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Does Cardiopulmonary Bypass Alter Enflurane Requirements for Anesthesia?

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This study on dogs determined whether the requirement for enflurane anesthesia was different pre- *versus* postcardiopulmonary bypass (CPB). Male mongrel dogs (n = 16) were anesthetized with enflurane in oxygen. Tracheal intubation was performed, monitors placed, and end-tidal enflurane concentration measured *via* a Puritan-Bennett Anesthesia Agent Monitor.® MAC was determined by the tail-clamp method. CPB was then initiated using aortoatrial (n = 6, group 1) or femoral artery-vein (n = 4, group 2) cannulation or none (n = 6, group 3, control). CPB was maintained for 1 h using a bubble oxygenator, a crystalloid prime, and flows of approximately 70–80 ml/kg with a mean systemic pressure maintained between 50–70 mmHg. Following separation from CPB, MAC was again determined. The reduction in enflurane MAC following CPB was 30.1 ± 21.5% (mean ± SD; $P < 0.05$ *vs.* pre-CPB) in group 1 but there was a wide range of reduction produced (3.8–58.8%). The degree of MAC reduction (19.8 ± 8.6%; $P < 0.05$ *vs.* pre-CPB) produced by CPB in group 2 was much less variable in degree (range 13.0–32.4%) but did not differ from group 1. Although pre- *versus* post-CPB mean systemic pressure fell from 83 ± 13 to 69 ± 15 mmHg ($P < 0.05$), this is above the level likely to produce a reduction in MAC. No other significant hemodynamic changes were observed. Temperature pre- *versus* post-CPB was not different. The degree of hemodilution and acid-base disturbances are unlikely to be the explanation. In group 3, MAC did not differ significantly when measured repeatedly over 8.7 ± 1.5 h (2.13 ± 0.26% at the beginning of the experiment *vs.* 2.14 ± 0.35% at the end), although the gradient between inspired and expired concentration was significantly reduced (0.15 ± 0.05 to 0.06 ± 0.05%; $P < 0.05$). This suggests that contamination of end-tidal gas by dead-space gas is also an unlikely explanation for our results. The authors conclude that normothermic CPB alters the requirements for enflurane anesthesia in dogs. (Key words: Anesthetics, volatile: enflurane. Potency, anesthetic: MAC. Surgery, cardiovascular: cardiopulmonary bypass.)

TO REDUCE THE DEGREE of myocardial depression and promote easy separation from cardiopulmonary bypass (CPB), a common clinical practice involves a reduction in anesthetic level prior to separation from CPB. Despite having a minimal degree of anesthesia present, no reports describe the presence of awareness under anesthesia at this time.[1] Our clinical impression is that there is a reduced requirement for anesthesia following surgery requiring the use of CPB. Factors known to influence volatile anesthetic requirements include temperature,[2] hypotension,[3] and other central nervous system depressants.[4–7] This study on dogs sought to determine whether normothermic CPB alone reduced the requirements for enflurane anesthesia. Our null hypothesis was that there are no changes in anesthetic drug requirements following CPB. There should therefore be no change in enflurane requirements for anesthesia following CPB.

Methods

This study was approved by the Dalhousie University Animal Care and Use Committee and followed the standards established by the Canadian Council of Animal Care. Fasted, hydrated male mongrel dogs (n = 16) weighing 20 ± 3 kg (all results mean ± SD) were each anesthetized by a specialized mask with enflurane in oxygen. Following induction of anesthesia, tracheal intubation and iv cannulation were carried out. Anesthesia was maintained by enflurane in oxygen delivered *via* a calibrated vaporizer. Heart rate and rhythm were recorded continuously. The femoral artery was cannulated for monitoring of systemic blood pressure and for the procurement of blood for gas analysis. A flow-directed pulmonary artery catheter was inserted into the pulmonary artery *via* the right external jugular vein for measurement of pulmonary artery, central venous, and pulmonary artery occlusion pressures and cardiac output *via* thermodilution technique. All parameters were continuously recorded on a Hewlett Packard® recording device Model No. HP7754A. Temperature was recorded from the tip of the pulmonary artery catheter and from the bladder *via* a urinary catheter. End-tidal enflurane concentration was measured *via* a Puritan-Bennett Anesthesia Agent Monitor® (sensitivity 0.1%) which was calibrated prior to each experiment. Arterial blood gases were measured prior to initiation of CPB (n = 10), during CPB (n = 7), and following termination of CPB (n = 7). Gas flows

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were adjusted to maintain arterial partial pressures of CO_2 in the normal range. Enflurane MAC was determined using a modification of the tail-clamp method of Eger *et al.*[8] Warming blankets maintained body temperature in the 35–37° C range.

