ± 0.21</td>
<td>2.4 ± 0.18</td>
<td>N.S.</td>
</tr>
<tr>
<td>SWI</td>
<td>65.7 ± 5.9</td>
<td>41.2 ± 2.3</td>
<td>N.S.</td>
</tr>
<tr>
<td>SVI</td>
<td>35.7 ± 5.0</td>
<td>38.6 ± 3.8</td>
<td>0.02</td>
</tr>
<tr>
<td>Wedge mm Hg</td>
<td>21 ± 2.2</td>
<td>12 ± 1.4</td>
<td>0.03</td>
</tr>
<tr>
<td>SVR</td>
<td>1547 ± 280</td>
<td>1168 ± 161</td>
<td>0.02</td>
</tr>
<tr>
<td>RPP</td>
<td>1028 ± 1010</td>
<td>6585 ± 724</td>
<td>0.02</td>
</tr>
<tr>
<td>CSF ml/min</td>
<td>85.6 ± 10.2</td>
<td>69.3 ± 18.3</td>
<td>N.S.</td>
</tr>
<tr>
<td>CI.</td>
<td>6.3 ± 0.6</td>
<td>7.4 ± 0.9</td>
<td>0.04</td>
</tr>
<tr>
<td>MVO2 ml/min</td>
<td>8.7 ± 1.0</td>
<td>5.7 ± 1.2</td>
<td>N.S.</td>
</tr>
<tr>
<td>Lact. Ext. %</td>
<td>26.3 ± 4.5</td>
<td>28 ± 3.4</td>
<td>N.S.</td>
</tr>
</tbody>
</table>

**Haemodynamic Responses and Serum Fentanyl Levels During Fentanyl Infusion Anaesthesia.**


**Introduction:** It has been shown that high dose fentanyl (100 µg·kg⁻¹) and oxygen produce stable haemodynamics during induction and early surgical stimulation in patients with good ventricular function undergoing aortocoronary bypass surgery (ACBP). However, in the period between sternotomy and the initiation of cardiopulmonary bypass (CPB), many patients develop undesirable systemic hypertension which requires treatment. We wished to determine whether fentanyl 100 µg·kg⁻¹ divided into various loading doses and infusion rates could produce more stable haemodynamics and be associated with stable serum fentanyl levels.

**Methods:** Thirty patients scheduled for ACBP were divided into three groups of 10, each with similar demographic data. All patients were premedicated with diazepam, morphine and scopolamine. Group 1 received fentanyl 30 µg·kg⁻¹ intravenously as a loading dose followed by an infusion of 0.3 µg·kg⁻¹·min⁻¹. Group 2 received 40 µg·kg⁻¹ as a loading dose and an infusion of 0.4 µg·kg⁻¹·min⁻¹ and Group 3 received 50 µg·kg⁻¹ as a loading dose and an infusion of 0.5 µg·kg⁻¹·min⁻¹. A control haemodynamic profile was obtained before induction. Haemodynamic profiles were done following the loading dose of fentanyl, which was given at the rate of 1 mg·min⁻¹, and after tracheal intubation, skin incision, sternotomy and aortic root dissection. Blood samples for radioimmunoassay determinations of fentanyl were taken at 5, 10, 20, and 30 minutes and then half-hourly from the beginning of the induction of anaesthesia.

The infusion of fentanyl was continued until the patient had received a total of 100 µg·kg⁻¹ or rewarming was begun on CPB.

**Results:** The serum fentanyl concentrations were significantly different between Groups 1 and 3 in the 5 to 30 minute time interval. Thereafter there were no significant differences in serum concentrations of fentanyl between the groups. However, it was seen that for the first 90 minutes there appeared to be a trend for the patients who received the highest infusion rate to have the highest serum levels. Serum fentanyl levels decreased by an average of 30 per cent when CPB was instituted but returned to their approximate pre-bypass levels with 30 minutes.

No significant differences between the groups were demonstrated in the haemodynamic measurements and derived indices. In addition each event was compared to control and to the previous event within each group regardless of the addition of supplemental anaesthesia. No changes from control were noted in central venous pressure, pulmonary capillary wedge pressure or left ventricular stroke work index within any group. Significant changes in heart rate, cardiac index and systemic vascular resistance occurred in Group 1. In Group 2 significant changes were seen in initial 20 minutes, systolic blood pressure and systemic vascular resistance, while in Group 3 such changes were seen only in heart rate. Thus patients who received the highest dose of fentanyl had fewer significant haemodynamic changes.

Nine patients in Group 1, seven in Group 2, and five in Group 3 required treatment of hypertension or tachycardia.

**Conclusions:** We conclude that a loading dose of fentanyl 50 µg·kg⁻¹ followed by an infusion of 0.5 µg·kg⁻¹·min⁻¹ to a total dose of 100 µg·kg⁻¹ will produce a serum fentanyl level of approximately 1.5 ng·ml⁻¹ before CPB. This provides haemodynamic stability in about 50 per cent of patients and produces baseline anaesthesia enabling easy control of any undesirable haemodynamic changes.

Introduction: High dose fentanyl and oxygen anaesthesia has been shown to produce stable haemodynamics during induction of anaesthesia and early surgical stimulus in patients with good ventricular function undergoing aortocoronary bypass surgery (ACBP). We wished to determine if patients with poor ventricular function undergoing ACBP would differ in their haemodynamic response and serum concentrations of fentanyl from patients with good ventricular function when both groups were anaesthetized with an identical fentanyl infusion technique.

Methods: Six patients (Group 1) with poor ventricular function (ejection fraction < 0.3 and LVEDP > 20 torr) and ten patients (Group 2) with good ventricular function (ejection fraction > 0.3 and LVEDP < 15 torr) were studied. All patients were premedicated with diazepam, morphine and scopolamine. Anaesthesia consisted of a loading dose of fentanyl 30 μg kg⁻¹ followed by a fentanyl infusion of 0.3 μg kg⁻¹ min⁻¹. The loading dose was given at the rate of 1 mg min⁻¹ and the infusion was continued until warming was commenced on cardiopulmonary bypass. Muscle paralysis was induced with pancuronium (0.1 mg kg⁻¹) and the patients were ventilated with 100 per cent oxygen to normocarbia. A control haemodynamic profile was obtained before the induction of anaesthesia and repeated following induction, tracheal intubation, skin incision, sternotomy and incision for the treatment of hypertension and tachycardia. HR decreased on induction and aortic dissection respectively but did not differ from control or between study periods at any other time interval.

Discussion: Patients with poor ventricular function undergoing ACBP surgery who are anaesthetized with a fentanyl infusion technique require less intervention for the treatment of hypertension and tachycardia than patients with good ventricular function anaesthetized identically. The similarity in serum fentanyl levels between the two groups would indicate similar brain concentrations of fentanyl and presumably similar depths of anaesthesia. Thus, the difference of clinical response of the two groups to anaesthesia and surgical stimulation. HR increased after induction and remained elevated throughout. The change in HR was reflected in CI which increased in patients with poor ventricular function undergoing ACBP would differ in their haemodynamic response and serum concentrations of fentanyl from patients with good ventricular function when both groups were anaesthetized with an identical fentanyl infusion technique.


Normal leucocyte function, characterized by chemotactic migration, phagocytosis and the ability to kill invading organisms is important in the immunological defence against infection. Halothane has been shown to reversibly inhibit phagocytosis and killing, and phagocytosis is inhibited by intravenous anaesthetic agents.

A major mechanism of bacterial killing by PMNL is excited oxygen radical (EOR) generation. This is associated with the emission of photons, and the phenomenon of chemiluminescence. We have explored whether intravenous anaesthetic agents depress leucocyte function by an effect on this system. Leucocyte activation was achieved by Cyb receptor stimulation using opsonized Zymosan, and the magnitude and kinetic characteristics of the EOR generation was quantified by measurement of light emission with a Beckman Scintillation Counter. Within this system, the effects of the thiopentone and alfathesin on basal and stimulated EOR generation were studied. The drugs were incubated with the leucocytes for one hour, in concentrations chosen to reflect those achieved in vivo. Following stimulation of the cells, measurements of light emission were made at 10
minute intervals for one hour. Peak activity occurred 20–30 minutes following stimulation. The area under the curve was used as an index of energy output by the cell preparation.

Basal activity was unaffected by the presence of the drugs but peak activity was depressed in a dose dependent manner. The percentage change of area under the curve shows a statistically significant (p < 0.01) 25 per cent depression of activity by thiopentone at 5 µg/ml and 50 per cent depression of activity by alfathesin at 1.25 µg/ml. These levels were chosen to reflect the free plasma concentration at sleep levels of anaesthesia. Extensive washing of the cells with buffered saline returned activity to that of the control cells.

