Meeting abstracts

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Jugular bulb desaturation during rewarming from cardiopulmonary bypass is influenced by isoflurane

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Introduction: Jugular bulb oxyhaemoglobin desaturation ($SjO_2 \leq 50\%$) during the rewarming phase of cardiopulmonary bypass (CPB) is associated with postoperative cognitive deficits [1]. Isoflurane effects cerebral blood flow and cerebral metabolic rate, both of which affect SjO_2 [2]. We report the effect of isoflurane on the incidence of desaturation during rewarming from CPB for coronary artery surgery.

Materials and methods: One hundred and nine men and 16 women of mean age 60 years (standard deviation 9 years) were studied. Isoflurane 1% was used on CPB for hypnosis in 61 patients and 64 received either propofol or a combination of morphine and midazolam. A catheter was positioned in the right jugular bulb. At 36°C, during rewarming, paired jugular bulb and arterial samples were taken for blood gas and SjO_2 measurements. Nasopharyn-

Table 1

Blood gas and blood pressure results

	I group ($n = 61$)	NI group ($n = 64$)	*P*
SjO_2 (%)	64.6 (9.5)	58.3 (11.6)	0.001
SjO_2 carbon dioxide corrected (%)	70.6 (8.4)	63.5 (10.7)	0.001
$SjO_2 \leq 50\%$ (*n*)	3 (4.9%)	16 (25%)	<0.01
SjO2 ≤50% carbon dioxide corrected (*n*)	1 (1.6%)	3 (4.7%)	>0.2
$PaCO_2$ (kPa)	4.49 (0.55)	4.59 (0.54)	0.286
MAP (mmHg)	58.8 (15.2)	64.5 (15.6)	0.065
Haemoglobin (g/dl)	8.3 (0.98)	8.6 (1.2)	0.258
SaO_2 (%)	98.0 (0.6)	98.0 (0.5)	0.948
CPB (min)	88 (24)	86 (34)	0.661
Min temp CPB (°C)	31.0 (2.0)	30.9 (1.8)	0.797
Rewarm rate (°C/min)	0.21 (0.08)	0.26 (0.09)	0.001

Values are expressed as mean (standard deviation), unless otherwise indicated. CPB, cardiopulmonary bypass; I, isoflurane; MAP, mean arterial pressure; NI, morphine and midazolam; $PaCO_2$, arterial carbon dioxide tension; SaO_2, arterial oxygen saturation; SjO_2, oxyhaemoglobin desaturation.

geal temperature was measured throughout. SjO_2 values were analyzed as measured and also after correction to an arterial carbon dioxide tension of 5.3 kPa. The number of patients who desaturated in each group was analyzed by χ^2 test and the mean differences in the variables by Student's *t*-test.

Results: Blood gas and blood pressure results are summarised in Table 1. Correcting for carbon dioxide significantly reduced the number of patients who desaturated in the morphine and midazolam group (25–4.7%, $\chi^2=10.4$; $P<0.01$) but not the isoflurane group (4.9–1.6%; $P>0.2$).

Conclusion: The incidence of desaturation during rewarming was significantly reduced by isoflurane. This suggests the balance between cerebral blood flow and cerebral metabolic rate during the rewarming phase of CPB is better preserved in the presence of isoflurane. Different arterial carbon dioxide tension levels cannot explain this effect, but the rate of rewarming may be one factor. Whether prevention of desaturation by isoflurane improves cognitive outcome is yet to be determined.

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Can extubation time be predicted?

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Introduction: Fast-tracking has become an established practice in many cardiac units. We have attempted to identify the factors that may result in prolonged ventilation in our unit.

Materials and methods: The audit was conducted prospectively over an 8-week period during February and March 1999. The audit forms of a total of 156 patients who passed through the intensive care unit were analyzed. Appropriate criteria for extubation were set out beforehand, as were guidelines for management of pain, shivering, agitation and confusion, and poor gas exchange. The following data was collected: patient details; operation, anaesthetist and surgeon; anaesthetic technique; preoperative risk stratification (Parsonnet and Euro-scores); time to extubation; principal reason for continued ventilation (recorded every 2 h for 24 h); and hospital discharge date.