After determination of control enflurane MAC in six dogs (group 1), anesthesia was deepened (approximately 0.5% greater concentration than MAC) and sternotomy was performed. Following administration of 4 mg/kg heparin, cannulation of the aorta and right atrium was performed and CPB initiated. The bypass circuit was primed with Plasmalyte®. Circuit flows were adjusted to provide an estimated flow of 70–80 ml/kg and a mean systemic pressure of 50–70 mmHg. Sustained (> 3 min) decreases in mean systemic pressure below 50 mmHg were treated with additional increases in flow, additional Plasmalyte,® and if necessary, small incremental doses of neosynephrine (never required). Bubble oxygenators (Bentley B10 [n = 5]; Harvey H1700 [n = 1]) were employed and enflurane was added to the circuit in a concentration sufficient to prevent movement by the animal. Ventilation of the lungs was terminated during CPB. Temperature was maintained in the 36–38° C range by a heat exchanger.

After 1 h CPB was discontinued, protamine given to reverse the effects of heparin, hemostasis secured, and MAC was again determined. Transfusion of the contents of the oxygenator was performed to improve oxygen-carrying capacity and maintain hemodynamics while MAC was being determined.

To determine whether the variability of the results obtained in group 1 could be explained by bleeding and hemodynamic disturbances (likely to be greatest with CPB employing sternotomy and aortoatrial cannulation), a second group of dogs (n = 4, group 2) were treated in the same fashion as group 1 except that femoral artery-vein cannulation was performed and the lungs were ventilated during CPB. Oxygenators employed were Harvey H1700 (n = 3) and Shiley S100A (n = 1). Hematocrit was determined pre- and post-CPB.

In group 3 (n = 6, control), following determination of each animal's control enflurane MAC, anesthesia was maintained and MAC was repeated 1 h later. This process was repeated until five determinations of MAC had been made. A record was kept of the gradient between inspired and expired concentration of enflurane at each determination of MAC.

Paired Student's *t* tests determined differences ($P < 0.05$) between the degree of MAC reduction pre- *versus* post-CPB, hemodynamic changes (groups 1 and 2) and changes in hematocrit for group 2. For group 3, an analysis of variance techniques with Scheffe's *post hoc* analysis for intergroup means ($P < 0.05$) determined differences between the values obtained for each determination of MAC. For group 3, the value for MAC was normalized by dividing the result obtained at each MAC determination by the value obtained during the first MAC determination for each animal prior to statistical analysis.

Results

Control enflurane MAC was 2.15 ± 0.29%. (All results are mean ± SD.) Following CPB, in group 1, MAC was reduced in each animal with a mean reduction of 30.1 ± 21.5% ($P < 0.05$) (table 1). The time required to determine MAC following separation from CPB was 1.2 ± 0.5 h with a total experimental time of 5.1 ± 2.6 h. There was no significant difference between the temperatures measured pre- *versus* post-CPB either from the bladder or pulmonary artery. Moreover, uniform temperature within each dog was maintained at each measurement point as there was no significant difference be-

TABLE 1. MAC Reduction Due to Cardiopulmonary Bypass Employing Aorto-atrial Cannulation in Six Dogs Anesthetized with Enflurane at Normothermia

Dog Number	Control MAC (%)*	Temperature (°C)†	Post-CPB MAC (%)‡	Reduction (%)§	Post-CPB Temp (°C)¶
11	1.50	34.8	0.90	40.0	34.8
12	2.10	32.3	1.62	22.9	36.4
13	2.10	37.1	2.02	3.8	36.2
15	2.33	36.6	2.10	9.9	36.4
16	2.37	38.2	1.30	45.3	35.0
18	1.70	35.8	0.70	58.8	34.9
Mean ± SD	2.02 ± 0.35	35.8 ± 2.1	1.44 ± 0.58**	30.1 ± 21.5	35.6 ± 0.8

* Control enflurane MAC determined prior to initiation of cardiopulmonary bypass.