These results show the depression of EOR generation by thiopentone and alfathesin. The general shape of the response curves was unchanged, suggesting that this effect is probably a generalized quenching of EOR. The site of action of these agonists is unclear at the present time, but clinically the depression of EOR production reflects a decreased competence of polymorphonuclear leucocytes and may be a factor contributing to impaired host resistance in the postoperative period.

### Area Under Curve

<table>
<thead>
<tr>
<th>Dose (µg/ml)</th>
<th>Thiopentone % Control (± SEM)</th>
<th>Alfathesin % Control (± SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>9 ± 2</td>
<td>2.5 ± 1</td>
</tr>
<tr>
<td>50</td>
<td>3 ± 5</td>
<td>1.25 ± 0.5</td>
</tr>
<tr>
<td>25</td>
<td>7 ± 4</td>
<td>0.5 ± 0.5</td>
</tr>
<tr>
<td>10</td>
<td>7 ± 6</td>
<td>0.25 ± 0.4</td>
</tr>
<tr>
<td>5</td>
<td>2 ± 6</td>
<td>0.125 ± 0.4</td>
</tr>
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</table>

### REFERENCES


### Error in Estimating Sensible Heat Loss from the Respiratory Tract

Conventionally, sensible heat loss from the respiratory tract is calculated by the product of minute volume, density of air, specific heat of air and the difference between the expired and inspired air temperature (T). This assumes that all the expired air is at the same temperature, thus describing a square wave. It can be shown, however, that the initial portion of the expired temperature describes a curve. Therefore there should be an overestimation of sensible heat loss.

Air temperature was measured continuously by a 0.122 mm copper-constantan thermocouple (60 per cent response time of 40 ms) mounted in the mouthpiece of a T-piece breathing system equipped with one way valves. Using a pneumotachograph and magnetic tape recorder, changing air temperature at the mouth and expired air volume (VT) were recorded simultaneously while the subject breathed voluntarily at different tidal volumes (2000, 1500, 1000, 500 ml) and rates (3–18, 28–48 breaths per minute). Inspired temperatures were controlled at 12.05°C, 21.80°C and 27.74°C at a constant dewpoint temperature of 4–5°C.

Temperature-volume "loops" were constructed using a X-Y plotter. The areas of each "loop" and enclosing rectangle (T × VT) were cut out and weighed on an analytical balance. The difference was divided by the weight of the rectangle to give the percentage of overestimation of sensible heat loss. This ranged from 6.4 to 15.5 per cent. It was not affected by the inspired air temperature but increased significantly (p < 0.001) with decreasing VT (y = 13.2 – 3.21 x, where VT is in litres). Fast breathing further increased the error systematically by an additional two per cent over the same VT at normal or slow breathing rates (y = 15.2 – 2.31 x).

### Local Anaesthetics Inhibit Platelet Aggregation

**Alexander W. Gotta and Colleen A. Sullivan.**

**Introduction:** Local anaesthetics inhibit flux of sodium and potassium in the nerve membrane, thus impeding impulse transmission. Ionic flux in red blood cells is similarly impeded. Since maintenance of platelet membrane permeability and transmembrane flux of adenosine diphosphate and calcium are essential for platelet aggregation, local anaesthetic-induced inhibition of ionic and molecular flux could decrease platelet aggregation and limit the primary haemostatic mechanism.

**Methods:** Twenty-seven ml of whole blood was collected from fasting healthy volunteers, with no known bleeding dyscrasia or recent exposure to drugs with anti-platelet activity. The blood was mixed with 0.11M sodium citrate 3 ml and centrifuged at 20°C for 10 minutes at 150 g. Platelet-rich plasma was removed and the remaining blood was centrifuged at high speed for 25 minutes, so that the initial portion of the expired temperature describes a curve. Therefore there should be an overestimation of sensible heat loss.
Period. Determined by Student’s t test with P < 0.05. Platelet aggregation and collagen lag period was determined again. The significance of alteration on platelet aggregation and collagen lag period was determined by Student’s t test with P < 0.05 considered significant.

Results: Local anaesthetics induce significant decreases in ADP and collagen-induced platelet aggregation, and significant increases in collagen lag period.

<table>
<thead>
<tr>
<th>Anaesthetic</th>
<th>ADP</th>
<th>Collagen</th>
<th>Lag Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupivacaine</td>
<td>250</td>
<td>500</td>
<td>150</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>750</td>
<td>1500</td>
<td>750</td>
</tr>
<tr>
<td>Chloroprocaine</td>
<td>500</td>
<td>*</td>
<td>250</td>
</tr>
<tr>
<td>Tetracaine</td>
<td>200</td>
<td>200</td>
<td>100</td>
</tr>
</tbody>
</table>

*No significant inhibition up to 500 µg/ml.

Discussion: Platelet aggregation in response to ADP and collagen was significantly reduced by four local anaesthetics, but only at toxic plasma concentrations. The indication of an alteration in platelet function induced by local anaesthetics was an increase in collagen lag period which was independent of total aggregation. This probably represents a decrease in platelet membrane permeability and inhibition of trans-membrane flux of ADP and calcium. The platelet may thus serve as a useful readily-available tool for studying local anaesthetic-induced alteration in membrane permeability which is the basic mechanism of local anaesthetic action.

Nitrous Oxide Effects on PO2 Measurements in the Operating Room: Shift of the Oxygen-haemoglobin Curve. Louis Fournier and Diane Major.

Since 1978, we know that oxygen electrodes are sensitive to nitrous oxide, so that our measurements of PO2 during anaesthesia with nitrous oxide are not as accurate as we would like.

To obviate this problem we started to measure oxygen saturation directly in our patients receiving nitrous oxide during an operation. This did not solve the question since the results were not as expected. We then asked ourselves if nitrous oxide had a significant influence on the HbO2 curve, contrary to what has been reported to date.

We selected 20 normal patients (ASA-1) scheduled to have an operation where the maintenance of anaesthesia would be a mixture of nitrous oxide and oxygen with curare, without any other inhalation agent.

We drew a blood sample from each patient before induction of anaesthesia. On this sample we did:

1. The HbO2 curve on an Hem-O-Scan, tonometrying from 0 to 25 per cent oxygen.
2. An HbO2 curve using a mixture containing a constant concentration of nitrous oxide 50 per cent, carbon dioxide 5.6 per cent, tonometrying from PO2 zero to PO2 180 mm Hg.

Before doing this curve, we offset the nitrous oxide interference on PO2 determination by zeroing the electrode with a mixture of nitrous oxide 50 per cent, carbon dioxide 5.6 per cent and the balance nitrogen.

After 30-60 minutes of anaesthesia with nitrous oxide and oxygen a second blood sample was drawn. The same HbO2 curves were drawn for this blood.

Results: a) The 20 patients showed a normal preoperative HbO2 curve. b) The HbO2 curves with 50 per cent nitrous oxide both in vivo and in vitro, were all significantly shifted to the left for a mean of 9 torr, contrary to previous published results. c) The functioning fraction of 2,3-DPG had a tendency to decrease and this may contribute to shift the HbO2 curve to the left.

In conclusion we can say that nitrous oxide not only affects the PO2 electrode to give us false PO2 results in the operating room but also shifts the HbO2 curve significantly to the left.

REFERENCES

acoustic admittance. The value of acoustic admittance is a composite of three factors: conductance or the reciprocal of resistance (friction), susceptance or the reciprocal of reactance (sum of mass and rigidity). The acoustic impedance on the other hand can be best described by the following equation: 

\[ Z = \frac{1}{r} + \frac{1}{2 \pi f m} + \frac{S}{2} \]  

where \( Z \) is the acoustic impedance, \( r \) is friction, \( m \) is mass, \( S \) is rigidity, \( f \) is the frequency of the probe tone.

It is evident from the previous equation that when a low frequency tone (220Hz) is used to measure acoustic impedance, pathology involving the rigidity of the tympano-ossicular system can be more precisely evidenced, whereas when a high frequency tone (660Hz) is used to measure acoustic impedance, pathology involving mass of the tympano-ossicular system is more precisely evidenced.

Data were analyzed according to the two kinds of measurement with two different probe tones. Results from the data available at this time on 30 subjects show, first, that the values of the acoustic admittance are highly variable from one individual to the other during general anesthesia and, second, that the shape of the tympanograms become highly similar to the pathognomonic tympanogram found in patients presenting tympanic membrane abnormalities and/or ossicular luxations. These results were compared to two control groups, a surgery group which received nitrous oxide and oxygen but did not have any impedance measurement done during the operation and a non-surgery group which did not receive nitrous oxide and oxygen but had impedance measurement done at successive intervals for 90 minutes. Discussion of the results suggests that diffusion of gases in the middle ear system influences the shape of the tympanograms by changing the elastic properties of the whole system.

Finally, diffusion of gases in the middle ear system seems to induce changes in the oto-labyrinthic function in such a way that nausea and vomiting in the recovery room are more frequent in patients who present high negative pressure in the middle ear.