Results: The patients were divided into four principal groups according to their extubation times: less than 6 h, 6–12 h, 12–24 h and longer than 24 h. We focused particularly on the group of patients with extubation times less than 6 h and found that 25.7% were extubated during this period (as compared with only 3% from previous audit figures in 1997). Neither the Parsonnet or Euroscore predicted extubation times well. The percentage of patients extubated in under 6 h divided into low, medium and high risk groups for Parsonnet were 29.3, 15.15 and 34.6%, and for Euroscore 26.5, 29.3 and 16.7%. Very high scores were associated with longer ventilation times as expected. The percentage of patients in the less than 6 h group was found to vary between individual anaesthetists from 8.0 to 50% and surgeons 7.7–31.6%. This degree of variation could not be explained by preoperative risk stratification alone. Patients first on the theatre list (am) were more likely to be extubated within 6 h (32.1%) compared with patients who were later on the list (pm; 18.2%; $P<0.05$). This could not be explained by risk stratification. Of 'am patients' 74.1% were discharged by day 6 compared with 60% of 'pm patients' ($P=0.08$). When we examined the effects of coexistent disease we found that smoking had little effect (25.8% <6 h), presence of chronic obstructive pulmonary disease delayed extubation (16.7%) and excessive alcohol intake appeared to expedite extubation (37.5%) compared with all patients (25.6%), but these associations did not reach statistical significance. The drugs used to provide hypnosis and analgesia on cardiopulmonary bypass were recorded, and the percentage of patients extubated in under 6 h were as follows: midazolam 13.7%, volatile on bypass 16.1%, propofol infusion 30.3% and methohexitone 44.4%, remifentanil 14.3%, fentanyl 25.0% and alfentanil 38.5%. The common causes of continued ventilation at 6 h were 'too drowsy' (70%) and 'poor gases' (28%), but at 24 h were 'inotropic support' (86%), 'confusion' (43%) and the use of 'intra-aortic balloon pump' (37%) were cited by the attending nurse. The percentages of patients discharged by the sixth postoperative day were 80.0% in the less than 6 h group, 70.6% in the 6–12 h group, 57.6% in the 12–24 h group and 0.0% in the longer than 24 h group ($P<0.05$).

Conclusion: Early extubation may expedite recovery and hospital discharge. Extubation time was influenced by both anaesthetist and the anaesthetic technique used. Current preoperative risk scoring systems are insensitive predictors of ventilation times. Patients that had their operations later in the day were more likely to be ventilated overnight, perhaps unnecessarily. Clinical audit changes practice and can be a very useful tool.

A comparison of sequential total and activated white cell count in patients undergoing coronary artery bypass grafting, using cardiopulmonary bypass, with and without a white cell filter

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Introduction: Cardiopulmonary bypass (CPB) has been shown to induce a systemic inflammatory response similar to the local reaction seen after tissue damage [1]. This leads to the release of toxic substances, such as elastase, which cause endothelial damage and may adversely affect outcome [2]. Use of a leucocyte depleting arterial line filter is one of many anti-inflammatory strategies that are undergoing evaluation. Leucocyte depleting filters may be capable of selectively removing activated white cells [3], but this has not been proved *in vivo*. The aim of the present study was to compare sequential total and activated white cells during CPB, using either a leucocyte depleting or standard arterial line filter.

Materials and methods: After local ethical committee approval, 20 patients undergoing coronary artery bypass grafting using CPB were prospectively randomly allocated to have either a Leukogard LG-6 (Pall Biomedical, Portsmouth, UK) or a nonleucocyte depleting filter inserted into the arterial line of the CPB circuit. Arterial limb blood samples were taken immediately after institution of CPB (0 min) and at 10-min intervals throughout the bypass period. Activated white cells were identified using nitroblue tetrazolium, then both total and activated white cell numbers counted after staining with Leucoplate.

Results: Table 2 shows the number of white cells counted/1.25 µl (volume of a single channel of Nageotte counting chamber) using light microscopy (× 25).

Conclusion: The LG6 leucocyte filter reduces the total white cell count and is capable of selectively removing activated white cells during CPB. The exact relationship between leucocyte depletion and improved patient outcome still remains unclear.