† Temperature (°C) measured from the pulmonary artery at time of determination of each dog's control enflurane MAC.

‡ MAC determined following separation from cardiopulmonary bypass that had been maintained for 1 h.

§ Percent reduction of enflurane MAC due to cardiopulmonary bypass.

¶ Temperature (°C) measured from the pulmonary artery after MAC determination following separation from cardiopulmonary bypass.

** $P < 0.05$ *versus* control MAC.

TABLE 2. MAC Reduction Due to Cardiopulmonary Bypass Employing Femoral Artery–Vein Cannulation in Four Dogs Anesthetized with Enflurane at Normothermia

Dog Number	Control MAC (%)*	Temp (°C)†	Post-CPB MAC (%)‡	Reduction (%)§	Post-CPB Temp (°C)¶
20	2.42	36.9	2.01	16.9	37.2
21	2.29	37.5	1.90	17.0	37.0
22	2.30	37.6	2.00	13.0	37.0
23	2.50	36.8	1.69	32.4	35.7
Mean ± SD	2.38 ± 0.10	37.2 ± 0.4	1.90 ± 0.15**	19.8 ± 8.6	36.7 ± 0.7

* Control enflurane MAC determined prior to initiation of cardiopulmonary bypass.
† Temperature (°C) measured from the pulmonary artery at time of determination of each dog's control enflurane MAC.
‡ MAC determined following separation from cardiopulmonary bypass which had been maintained for 1 h.
§ Percent reduction of enflurane MAC due to cardiopulmonary bypass.
¶ Temperature (°C) measured from the pulmonary artery after MAC determination following separation from cardiopulmonary bypass.
** $P < 0.05$ *versus* control MAC.

tween the pulmonary artery and bladder temperatures measured in each dog during each determination of MAC.

In group 2, following CPB, MAC was reduced in each animal with a mean reduction of 19.8 ± 8.6% ($P < 0.05$) (table 2). This degree of MAC reduction did not differ statistically from that achieved in group 1 although there was considerably less variability about the mean. The time required to determine MAC following separation from CPB was 1.1 ± 0.8 h with a total experimental time of 4.0 ± 2.4 h. Again there was no significant difference between the temperature measured pre-*versus* post-CPB, whether measured from the bladder or pulmonary arterial site, and uniform temperature within the animal was maintained. Hematocrit was 39.8 ± 6.1% pre-CPB and decreased to 31.0 ± 4% post-CPB ($P = 0.06$; table 3).

As there were no significant changes in the degree of MAC reduction produced by CPB in group 1 *versus* group 2, the hemodynamic and acid-base data were pooled. The hemodynamic changes pre-*versus* post-CPB are presented in table 4. Mean arterial pressure decreased following CPB (83 ± 13 to 69 ± 15 mmHg; $P < 0.05$).

The acid base data are provided in table 5. An oversight prevented us from determining the acid base changes during and following CPB in the first three dogs and data for these animals are excluded. There was no significant difference in the arterial *p*H or P_{CO_2} pre-*versus* post-CPB. The arterial P_{O_2} decreased following CPB (443 ± 43 to 386 ± 87 mmHg; $P < 0.05$).

In group 3 (control), MAC did not differ from the initial value obtained when repeatedly measured over 8.7 ± 1.5 h (table 6). The gradient between inspired and expired concentration of enflurane decreased from 0.15 ± 0.05 to 0.06 ± 0.05% ($P < 0.05$) over the duration of the experiment. There was no difference in either the pulmonary artery or bladder temperatures over the course of the experiment and apart from a reduction in systemic vascular resistance (2898 ± 678 to 1762 ± 522 dyne · s^{-1} · cm^{-5}; $P < 0.05$) no significant changes in hemodynamic parameters were observed (table 7). Hematocrit did not differ significantly (38.1 ± 3% at the beginning *versus* 35.8 ± 3.1% at the end of the experiment).

TABLE 3. Changes in Hematocrit Following Cardiopulmonary Bypass Employing Femoral Artery–Vein Cannulation in Four Dogs Anesthetized with Enflurane at Normothermia

Dog Number	HCT Pre-CPB (%)*	HCT Post-CPB (%)†
20	40.3	30.0
21	47.0	32.7
22	40.0	26.0
23	32.0	35.3
Mean ± SD	39.8 ± 6.1%	31.0 ± 4%

* Hematocrit (percent of total volume) measured prior to initiation of cardiopulmonary bypass.
† Hematocrit (percent of total volume) measured following cardiopulmonary bypass.