REFERENCES


Heparin rebound is the reappearance of the anticoagulant effect of heparin 1–18 hours after its complete neutralization with protamine sulphate. The mechanism of heparin rebound is uncertain and the fate of the heparin-protamine complex in the body is unknown. Clinically, relapse into the anticoagulant state can cause significant postoperative bleeding in patients who have been sustained with extracorporeal circulation. This has prompted the present study in which the pharmacokinetics of heparin before and after combination with protamine was investigated.

Methods: Dogs anaesthetized with pentobarbitone were given 35S labelled heparin 1.0 mg-kg⁻¹. Heparin anticoagulant levels were measured by artificial substrate (Protopath) and APTY as well as scintillation counting were carried out on blood and urine samples taken before (control) and at 15 or 30 minute intervals after heparin was given. In one group of dogs, the heparin was neutralized with an equivalent dose of protamine sulphate after an interval, usually 60 minutes but also 30 minutes and 90 minutes. Blood and urine samples were tested as before neutralization. The studies were continued for 4–7 hours and, after the dogs had been killed, specimens of organs were taken for scintillation counting.

Results: In the dogs given heparin alone, blood heparin anticoagulant activity and radioactivity were highest immediately after the drug was given and declined thereafter. The same pattern of heparin elimination was observed before neutralization in the dogs given protamine. Immediately after protamine the heparin anticoagulant activity disappeared from the blood and urine, as expected, and remained near control levels. At the same time there was a sudden unexpected drop in plasma and urine radioactivity. Thus the observed plasma radioactive count 30 minutes after neutralization had fallen to 24.8 ± 9.8 per cent (S.D.) of the value predicted by extrapolation of the pre-neutralization heparin elimination curve to the same time point. This change was 90 per cent complete after five minutes. Post-neutralization values either stayed near this level for the remainder of the study or rose to a higher plateau level, so mimicking the pharmacokinetic pattern seen when a drug is given by constant infusion. As urinary radioactivity fell at the same time as that of plasma, loss of the label could not be attributed to increased urinary excretion. Counts of radioactivity in the organs sampled were highest in the liver and kidney, but were not high enough to suppose that the fall in plasma radioactivity could be explained by shift of the label in these organs.

Conclusion: Our results indicate that, after its formation, the heparin-protamine complex undergoes rapid compartmental shift from the plasma. At present its fate is not clear but there is no evidence to suggest that it migrates to an organ normally associated with drug storage, such as the liver. The slow return of radioactivity to the circulation indicates the release of either free or bound heparin. Although heparin activity did not return to anticoagulant levels in our experiments, nevertheless this could be the mechanism underlying heparin rebound. Further studies to identify possible storage sites for the complex will be discussed and a hypothesis proposed to explain the results.

REFERENCES

A prospective survey of prehospital patients in cardiac arrest or with "high risk" symptoms was undertaken to document cardiac rhythms in these patients before arrival in hospital. Of 21 patients in cardiac arrest a tachycardia (mainly ventricular fibrillation) was found initially in 10 and was the predominant rhythm during transport in 16, while basic life support cardiopulmonary resuscitation and ventilation with oxygen were being administered. Emergency room electrocardiographic tracings revealed, however, that deterioration of cardiac rhythms had occurred so that only five remained in a tachycardia and 15 were asystolic. Eighty high risk patients with cardiorespiratory symptoms were also monitored. In this group 129 different rhythms were observed during transport, of which 34 (occurring in 26 patients) were of ventricular origin. The incidence of complex ventricular arrhythmias was significantly greater than in a similar group of control patients.

These data demonstrate that significant rhythm deterioration occurs in cardiac arrest victims when only basic life support is provided before hospital arrival. Untreated "high risk" patients also exhibit a high incidence of threatening ventricular ectopic rhythms during ambulance transport.


Epidemiological and animal studies suggest that chronic exposure to an operating room environment may adversely affect pregnant women and their unborn children, resulting in an increased risk of spontaneous abortion or a child with congenital abnormalities. Anaesthetic agents are implicated as the potential cause for this possible toxicity. However, little work has been done to examine the reproductive consequences to the female of exposing males to anaesthetic agents before mating.

Male rats were exposed to halothane 50 ppm, or 1700 ppm, or air eight hours daily for 12 days, and mated two days later. The impregnated females and their litters were carefully studied. Foetuses recovered on day 20 of gestation showed no external or visceral malformations. Litter size, foetal loss and foetal weights were unaffected. Exposure of male rats to halothane before mating did not impair fertility and reproductive consequences to the female of exposing males to anaesthetic agents before mating.


A prospective survey of prehospital patients in cardiac arrest or with "high risk" symptoms was undertaken to document cardiac rhythms in these patients before arrival in hospital. Of 21 patients in cardiac arrest a tachycardia (mainly ventricular fibrillation) was found initially in 10 and was the predominant rhythm during transport in 16, while basic life support cardiopulmonary resuscitation and ventilation with oxygen were being administered. Emergency room electrocardiographic tracings revealed, however, that deterioration of cardiac rhythms had occurred so that only five remained in a tachycardia and 15 were asystolic. Eighty high risk patients with cardiorespiratory symptoms were also monitored. In this group 129 different rhythms were observed during transport, of which 34 (occurring in 26 patients) were of ventricular origin. The incidence of complex ventricular arrhythmias was significantly greater than in a similar group of control patients.

These data demonstrate that significant rhythm deterioration occurs in cardiac arrest victims when only basic life support is provided before hospital arrival. Untreated "high risk" patients also exhibit a high incidence of threatening ventricular ectopic rhythms during ambulance transport.


Epidemiological and animal studies suggest that chronic exposure to an operating room environment may adversely affect pregnant women and their unborn children, resulting in an increased risk of spontaneous abortion or a child with congenital abnormalities. Anaesthetic agents are implicated as the potential cause for this possible toxicity. However, little work has been done to examine the reproductive consequences to the female of exposing males to anaesthetic agents before mating.

Male rats were exposed to halothane 50 ppm, or 1700 ppm, or air eight hours daily for 12 days, and mated two days later. The impregnated females and their litters were carefully studied. Foetuses recovered on day 20 of gestation showed no external or visceral malformations. Litter size, foetal loss and foetal weights were unaffected. Exposure of male rats to halothane before mating did not impair fertility and reproductive consequences to the female of exposing males to anaesthetic agents before mating.


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Ranitidine is a new histamine H2 receptor blocking agent, and would appear to be more potent and longer acting than cimetidine. Previous studies have shown that preoperative administration of cimetidine is partially effective in raising gastric pH to protect against aspiration syndrome. However, 10–16 per cent of patients may still have a pH of less than 2.5 at intubation. This double-blind study compared the effectiveness of preoperative cimetidine, ranitidine, and placebo in raising gastric pH.

**Methods:** Institutional approval of the protocol was obtained and all patients gave written, informed consent. One hundred and ninety patients of ASA status I and II, 18 to 70 years of age and having elective operations requiring tracheal intubation were studied. They were divided into two groups. Group A – 100 patients were randomly assigned to receive either cimetidine 300 mg, ranitidine 40 mg, ranitidine 80 mg, or placebo administered intravenously one hour before operation. Group B – 90 patients were randomly assigned to receive either cimetidine 300 mg, ranitidine 150 mg, or placebo administered orally two or four hours before operation.

Narcotic and anticholinergic premedicants were avoided. Following tracheal intubation a 16 French gauge Salem naso-gastric tube was inserted. The gastric contents were aspirated after tracheal intubation and also before extubation, by an observer unaware of the medication used. Volumes were recorded and pH was measured using a Fisher Accumet 320 pH meter.

**Results:** The groups were similar with respect to age, weight, height, and duration of fasting. The volume and pH of aspirate at the time of tracheal intubation are shown in the tables. The extubation results were similar to those at intubation. In both groups, cimetidine and ranitidine raised the gastric pH significantly compared to placebo. In Group A, ranitidine did not raise the gastric pH significantly compared to cimetidine, but in group B the gastric pH following ranitidine was significantly higher than following cimetidine (p < 0.009 at two hours and p < 0.01 at four hours). There were also fewer patients with a pH < 2.5 following ranitidine compared to cimetidine.

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nous diazepam (0.05 mg. kg\(^{-1}\)) have been shown to reduce the muscle pains following succinylcholine (SCH) injection. Therefore, we were interested in studying the influence of oral diazepam premedication on SCH myalgias. Previous studies have been criticized for lacking standardization of the many factors believed to influence the incidence of SCH-induced muscle pains. Therefore we undertook a double-blind randomized trial of patients undergoing a single operative procedure, with a standardized anesthetic regimen, and who were all ambulatory in the immediate postoperative period.