Table 2

Mean total and activated white cell counts

	NLDF control group		LG6 filter study group	
Time (min)	Mean total WCC (range)	Activated WCC (range)	Mean total WCC (range)	Activated WCC (range)
0	684 (282–1155)	38 (1–328)	417 (253–531)	5 (2–8)
10	680 (260–1384)	37 (1–318)	351 (283–478)	4 (1–18)
20	767 (260–1684)	21 (2–152)	335 (222–526)	4 (0–20)
30	798 (305–1572)	54 (1–477)	294 (195–796)	5 (1–24)
40	900 (372–1802)	33 (2–266)	420 (302–709)	5 (1–20)
50	948 (277–1911)	50 (2–302)	490 (251–672)	7 (1–18)
60	969 (433–1707)	58 (2–351)	545 (403–740)	5 (0–14)
70	746 (500–1233)	11 (1–18)	587 (525–650)	7 (6–9)
80	662 (548–762)	12 (2–20)	541	6
90	847 (656–1038)	9 (5–12)	–	–
100	732	6	–	–

NLDF, nonleucocyte depleting filter; WCC, white cell count.

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Correlation between preoperative platelet levels and heparin response

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Introduction: Identification of factors responsible for the development of reduced sensitivity to heparin have important implications for cardiac surgery with cardiopulmonary bypass, because inadequate anticoagulation during this procedure can have profound thrombotic and haemorrhagic consequences. Recently, it was noted [1,2] that preoperative platelet levels are higher in heparin-resistant patients than in those who are heparin sensitive. In the present study, a possible relationship between preoperative platelet levels and heparin response was investigated.

Materials and methods: After local regional ethics committee approval and patients' informed consent was obtained, 87 patients undergoing either coronary artery bypass surgery ($n=73$), valvular surgery ($n=8$) or a combination of both ($n=6$) were studied. Both preoperative platelet count and the heparin dose response (HDR) [measured using the Hepcon Hemostasis Management System (Medtronic, USA)] were determined for each patient. Patients with an HDR slope of 80 s/unit heparin per ml of blood or less were considered to have a reduced heparin sensitivity and were studied further. Heparin administration was standardized in all patients and coagulation status was determined by measuring the activated clotting time (ACT). If an ACT of 480 s or greater was not achieved after administration of 300 U/kg heparin, then a further 100 U/kg was given. Patients were considered heparin resistant if the ACT was 480 s or less after the second heparin dose. Patient data were compared using the Mann-Whitney U-test with results expressed as median (interquartile range) where appropriate. Correlation analysis was by Spearman's rank sum correlation.

Results: From the original 87 patients, 30 had an HDR slope of greater than 80 s/U per ml (group 1). From the remaining 57 patients, 42 had an ACT of 480 s or greater after the first heparin dose (group 2), eight had an ACT of 480 s or greater after the additional heparin dose (group 3) and seven were considered to be heparin resistant (group 4). A significant correlation was measured between preoperative platelet levels and a reduced sensitivity to heparin (measured by the HDR slope; $P<0.001$). No correlation with preoperative platelet levels was determined for either the baseline ACT or the ACT after the first heparin dose. Preoperative platelet count was shown to be significantly higher in groups 3 [252 (221–270) $\times$ 10^9/l) and 4 [262 (222–314) $\times$ 10^9/l), compared with 194 (165–223) $\times$ 10^9/l in group 1 ($P<0.05$).

Conclusion: Preoperative platelet levels have been shown to correlate with a reduced sensitivity to heparin. This can probably be explained by the fact that patients with a higher platelet count have a greater capacity to produce platelet factor-4, which is released when platelet aggregation takes place. This mediator has a heparin neutralizing effect. We conclude therefore that assessment of preoperative platelet levels might be a useful diagnostic tool in identifying patients who have a reduced sensitivity to heparin.

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Coagulation and neonatal bypass: an assessment of changes in coagulation factor concentration during cardiopulmonary bypass in neonates, with modified ultrafiltration

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Introduction: Bleeding is of major concern in neonates after cardiopulmonary bypass. More severe coagulopathy can be expected in children who weigh under 8 kg. The effect of cardiopulmonary bypass on factor concentration

has been described previously using a prime of fresh whole blood. Fresh whole blood is not generally available in the UK. In addition we describe the effect of modified haemofiltration and changes in factor V concentration, which has not previously been described.