Discussion

In dogs receiving aortoatrial cannulation, enflurane MAC was significantly reduced following CPB (30 ± 21%), but there was a large variability in the degree of reduction in this small sample size (n = 6). In four dogs receiving femoral artery-vein cannulation, the degree of MAC reduction was similar (20 ± 9%) with less variability. The degree of variability does not appear to be explained by hemodynamic differences between the two groups (table 4). Because no anesthetic agents other than enflurane were employed, the influence of other central nervous system depressants on MAC reduction was eliminated. The only other possible explanations for the reduction in enflurane MAC are then related to physical factors such as hypothermia, acid-base changes, significant hemodynamic disturbances, or falsely high pre-CPB MAC measurement due to contamination of end-tidal gas by gas from a nonperfused lung (dead space).

TABLE 4. Hemodynamic Changes Pre- *Versus* Post-Cardiopulmonary Bypass in Ten Dogs Anesthetized with Enflurane Alone at Normothermia

	Dog Number										
	11	12	13	15	16	18	20	21	22	23	Mean ± SD
HR											
Pre*	99	81	117	129	132	93	110	120	120	120	112 ± 16
Post†	96	94	115	121	176	138	100	130	102	84	116 ± 27
MAP											
Pre*	79	66	89	60	102	92	92	81	87	82	83 ± 13
Post†	49	55	68	56	65	75	91	65	67	95	69 ± 15‡
PAP											
Pre*	11	5	9	6	8	4	21	10	5	7	9 ± 5
Post†	8	5	9	8	10	5	16	9	6	8	8 ± 3
RAP											
Pre*	4	0	7	2	3	1	8	4	6	2	4 ± 3
Post†	0	0	8	3	2	1	3	2	1	4	2 ± 2
PAOP											
Pre*	4	0	7	2	5	1	10	4	4	2	4 ± 3
Post†	0	0	7	3	2	5	6	6	3	4	4 ± 2
CO											
Pre*	4.81	2.14	5.95	2.51	1.56	2.05	4.40	3.23	5.43	3.35	3.54 ± 1.53
Post†	4.26	3.12	7.80	2.68	5.50	2.20	4.50	1.77	2.29	2.10	3.62 ± 1.91
SVR											
Pre*	1247	2467	1102	1849	5077	3551	1290	1907	1193	1910	2159 ± 1265
Post†	920	1410	615	1582	916	2690	1554	1307	2306	3467	1677 ± 891
PVR											
Pre*	117	187	27	127	256	117	200	149	15	119	131 ± 74
Post†	131	128	21	149	116	36	177	136	175	152	122 ± 53

HR = Heart rate (beat per min). MAP = Mean systemic arterial pressure (mmHg). PAP = Mean pulmonary arterial pressure (mmHg). RAP = Right atrial pressure (mmHg). PAOP = Pulmonary artery occlusion pressure (mmHg). CO = Cardiac output (l/min). SVR = Systemic vascular resistance (dyne·s^{-1}·cm^{-5}). PVR = Pulmonary vascular resistance (dyne·s^{-1}·cm^{-5}).

* Values measured following the determination of control enflurane MAC and prior to the initiaton of cardiopulmonary bypass.

† Values measured after the determination of MAC following separation from cardiopulmonary bypass.

‡ $P < 0.05$ *versus* pre value.

While hypothermia is known to alter MAC for volatile agents,[1,9] in this study, although for individual animals temperature changes were noted, no consistent pattern emerged and there was no significant difference in the temperature pre- *versus* post-CPB, whether measured from the pulmonary artery or bladder (tables 1 and 2).

Severe anemia with a reduction in oxygen content below 4.3 ml of oxygen/100 ml of blood has been shown to reduce halothane MAC.[10] The degree of hemodilution imposed by our study methods was approximately 10% in group 2 (table 3). We believe that this would still provide the animal with sufficient oxygen-carrying capacity to prevent the tissue acidosis and hypoxia responsible for MAC reduction due to hemodilution. The animals were all ventilated with oxygen at an FI_{O_2} of 1 and were transfused the contents of the oxygenator following separation from CPB.