**Method:** Written informed consent was obtained from forty patients scheduled to undergo septoplasty operations. Their preoperative anxiety was scored on a scale of 0 to 3+ by the patient (subjective assessment) and by the anaesthetist (objective assessment). Ninety minutes before operation the patients received either diazepam 10 mg orally or placebo, with a sip of water.

The patient's anxiety level was assessed again in the operating room. Anaesthesia was induced with thiopentone 5 mg. kg\(^{-1}\) and succinylcholine 1 mg. kg\(^{-1}\). The level of fascinations and ease of tracheal intubation were noted. The trachea was sprayed with lignocaine aerosol 1 mg. kg\(^{-1}\). After tracheal intubation anaesthesia was maintained with halothane one per cent in 66 per cent nitrous oxide. Ventilation was by IPPB with a Bain circuit (fresh gas flow of 70 ml. kg\(^{-1}\) h\(^{-1}\)).

Thirty to forty hours later the patients were interviewed using a fixed questionnaire to assess levels of amnesia, nausea, surgical pain and sore throat. The second last of eight questions concerned muscle pain or stiffness. If it was present, the location and intensity (scale 1 to 3+) were noted.

**Summary:** There were no significant differences between the control and the diazepam groups in regard to age, sex distribution, premedication anxiety or ease of tracheal intubation. Only one of 20 patients treated with diazepam had increased subjective anxiety immediately before induction compared to nine placebo patients. (Chi-square = 8.6, p < 0.01)

In the postoperative period, only three of 20 diazepam patients (15 per cent) had myalgias compared to 10 of 20 placebo patients (50 per cent), a significant difference (Chi square = 5.8, p < 0.02). There were no significant differences in postoperative sensory pain, nausea, vomiting or recall after premedication.

**Results:** Patients in each group were similar with respect to age, weight and height and there were no significant differences between the interval from premedication to induction of anaesthesia and total anaesthetic time. Postoperative remedication rates were significantly lower in the zomepirac group (p = 0.01). During the first three hours following termination of anaesthesia, 27 (90 per cent) patients receiving meperidine had received analgesic medication compared to 17 (57 per cent) of the zomepirac group (X\(^2\) = 8.52, p < 0.01). Pain intensity scores were similar for each group during early recovery but were lower in the zomepirac patients during the later recovery period. Recovery and street fitness times tended to be longer in the meperidine group, but this difference was not statistically significant. Postoperative nausea and vomiting occurred in 11 (36 per cent) of meperidine patients and 7 (23 per cent) of zomepirac patients (p = 0.40), and the incidence of postoperative drowsiness was 13 and 3 per cent respectively (p < 0.35).

**Conclusions:** On the basis of remedication rates and postoperative pain levels, zomepirac appeared to be significantly more effective than meperidine in preventing postoperative pain, and would seem to have a longer duration of analgesic action. There was a tendency for the incidence of side effects to be lower with zomepirac than with meperidine. It is therefore concluded that zomepirac is preferable to meperidine for prevention of postoperative pain in dental short stay patients.
and more easily antagonized with anticholinesterases
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randomly divided into three groups: Group A received

dantrolene 5 mg/70 kg, Group B 10 mg/70 kg, and

neuromuscular blocking regimen. Follow-

ing induction of anaesthesia they received either

suxamethonium, 1 mg/kg or NC45 in doses of 50,

and pancuronium for relaxation during maintenance.

combination of succinylcholine for tracheal intubation

Dantrolene was administered in doses that would

produce depression of muscle twitch response similar

to the commonly used doses of non-depolarizing

muscle relaxants.

Methods: Thirty patients were studied and were

randomly divided into three groups: Group A received
dantrolene 5 mg/70 kg, Group B 10 mg/70 kg, and

Group C a placebo of normal saline. Three minutes

later, anaesthesia was induced with a sleep dose of
tubocurarine and succinylcholine. Muscle fascicula-
tions and tracheal intubation conditions were observed

and graded. Each patient was visited on the first

postoperative day and enquiries were made for the

presence or absence of muscle pains.

Results: Fasciculations were mild in five patients,

moderate in thirteen, severe in nine and absent

in three. Intubating conditions were good in all subjects

except one.

Only six patients admitted to having muscle pains

unrelated to the surgical incision and these were

evenly distributed between the three groups.

Conclusion: Dantrolene given intravenously in

small doses was ineffective in reducing the incidence

of either fasciculations or muscle pains after succinyl-

choline.

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ORG-NC45 As The Sole Muscle Relaxant. A.

Williams, H. K. Gyasi and D.R. Bevan.

ORG-NC45, a monoquaternary analogue of pan-

curonium, is a neuromuscular blocking drug undergo-

ing clinical trials in North America. Previous studies

have shown that it is faster in onset, of shorter duration

and more easily antagonized with anticholinesterases

than pancuronium and it has been recommended for

use as the sole muscle relaxant. However, it has not

been compared directly with existing drugs in clinical

practice. This study was designed to compare NC45 as

the single neuromuscular blocking drug with the

combination of succinylcholine for tracheal intubation

and pancuronium for relaxation during maintenance.

Methods: Forty patients, ASA I or II, scheduled for

elective operations, were studied. Anaesthesia was

induced with thiopentone and maintained with nitrous

oxide and oxygen supplemented with fentanyl. Neu-

romuscular transmission was monitored using train-of-

four stimulation. The patients were divided randomly

into four groups with 10 patients in each group for

choice of neuromuscular blocking regimen. Follow-

ing induction of anaesthesia they received either

succinylcholine, 1 mg/kg or NC45 in doses of 50,

70 or 90 &g/kg and intubation was attempted 90

seconds later, when twitching conditions were assessed

on a scale of 0–3 as described by Fahey et al.1 Muscle

relaxation was maintained in the NC45 group with

further increments of 10 &g/kg when the first twitch

of the train-of-four recovered to 10 per cent of control,

and in the succinylcholine group with pancuronium,

initially as a bolus of 40 &g/kg at full recovery from

tubocurarine, followed by increments of 5 &g/kg at

10 per cent recovery. At the end of the operation

neuromuscular block was antagonized with atropine

18 &g/kg and neostigmine 36 &g/kg at 10 per

cent recovery.

Results: All patients were intubated at 90 seconds.

Succinylcholine produced 100 per cent block with

uniformly excellent conditions whereas the three
doses of NC45 were associated with blocks of 7.5,

18.7 and 30.7 per cent and acceptable intubating

conditions in only 30 per cent of patients. The overall

requirements to maintain 90 per cent block with

pancuronium was 1.1 &g/kg min–1 compared with

1.28 &g/kg min–1 for NC45. No cumulative

effects were seen with either drug during the first hour

of neuromuscular blockade. Recovery of neuromus-

cular activity was more rapid with NC45 than pan-

curonium: five minutes after neostigmine the mean

train-of-four recovery was 50.6 ± 2.6 per cent after

NC45 compared with 41.6 ± 2.5 per cent after

pancuronium (P < 0.05).

Conclusion: We conclude that the lack of cumula-

tion, easy reversibility and lack of cardiovascular

effects2 suggests that NC45 has advantage over

currently available non-depolarizing muscle relax-

ants, but that its onset of action is too slow for rapid

intubation.

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(1980).

Guedel designed his oral airway in 1933 and Berman described his in 1950; both airways have been, and are, very popular. However, believing that in present day anaesthesia and resuscitation something more should be expected from an oropharyngeal airway, an airway intubator was designed in 1979. Its proximal half is cylindrical in shape and its distal half is open on the lingual surface. In addition to its use as an oropharyngeal airway, it has the following four advantages over other commonly used airways:

1. Partial airway obstruction despite the presence of an airway can be relieved by the passage of a tracheal tube through the airway intubator.
2. Suctioning of the pharynx can be effected by insertion of even a tonsil sucker through the airway intubator.
3. Indirect oral (“blind”) intubation can be done easily in the awake or unconscious patient by both experienced (anaesthetists) and inexperienced (surgeons, nurses, dentists, paramedics) intubators.
4. An excellent guide is provided for fibre-optic laryngoscopy.

The technique of use of the airway in each of these four situations will be described and case examples given.


The use of a venturi system of jet ventilation has been recommended as an alternative to spontaneous ventilation during bronchoscopy in children. Although this technique has been used safely, it is important to recognize that peak flow rates and inflation pressures may vary considerably with only small changes in the diameter of the injector or its angle from the axial line. These factors vary between manufacturers and it is therefore essential to investigate the characteristics of individual systems.

We compared the Hollinger bronchoscope (Pilling) with its injector of 0.89 mm internal diameter used in the axial line of the bronchoscope to the Storz bronchoscope which is equipped with an injector of 1.5 mm internal diameter that enters the instrument through a sidearm at an angle of 20 degrees to the axial line. Bronchoscopes 3.0, 4.0 and 5.0 millimeter diameter were assessed in a test lung at various driving pressures.