Materials and methods: Ethical approval was gained and consent was obtained from the patient's parents. An observational design was adopted for the present study. Cardiopulmonary bypass was conducted as is routine at the Freeman Hospital. The pump prime had an average volume of 900 ml. This consisted of one unit of fresh frozen plasma, packed cell to target haematocrit of 25%, sodium bicarbonate, heparin, and a balanced crystalloid solution. All patients were subjected to extreme hypothermia (17–21°C), received heparin (3 mg/kg) and protamine reversal, and received modified ultrafiltration after separation from bypass. Blood samples were taken before bypass, on full flow, at minimum temperature, after rewarming, after modified ultrafiltration and on return to intensive care. The samples were analyzed for haemoglobin, platelets, standard coagulation tests and colloid osmotic pressure. The samples were stored for analysis of factors II, V, VII, VIII, IX and X, antithrombin III, and markers of activation (TAT, PTf 1+2, D-dimers).

Results: Fourteen patients were recruited (age 3–21 days). Thirteen patients had arterial switch procedures, one patient had repair of an interrupted aortic arch. Weights were 2.2–4.4 kg.

Before bypass most levels were at the low end of the expected range for neonates of this age. After initiation of bypass, factor concentrations fell to extremely low levels. With the exception of factors V and VII, the change was predictable from the degree of haemodilution with the pump prime. Factor V levels fell to less than 50% of predicted activity. During hypothermic bypass there was little change in factor activity or evidence of blood activation.

After discontinuation of bypass and modified ultrafiltration, factor concentrations rose to an unpredictable degree. Although factor V activity increased by almost 200%, platelet counts rose by only 4%. In addition there was evidence of marked activation at this stage with increases in TAT, PTf 1+2, and D-dimers levels. On return to intensive care factors V and VIII levels were below the expected range in the majority of patients (11 and 7 patients, respectively). Fibrinogen levels were below age normal in eight patients, but were greater than 0.5 g/dl in all but one.

Discussion: The low levels of factor V on bypass are of interest. Further work has demonstrated that loss of factor V occurs as soon as the FFP is added to the circuit (without connection to the patient). This suggests absorption into the circuit plastics.

The factor deficiencies during bypass are profound but predictable. The increase after ultrafiltration points to a further advantage of this technique, but evidence of platelet consumption is a concern. Continuing deficiencies of factors VIII and V may add to bleeding postoperatively. Factor V concentrate is not available.

Effects of clomethiazole on neuropsychological outcome following coronary artery bypass graft surgery

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Introduction: The γ-aminobutyric acid A receptor agonist clomethiazole has been shown to have neuroprotective properties in animal models of global and focal brain ischaemia. In the present study we investigated the efficacy of clomethiazole in improving neuropsychological outcome after coronary artery bypass surgery.

Materials and methods: Two hundred and forty-five patients scheduled for coronary artery bypass surgery were prospectively randomized at two centres to intravenous clomethiazole edisilate (8 mg/ml) or placebo (0.9% sodium chloride) in a double-blind trial. The drug was infused after induction of anaesthesia and continued until the end of surgery. Coronary artery grafting was completed during mild-to-moderate hypothermia (28–32°C) cardiopulmonary bypass. Baseline neuropsychological assessment was made the day before surgery, using a battery of eight tests, and repeated 4–7 weeks after surgery. Neuropsychological outcome was evaluated by two methods: postoperative change compared with baseline of a global test score, which combined the scores from the eight tests; and the change in individual test scores after surgery compared with baseline.

Results: Neuropsychological assessments were completed in 219 patients (110 clomethiazole and 109 placebo). The mean age in both groups was 64.5 years (range 50–84 years) with a male sex distribution of 89%

in the clomethiazole and 76% in the placebo group. There was no difference between the two groups in the change before and after surgery of either the global or individual test scores.

Conclusion: Clomethiazole was not found to influence neuropsychological outcome in patients undergoing coronary artery surgery.

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