The Storz bronchoscopes produced consistently higher inflation pressures and peak flow rates at all driving pressures. In the 3.0 mm Storz bronchoscope, dangerously high inflation pressures were reached, 7.35 kPa (75 cmH\(_2\)O) with a driving pressure of only 207 kPa (30 psi), while with the Hollinger system, a maximum inflation pressure of only 3.14 kPa (32 cmH\(_2\)O) was produced with a driving pressure of 276 kPa (40 psi). To use the Storz system safely in infants, driving pressures should be maintained below 18 kPa (20 psi) or an injector of smaller diameter should be substituted.

The introduction of new injector equipment for paediatric bronchoscopy demands careful evaluation before use in infants, as small changes in the specifications may affect the safety of the system.

Physical Characteristics of Paediatric Tracheal Tubes. B.G. Anderson and D.J. Steward.

Paediatric tracheal tubes should be thin-walled and should conform readily to the shape of the airway but should resist kinking or compression by external pressure. Though studies have been reported of the physical characteristics of adult tracheal tubes, little information is available concerning paediatric tubes. Methods: We have tested a range of each of 10 different models of paediatric tracheal tubes of sizes 3.0 mm - 5.5 mm inclusive. The measurements included:

1. Internal diameter (I.D.) and wall thickness, from which the external diameter (E.D.) for each tube was derived.
2. External force (gram Newtons) required to compress each tube to a point at which resistance to flow is increased by 50 per cent (gram Newtons R + 50).
3. The angle at which each tube kinked to produce a 50 per cent increase in resistance to flow (\(\theta\) bend R + 50).

Measurements 2 and 3 were made with the tracheal tubes at a temperature of 40\(^\circ\)C ± 1°C. Results: I.D., wall thickness, and E.D. varied significantly among tubes tested of similar labelled I.D. The true calculated E.D. frequently differed from that marked on the tube. The compressibility (gram Newtons R + 50) decreased with increasing tube size (mm I.D.) and with increasing wall thickness in similar I.D. tubes. Differing compressibility in tubes of identical I.D. and wall thickness is a function of the plastic material of the tubes which can thus be documented. The angle at which kinking resulted in increased flow resistance (\(\theta\) bend R + 50) decreased with increasing wall thickness in tube of similar I.D. size.

Discussion and Conclusions: It is important to define the physical characteristics which will result in a tracheal tube with ideal clinical performance.

1. The tendency of a tube to collapse due to external pressure is determined by physical principles (Lamé's Law) and the material of the tube. The standardized test which we have used can be used to document these factors for each tube.
2. The tendency of a given size tracheal tube to kink is largely determined by wall thickness, though tracheal tube design must involve a compromise between the adequacy of the I.D., and the wall thickness. The design of improved tracheal tubes will require standardized tests to select ideal properties for plastic materials.


It is recognized that isoflurane potentiates the neuromuscular blocking effect of d-tubocurarine (\(\alpha\)TC) to a greater extent than other commonly used volatile anaesthetic agents. The extent of this potentiating effect has not been reported for the newborn human nor has the reversibility of this effect on withdrawal of the volatile agent been documented.
Neuromuscular blockade was monitored in a series of infants (aged newborn to two months) following intravenous administration of dTc in a dose of 0.1 mg·kg⁻¹·min⁻¹. Isometric contraction of the adductor pollicis muscle was recorded by a Grass FT103C force displacement transducer. The ulnar nerve was stimulated through surface electrodes and the response to single repeated stimuli (1 Hz and 0.2 Hz) and train-of-four stimuli was recorded on a chart recorder. Measurements were made during nitrous oxide, halothane, and isoflurane anaesthesia. End-tidal carbon dioxide was recorded using a Puritan Bennett carbon dioxide monitor and sampling from the distal tip of the tracheal tube.

**Results and Comments:**

1. In infants, as in adults, isoflurane potentiates dTc to a greater extent than halothane.
2. The potentiation of dTc is reversed when isoflurane anaesthesia is discontinued.
3. The extent of potentiation of neuromuscular block in infants is at least as great as that seen in adults.
4. The neuromuscular block of dTc potentiated by isoflurane anaesthesia is decreased during hypcapnia.
5. Because of the marked potentiating effect of isoflurane, the initial dose of dTc administered to infants receiving this agent should be reduced to 0.1 mg·kg⁻¹·min⁻¹ and repeat doses given as indicated by a "block aid" monitor or similar equipment.


After major surgery we compared the speed and degree of recovery of 25 children under five years of age (mean 3.33 ± 1.76 years) who were anaesthetized with 70 per cent nitrous oxide and 30 per cent oxygen, supplemented with one of the following:

- **Group I** (6 patients): Continuous intravenous morphine infusion 2 μg·kg⁻¹·min⁻¹ to achieve serum morphine level 87.3 ± 5.8 μg·l⁻¹
- **Group II** (11 patients): halothane 0.5 per cent.
- **Group III** (8 patients): isoflurane 1.0 per cent.

All patients were paralysed with metocurine and ventilated artificially to maintain good oxygenation and normocarbia.

**Recovery of consciousness,** spontaneous respiration, and limb movement were scored using a modification of the postoperative recovery scoring system by Steward. After the effect of the muscle relaxant was adequately reversed.

**When nitrous oxide was discontinued the three groups recovered to almost the same degree.** There was no statistically significant difference between the three groups. Thereafter GROUP I and III recovered with the same speed and to about the same degree, though the latter group scored slightly better after extubation. GROUP II scored poorly in the last three assessment periods.

**Conclusion:** The speed and degree of postanaesthetic recovery after morphine infusion at 2 μg·kg⁻¹·min⁻¹ and isoflurane one per cent was excellent and almost identical. The morphine group had the added advantage of not requiring immediate administration of postoperative analgesia and sedation.

**REFERENCES**


While a pure fentanyl anaesthetic is reported to avoid cardiac depression it may not prevent hypertension or decreased MVO₂. Halothane used alone avoids hypertension but may markedly depress the myocardium leading to decreased MVO₂, low cardiac output, hypotension and cardiac failure. The haemodynamic consequences of adding fentanyl to a halothane anaesthetic were evaluated in this study.

Ten patients for coronary artery bypass were induced with thiopentone 3 mg·kg⁻¹ and maintained with halothane 1–1.5 per cent inspired, with pancuronium as relaxant. The data were collected during a period of minimal surgical stimulation while veins were being prepared and after the halothane had been administered for at least one hour. Measured baseline data included mean arterial pressure (MAP), systolic pressure (SP), diastolic pressure (DP), pulmonary artery diastolic (PAD), heart rate (HR), and cardiac output (CO). Stroke volume (SV) and total peripheral resistance (TPR) were computed from the measured data. An index of ejection fraction (EFJ) was derived by the ratio (SV/PAD). Fentanyl 1 μg·kg⁻¹ was given through the right atrial line and measurements were repeated 8–10 minutes later. This procedure was repeated as additional fentanyl was given for a total dose 2, 5, and 10 μg·kg⁻¹ until MAP fell below 8 kPa (60 mmHg). Statistical significance was determined.
using analysis of variance for each measured or derived variable.

MAP, SP, DP all fell consistently with each dose increment and significantly over the dose range. Cardiac output did not change significantly nor was there a detectable trend (P < 0.950). HR, PA, PAD, and TPR decreased consistently and EFI increased consistently with each dose increment. However, the changes did not reach statistical significance due to large standard deviation and small sample size. Final dosage of 5 and 10 μg·kg⁻¹ were not reached in some patients due to MAP falling below 8 kPa (60 torr). Arterial pressure rose consistently as the halothane dosage of 5 and 10 μg·kg⁻¹ were not reached in some patients. The decrease in arterial pressure during low level halothane anaesthesia when fentanyl is added appears to be dose related, beginning with small dosages. The fall in arterial pressure can be dramatic, necessitating discontinuation of the halothane. A synergistic action is suggested by the stability of arterial pressure with halothane alone and then the return toward baseline when halothane is discontinued after fentanyl administration. Decreased TPR appears to explain the arterial pressure fall as CO did not change. The stability of CO was secondary to the fall in PAD and HR being offset by the increased EFI. Fentanyl should be given with great care to patients receiving halothane.

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Halothane anaesthesia in man abolishes the normal ventilatory response to isocapnic hypoxaemia, as well as responses to other physiological and pharmacological stimuli sensed by peripheral chemoreceptors. Furthermore, halothane in subanaesthetic or sedating doses markedly reduces these responses, while having little or no effect on ventilation or the ventilatory response to added carbon dioxide. This suggests a selective action of halothane on components of the peripheral chemoreflex arc that are distinct from the central carbon dioxide reflex, i.e. peripheral chemoreceptors, their central connections, or neural circuits which modulate their input. The purpose of this study was to test the hypothesis that this action is at the peripheral chemoreceptors themselves.

The subjects were seven fit volunteers. In each, isocapnic hypoxaemia (PETCO₂ 6.0 kPa) was induced and maintained steady by manipulating the composition of inhaled gas. When the subject was unaware, a small dose of halothane (0.15 per cent) was introduced in the inhaled gas to induce sedation, while isocapnic hypoxaemia was maintained. Upon exposure to halothane, hypoxaemic-driven ventilation decreased progressively over the first minute, and the relationship of end-tidal halothane concentration to ventilatory depression at 30 and 60 seconds was nearly identical to the relationship observed during steady states of halothane sedation, i.e. after 20 minutes of inhalation.

These results indicate that the site of the selective action of halothane on the peripheral chemoreflex arc is at a tissue in which the halothane level bears a nearly constant relationship to end-tidal concentration through the early period of sedation induction and in the steady state of sedation. That tissue would be located within a few seconds circulatory time from the lungs and to have a very high rate of perfusion to halothane capacity ratio. The only components of the peripheral chemoreflex arc which satisfy these requirements are the peripheral chemoreceptors themselves.
Isoflurane Anaesthesia.

Fentanyl Anaesthesia.

Nitrous Oxide

Results:

Discussion:

Methods:

Results:

ABSTRACTS OF PAPERS PRESENTED AT THE ANNUAL MEETING


Phosphodiesterase inhibition, stimulation of catecholamine synthesis and release, as well as altered calcium kinetics, are actions of aminophylline possibly responsible for its arrhythmogenic properties. These cardiac effects can result in potentially lethal arrhythmias. In an effort to better understand these arrhythmogenic properties and to provide a more rational approach to pharmacological management, we explored the usefulness of the calcium blocker verapamil and the beta adreno-receptor blocker propranolol in aminophylline toxic dogs. Verapamil was studied because of its effects on calcium kinetics mediated by cyclic AMP.

Method: Eighteen dogs were intubated and ventilated after induction of anaesthesia with pentobarbital 30 mg.kg⁻¹ and pancuronium 0.1 mg.kg⁻¹. Electrocardiogram, arterial blood pressure and left ventricular pressure were monitored continuously. Cardiac output and systemic vascular resistance, calcium, arterial blood gases and serial aminophylline levels were measured. All animals were rendered toxic by aminophylline infusion, an initial dose of 50 mg.kg⁻¹ over five minutes with subsequent doses of 10 mg.kg⁻¹ over 30 seconds. Twenty minutes after each aminophylline infusion, the dog was challenged with phenylephrine 10 to 20 μg.kg⁻¹. This resulted in hypertension of short duration and reproducible emergence of ventricular arrhythmias. The dogs continued to receive additional aminophylline infusion until these arrhythmias became persistent for longer than a 120 second observation period. Arrhythmias were defined as frequent PVC's, ventricular tachycardia, or ventricular fibrillation. The dogs were divided into three groups of six animals each. Group I (control) received no anti-arrhythmics whereas Group II received verapamil 0.2 mg.kg⁻¹ and Group III received propranolol 0.1 mg.kg⁻¹ for the treatment of persistent ventricular arrhythmias.

Results: All dogs in Group I died of ventricular arrhythmias when the serum aminophylline level reached 152 ± 23.3 μg per cent (mean ± SD). There was no statistically significant difference between the serum aminophylline level at the time of persistent ventricular arrhythmias in all three groups. In Group

had only one visible twitch (out of four) at the end of the infusion. Train-of-four ratios after 10 minutes of spontaneous recovery were much smaller with isoflurane (14 ± 6 per cent) than fentanyl (54 ± 8 per cent). Discussion: Although tachyphylaxis was observed with isoflurane, it was followed by a subsequent increase in succinylcholine requirements which correlated with isoflurane. This corresponds to the establishment of profound non-depolarizing blockade. Two explanations, which are not mutually exclusive, could account for this "reversal of tachyphylaxis". It may be an intrinsic property of succinylcholine which would be observed with nitrous oxide-fentanyl anaesthesia if the infusion were sufficiently prolonged to allow full development of non-depolarizing blockade. It seems more likely, however, that during profound non-depolarizing blockade, isoflurane potentiates succinylcholine as it does tubocurarine, pancuronium and gallamine.

The Anti-Arrhythmic Effects of Verapamil and Propranolol in Aminophylline Toxic Dogs. 

Robert M. Friesen and Jorge F. Bonet.

Phosphodiesterase inhibition, stimulation of catecholamine synthesis and release, as well as altered calcium kinetics, are actions of aminophylline possibly responsible for its arrhythmogenic properties. These cardiac effects can result in potentially lethal arrhythmias. In an effort to better understand these arrhythmogenic properties and to provide a more rational approach to pharmacological management, we explored the usefulness of the calcium blocker verapamil and the beta adreno-receptor blocker propranolol in aminophylline toxic dogs. Verapamil was studied because of its effects on calcium kinetics mediated by cyclic AMP.

Method: Eighteen dogs were intubated and ventilated after induction of anaesthesia with pentobarbital 30 mg.kg⁻¹ and pancuronium 0.1 mg.kg⁻¹. Electrocardiogram, arterial blood pressure and left ventricular pressure were monitored continuously. Cardiac output and systemic vascular resistance, calcium, arterial blood gases and serial aminophylline levels were measured. All animals were rendered toxic by aminophylline infusion, an initial dose of 50 mg.kg⁻¹ over five minutes with subsequent doses of 10 mg.kg⁻¹ over 30 seconds. Twenty minutes after each aminophylline infusion, the dog was challenged with phenylephrine 10 to 20 μg.kg⁻¹. This resulted in hypertension of short duration and reproducible emergence of ventricular arrhythmias. The dogs continued to receive additional aminophylline infusion until these arrhythmias became persistent for longer than a 120 second observation period. Arrhythmias were defined as frequent PVC's, ventricular tachycardia, or ventricular fibrillation. The dogs were divided into three groups of six animals each. Group I (control) received no anti-arrhythmics whereas Group II received verapamil 0.2 mg.kg⁻¹ and Group III received propranolol 0.1 mg.kg⁻¹ for the treatment of persistent ventricular arrhythmias.

Results: All dogs in Group I died of ventricular arrhythmias when the serum aminophylline level reached 152 ± 23.3 μg per cent (mean ± SD). There was no statistically significant difference between the serum aminophylline level at the time of persistent ventricular arrhythmias in all three groups. In Group
Il, these arrhythmias were promptly terminated by verapamil. Apart from its anti-arrhythmic effect, verapamil produced a fall in blood pressure (~33 per cent) and systemic vascular resistance. In Group III, propranolol resulted in rapid but partial arrhythmia control. Three dogs required additional doses of propranolol. No significant haemodynamic changes other than heart rate were seen in this group. Subsequent challenge with phenylephrine could not re-institute these arrhythmias in Group II while transient ventricular ectopies were seen in four dogs in Group III.

Discussion: Verapamil and propranolol exerted an anti-arrhythmic effect in aminophylline-induced ventricular arrhythmias. The efficacy of verapamil was independent of a reduction in blood pressure and systemic vascular resistance as subsequent phenylephrine-induced hypertension could not re-institute these arrhythmias. Propranolol appeared less effective since it did not completely suppress the arrhythmias in three dogs and could not prevent emergence of PVC's in four after repeat phenylephrine challenge. Although mechanisms of anti-arrhythmic action remain speculative, these observations suggest that verapamil, and perhaps propranolol, hold promise in pharmacological management of aminophylline-induced cardiac arrhythmias.


Les travaux de McLivaine et collègues ont montré que l'anesthésie à base de morphinique 1.5 mg·kg⁻¹ semble prévenir l'hypertension paroxysmale post-opératoire dans la chirurgie du pontage coronarien. L'incidence observée a été de 3.8 pour cent versus 28 pour cent lorsque l'anesthésie était faite de fentanyl à petites doses complétées par des agents haloïliques.

Ce travail compare l'incidence de l'hypertension post-opératoire chez un groupe de 24 malades recevant morphine 1.5 mg·kg⁻¹ à un autre groupe de 24 malades recevant fentanyl 50 μg·kg⁻¹ (ces doses étant considérées comme équivalentes). Tous les patients recevaient d'autre part protoxyde d'azote-oxygène (0.5%) et avaient une fonction ventriculaire normale. La prémédication et la technique d'induction étaient identiques dans les deux groupes.

Résultats: Hypertension post-opératoire: On n'a observé aucun cas d'hypertension chez les malades recevant de la morphine contre sept cas sur 24 dans les malades du groupe fentanyl (29 pour cent).

Produit fréquence × pression: A la suite de l'intubation, le produit fréquence × pression a augmenté au delà de 1300 mmHg dans 23 (96 pour cent) dans le groupe morphine et en aucun cas dans le groupe fentanyl.

Durant l'intervention avant la CEC, on a dû employer la nitroglycérine dans 17 cas sur 24 (70 pour cent) dans le groupe morphine et dans 10 cas sur 24 (41 pour cent) dans le groupe fentanyl.

De même on a jugé bon d'employer l'indéral dans sept cas sur 24 (29.1 pour cent) dans le groupe morphine et deux sur 24 (8.3 pour cent) dans le groupe fentanyl.

Conclusion: Ces résultats montrent que l'anesthésie à la morphine possède un effet préventif de l'hypertension paroxysmale post-opératoire par rapport à des doses équivalentes de fentanyl.

Que durant la chirurgie pour la période précédant la circulation extra-corporelle, le fentanyl apparait supérieur à la morphine pour l'anesthésie du malade coronarien.

REFERENCE


The patient undergoing ocular surgery presents special problems. Satisfactory surgical conditions require a stationary eye; intraoperative coughing, bucking and vomiting must be avoided; intraocular pressure rises, which can cause extrusion of globe contents, must be avoided. Choice of muscle relaxant is of paramount importance. The ideal relaxant should be potent, with a rapid onset and appropriate duration of action, and be readily reversible. In addition autonomic and cardiovascular side effects should be minimal.

Metocurine, a non-depolarizing neuromuscular blocking agent, has been recently reintroduced into clinical practice. In doses of 0.3 mg·kg⁻¹ metocurine produced 96.1 mean twitch height depression within 4.8 ± 0.6 (SEM) minutes allowing easy tracheal intubation. Metocurine offers the clinically advantageous cardiovascular effects of stable heart rate and mean blood pressure. Combination of metocurine and pancuronium produces potentiation of neuromuscular blocking effect so that administration of small doses of both drugs, pancuronium 0.18 mg·kg⁻¹ and metocurine 0.072 mg·kg⁻¹, produces clinically effective neuromuscular blockade with stable haemodynamic parameters and rapid reversal of neuromuscular blockade.

This study was designed to examine the effects of metocurine 0.3 mg·kg⁻¹ and metocurine 0.08 mg·kg⁻¹ plus pancuronium 0.02 mg·kg⁻¹ combination on intraocular pressure and to assess their suitability for patients undergoing ocular surgery. Thirty-nine male and female subjects aged 16–50 years undergoing elective minor surgical procedures were studied. The patients were allocated to two treatment groups. Treatment Group 1: (N=20) Each patient was induced with sodium thiopentone 3.5–5 mg·kg⁻¹ and metocurine 0.3 mg·kg⁻¹.

Treatment Group 2: (N=19) Each patient was induced with sodium thiopentone 3.5–5 mg·kg⁻¹ plus metocurine 0.08 mg·kg⁻¹ plus pancuronium 0.02 mg·kg⁻¹.

The time interval between relaxant administration and complete peripheral nerve twitch suppression was recorded and the degree of vocal cord relaxation was evaluated at the time of intubation using the criteria of Land and Stovner.3

Intraocular pressure was recorded, using a portable
Perkins applanation tonometer, on arrival in the operating room (control) and every two minutes for a total of 10 minutes following relaxant administration. The results of the study showed that metocurine 0.3 mg.kg 

The pneumotachograph and with chest wall magnetometer and with continuous loads during anaesthesia. We have studied ventilatory compensation for continuous loads because of the long time interval when the airway is unprotected.

**REFERENCES**


**Ventilatory Compensation for Continuous Loads During Halothane Anaesthesia in Man. C.A. Moote, R.L. Knill and J.L. Clement.**

Ventilatory impedance or “loaded breathing” has been widely studied only in awake subjects. Surgical patients may experience a variety of loads created by prooperative disease states, anaesthetic equipment and surgical positioning. We have studied ventilatory compensation for continuous loads during anaesthesia.

Elastic loads were constructed from rigid drums of various sizes, linearized flow resistive loads from layers of wire mesh and sponge. Eighteen subjects were studied during steady state halothane 1.1 MAC anaesthesia. In each subject we tested the responses to both an elastic and a flow resistive load of small, medium or large size, i.e. loads which reduced initial tidal volume approximately 10, 30 or 50 per cent respectively. Loads were applied to the airway during inspiration only and continued for five minutes while halothane levels were maintained constant and PaO2 greater than 0.5. Ventilation was measured with a pneumotachograph and with chest wall magnetometers.

With the addition of each load we observed an initial reduction of ventilation followed by progressive compensation to a new steady state of ventilation over two or three minutes. After five minutes of loading, VCO2 and arterial halothane levels were unchanged from control. There were no consistent changes in the relative contributions of the rib cage and diaphragm to ventilation at any time during addition of loads. Steady state values of Vt and PaCO2, control and after five minutes of continued loading are given in the table below (means ± S.E.M.). PaO2 values remained greater than 135 torr.

Compensation for continuous loads was unexpectedly good, indeed for small and medium loads it was complete. This is difficult to explain on the basis of altered chemical drive alone, since there were no detectable change of PaCO2 values in the steady loaded state with small and medium loads. Furthermore, upon removal of the loads ventilation increased transiently above control values, a response which was also inexplicable on the basis of chemical drive. This suggests that other factors, reflex or neuromuscular in nature, played a role in stabilizing ventilation during loads.

### ELASTIC LOADS

<table>
<thead>
<tr>
<th>Load Size</th>
<th>Small</th>
<th>Medium</th>
<th>Large</th>
</tr>
</thead>
<tbody>
<tr>
<td>(cm H2O)</td>
<td>(4.0 ± 0)</td>
<td>(17.0 ± 2.0)</td>
<td>(57.0 ± 14.0)</td>
</tr>
<tr>
<td>W (min m2)</td>
<td>3.8 ± 0.2</td>
<td>3.5 ± 0.2</td>
<td>3.3 ± 0.1</td>
</tr>
<tr>
<td>loaded</td>
<td>3.6 ± 0.2</td>
<td>3.4 ± 0.3</td>
<td>2.6 ± 0.1*</td>
</tr>
<tr>
<td>PaCO2 (torr)</td>
<td>48.2 ± 1.5</td>
<td>44.5 ± 1.6</td>
<td>45.5 ± 2.2</td>
</tr>
<tr>
<td>loaded</td>
<td>48.3 ± 1.9</td>
<td>45.4 ± 1.3</td>
<td>51.1 ± 2.3*</td>
</tr>
</tbody>
</table>

### RESISTIVE LOADS

<table>
<thead>
<tr>
<th>Load Size</th>
<th>Small</th>
<th>Medium</th>
<th>Large</th>
</tr>
</thead>
<tbody>
<tr>
<td>(cm H2O - cm2)</td>
<td>(7.0 ± 0.1)</td>
<td>(20.0 ± 3.0)</td>
<td>(100.0 ± 25.0)</td>
</tr>
<tr>
<td>W (min m2)</td>
<td>3.8 ± 0.2</td>
<td>4.0 ± 0.4</td>
<td>3.5 ± 0.2</td>
</tr>
<tr>
<td>loaded</td>
<td>3.8 ± 0.2</td>
<td>3.6 ± 0.2</td>
<td>3.0 ± 0.1*</td>
</tr>
<tr>
<td>PaCO2 (torr)</td>
<td>48.1 ± 1.4</td>
<td>44.4 ± 1.6</td>
<td>45.0 ± 1.7</td>
</tr>
<tr>
<td>loaded</td>
<td>48.3 ± 1.3</td>
<td>44.4 ± 1.5</td>
<td>49.3 ± 1.8*</td>
</tr>
</tbody>
</table>

*Significantly different from control values. P < 0.01

**Haemodynamic Effects of Intravenous Nitroglycerin in Patients with Coronary Artery Disease. W.A.C. Mutch, J.D. Culligan and I.R. Thomson.**

**Introduction:** Previous reports of the haemodynamic effects of intravenous nitroglycerin infusion may be invalid because the investigators infused nitroglycerin by delivery systems containing polyvinyl chloride (PVC) plastic. Adsorption of nitroglycerin (NTG) to PVC results in reduced delivery of nitroglycerin. We employed a delivery system free of PVC to assess the haemodynamic effects of intravenous nitroglycerin 0.5 μg·kg−1·min−1 in awake premedicated patients with coronary artery disease.

**Methods:** Twenty patients about to undergo myocardial revascularization entered a randomized double-blind study comparing the haemodynamic
Effects of intravenous nitroglycerin (n9) vs placebo (P) (n1). All patients had angina unresponsive to medical management. Patients were fasted and had nitrates withheld from midnight of the day of the operation. Following premedication with diazepam 0.15 mg. kg\(^{-1}\) by mouth and intramuscular atropine 0.007 mg. kg\(^{-1}\), nasal oxygen (3 l/min) was administered. Intravenous, radial artery and thermodilution pulmonary artery catheters were inserted under local anaesthesia. Electrocardiograph leads V5 and II were monitored continuously. Haemodynamic variables were measured before and after 20 minutes of intravenous NTG/P infusion. Infusions were administered by a Sage pump from a polypropylene syringe with polyethylene tubing connected to a Teflon catheter in a PVC plastic from our intravenous delivery system.

**Results:** (Sec Table). The P and NTG groups did not differ before infusion for any haemodynamic variable. After 20 minutes of NTG/P infusion significant differences were noted between groups. Nitroglycerin caused significant decreases in MAP, MPAP, PCWP, CVP, and CI compared to P. DPTI/SPTI was improved by NTG.

**Discussion:** Intravenous NTG 0.5 μg. kg\(^{-1}\). min\(^{-1}\) produced significant haemodynamic effects, including myocardial oxygen supply/demand ratio at a dose below that previously reported to cause minimal haemodynamic changes. The apparent potency of NTG in our study is a direct result of the exclusion of PCW, plaque from our intravenous delivery system. Used in this way, intravenous NTG is a potent vasodilator which must be administered cautiously. Reports of haemodynamic effects of intravenous NTG should not be accepted unless details of administration techniques are provided.

### Tables

**Table 1:** Haemodynamic effects of Intravenous Protamine for Reversal of Heparin in Swine. Kent H. Rogers, Brian Milne and Tomas A. Salerno.

<table>
<thead>
<tr>
<th></th>
<th>Pre-infusion</th>
<th>20 Minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>P</td>
<td>NTG</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>7.0 ± 2.2</td>
<td>6.5 ± 4.3</td>
</tr>
<tr>
<td>MAP (torr)</td>
<td>105.7 ± 3.1</td>
<td>93.0 ± 4.7*</td>
</tr>
<tr>
<td>MPAP (torr)</td>
<td>23.1 ± 2.7</td>
<td>13.6 ± 1.7*</td>
</tr>
<tr>
<td>PCWP (torr)</td>
<td>14.7 ± 2.7</td>
<td>7.7 ± 1.2*</td>
</tr>
<tr>
<td>CVP (torr)</td>
<td>6.8 ± 1.0</td>
<td>3.6 ± 1.0*</td>
</tr>
<tr>
<td>CI (ml/min/m(^2))</td>
<td>2.90 ± 0.16</td>
<td>2.38 ± 0.14*</td>
</tr>
<tr>
<td>Si (ml/m(^2))</td>
<td>41.3 ± 2.4</td>
<td>34.9 ± 2.1</td>
</tr>
<tr>
<td>SVRI (dyne-sec-m(^2)/cm(^5))</td>
<td>2.757 ± 185</td>
<td>3726 ± 189</td>
</tr>
<tr>
<td>PVR (dyne-sec-m(^2)/cm(^5))</td>
<td>275.4 ± 30.9</td>
<td>247.9 ± 15.7</td>
</tr>
<tr>
<td>RPP (mm Hg)</td>
<td>9699 ± 572</td>
<td>9672 ± 797</td>
</tr>
<tr>
<td>DPTI/SPTI</td>
<td>0.99 ± 0.7</td>
<td>1.16 ± 0.11</td>
</tr>
</tbody>
</table>

* = p < 0.05 vs placebo.

**Table 2:** Comparison of hemodynamic effects of Intravenous Protamine (P) and Placebo (P) in patients with coronary artery disease. Anesthesiology 51 (3):S69 (1979).

<table>
<thead>
<tr>
<th></th>
<th>Pre-protamine</th>
<th>Post-protamine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IV</td>
<td>IA</td>
</tr>
<tr>
<td></td>
<td>15.6 ± 1.9</td>
<td>20.0 ± 5.1</td>
</tr>
<tr>
<td></td>
<td>3.20 ± 0.24</td>
<td>2822 ± 213</td>
</tr>
<tr>
<td></td>
<td>3711 ± 113</td>
<td>187 ± 54</td>
</tr>
<tr>
<td>LVEDP (cm Hg)</td>
<td>15.6 ± 1.9</td>
<td>20.0 ± 5.1</td>
</tr>
<tr>
<td></td>
<td>3.20 ± 0.24</td>
<td>2822 ± 213</td>
</tr>
<tr>
<td></td>
<td>3711 ± 113</td>
<td>187 ± 54</td>
</tr>
<tr>
<td>SVR (dynes/sec/cm(^5))</td>
<td>3.36 ± 0.43</td>
<td>3.20 ± 0.24</td>
</tr>
<tr>
<td></td>
<td>2882 ± 213</td>
<td>187 ± 54</td>
</tr>
<tr>
<td>Systolic PAP (mm Hg)</td>
<td>3.20 ± 0.24</td>
<td>2822 ± 213</td>
</tr>
<tr>
<td></td>
<td>3711 ± 113</td>
<td>187 ± 54</td>
</tr>
<tr>
<td>PVR dynes/sec/cm(^5))</td>
<td>3.36 ± 0.43</td>
<td>3.20 ± 0.24</td>
</tr>
<tr>
<td></td>
<td>2882 ± 213</td>
<td>187 ± 54</td>
</tr>
</tbody>
</table>

* = mean ± standard error of mean.

**References**


PAP (TV 76 per cent, IA 79 per cent) and PVR occurred at 60 seconds. The intra-aortic group showed a statistically significant drop in systolic blood pressure at five and 15 minutes compared to the intravenous group.

Conclusion: We conclude that, in contrast to the apparent effect in humans, intra-aortic injection of protamine does not prevent the haemodynamic changes associated with the intravenous route. The mechanism for the marked elevation of PAP and PVR is unknown but may indicate either the release of a vasoactive substance or a direct vascular effect. In addition, the marked increase in PAP seen in pigs has not been observed in humans (research in progress).

REFERENCES


Introduction: Despite the advent of high dose narcotic techniques undesirable hypertensive episodes continue to occur in patients undergoing coronary artery bypass graft surgery. The renin-angiotensin system has been implicated as a mediator of hypertension during this surgery. We wished to determine whether a continuous fentanyl infusion would attenuate adverse haemodynamic responses and if the renin-angiotensin system was associated with hypertensive episodes.

Methods: Twelve patients with comparable preoperative demographic data undergoing elective cardiac revascularization operations were studied. Premedication consisted of diazepam, morphine, and hyoscine. Supplemental oxygen was given en route to the operating room. Beta blockers and nitrates were continued to the time of operation. A haemodynamic profile and blood for plasma renin determination were obtained before induction of anaesthesia and after tracheal intubation, skin incision, sternotomy, and aortic dissection. Blood for plasma renin determination was subsequently obtained at regular intervals or before therapeutic intervention for the treatment of hypertensive episodes. Plasma for fentanyl assay was taken at intervals of 5, 10, 20, 30, 45, 60, 90 and 120 minutes. All patients were pre-oxygenated and then anaesthesia was induced with fentanyl 75 μg·kg⁻¹ at a rate of 1 mg·min⁻¹ and paralysis was produced with pancuronium 0.15 mg·kg⁻¹. Six of twelve patients received no additional fentanyl (Bolus Group). The remaining six patients received additional fentanyl 0.75 μg·kg⁻¹·min⁻¹ by infusion until either time of rewarming on cardiopulmonary bypass (CPB) or a cumulative dose of 200 μg·kg⁻¹ had been given (Infusion Group). Normocarbia was maintained throughout.

Results: In the period before CPB an increase of systolic blood pressure greater than 20 per cent of preinduction levels was considered an adverse response necessitating therapeutic intervention. Five of six patients in the bolus group versus one of the six in the infusion group required such intervention. Comparison of mean systolic blood pressures revealed a tendency to lower levels in the infusion group (Figure 1).

A mean arterial pressure on CPB greater than 13.3 kPa (100 mm Hg) at a flow rate of 1.8 l·m⁻² was considered unacceptable hypertension and was treated. All of the bolus group required treatment and one of the infusion group. Mean plasma fentanyl concentrations were greater in the infusion group from 20 minutes on, reaching statistical significance at 60 minutes. (Figure 2). Mean plasma renin values, although within normal limits, were greater in the bolus group than in the infusion group. There was no correlation of peak plasma renin values with hypertension in any patient.

Conclusions: A loading dose of fentanyl 75 μg·kg⁻¹ followed by an infusion of 0.75 μg·kg⁻¹·min⁻¹ provided a more haemodynamically stable anaesthetic with fewer additional pharmacological interventions when compared to a loading dose alone. Higher mean plasma fentanyl concentrations resulted in lower mean renin values. This study strongly suggests that hypertension encountered during aorto-coronary bypass surgery in patients under fentanyl anaesthesia is not due to the renin-angiotensin system.