Anemia may also change the solubility of anesthetics

TABLE 5. Acid Base Changes Pre- *Versus* Post-Cardiopulmonary Bypass in Seven Dogs Anesthetized with Enflurane Alone at Normothermia

	Pa_{CO_2} (mmHg)		*p*H (units)		Pa_{O_2} (mmHg)		Base Excess (mmoles)	
Dog Number	Pre*	Post†	Pre*	Post†	Pre*	Post†	Pre*	Post†
13	46	59	7.29	7.23	441	308	−4	−9
16	48	51	7.25	7.23	462	302	−7	−6
18	22	18	7.48	7.49	401	328	−4	−5
20	34	37	7.40	7.46	512	532	8	3
21	36	32	7.47	7.57	448	390	4	9
22	37	36	7.38	7.39	458	473	−2	−2
23	30	31	7.29	7.46	380	367	−10	0
Mean ± SD	36 ± 7	38 ± 14	7.37 ± 0.90	7.40 ± 0.13	443 ± 43	386 ± 87‡	−2 ± 6	−1 ± 6

* Value measured prior to initiation of cardiopulmonary bypass.

† Value measured following separation from cardiopulmonary bypass.

‡ $P < 0.05$ *versus* pre value.

TABLE 6. Enflurane MAC Values Determined Over Time in Six Dogs

Dog Number	Control MAC*	Time 1† (h)	MAC 2‡	Time§ (h)	MAC 3¶	Time§ (h)	MAC 4**	Time§ (h)	MAC 5††	Time§ (h)
27	2.30	0.80	2.30	2.90	2.30	4.00	2.28	6.10	2.30	7.20
	(1)		(1)		(1)		(0.99)		(1)	
28	2.31	1.67	2.72	3.90	2.71	6.25	2.71	7.67	2.72	9.25
	(1)		(1.18)		(1.17)		(1.17)		(1.18)	
29	1.98	2.92	2.00	4.47	2.00	6.32	2.00	7.95	2.00	9.75
	(1)		(1.01)		(1.01)		(1.01)		(1.01)	
30	1.71	3.45	1.70	5.58	1.70	7.73	1.70	9.55	1.71	10.80
	(1)		(0.99)		(0.99)		(0.99)		(1)	
31	2.40	1.67	2.21	3.03	2.20	4.37	2.21	5.68	2.21	7.02
	(1)		(0.92)		(0.92)		(0.92)		(0.92)	
32	2.10	1.17	1.90	2.00	1.92	4.30	1.92	5.78	1.92	7.28
	(1)		(0.90)		(0.91)		(0.91)		(0.91)	
Mean ± SD	2.13 ± 0.25	1.95 ± 1.02	2.14 ± 0.36‡‡	3.65 ± 1.28	2.14 ± 0.35‡‡	5.50 ± 1.49	2.14 ± 0.35‡‡	7.12 ± 1.54	2.14 ± 0.35‡‡	8.55 ± 1.60
	(1)		(1.0 ± 0.099)‡‡		(1.0 ± 0.093)‡‡		(0.998 ± 0.093)‡‡		(1.0 ± 0.097)‡‡	

Values in brackets represent the normalized value for each MAC determination and were obtained by dividing each MAC value by the result obtained at Control MAC.

* Value obtained (percent enflurane in end-tidal gas) during the initial determination of MAC.

† Time at which the first determination of MAC was completed. It is composed of induction time, time required to place monitors (accomplished with some difficulty in dogs 29 and 30), and time required to obtain MAC itself.

‡ Value for MAC (percent end-tidal gas) determined following a 1-h observation period after determining Control MAC.

§ Time at which the indicated determination of MAC was completed.

¶ Value for MAC (percent end-tidal gas) determined following a 1-h observation period after determining MAC 2.

** Value for MAC (percent end-tidal gas) determined following a 1-h observation period after determining MAC 3.

†† Value for Mac (percent end-tidal gas) determined following a 1-h observation period after determining MAC 4.

‡‡ P = NSD *versus* control.

in blood. With hemodilution of plasma proteins, solubility is decreased.[11] The effect of this in the present experiment might be a reduction in the rate of rise (but not the final level) of the brain anesthetic concentration following CPB. However, enflurane was continuously administered throughout the experiment in both groups, the degree of hemodilution was relatively small (approximately 10% in group 2), and the actual time for MAC determination (approximately 1 h) of sufficient duration that any affect on anesthetic uptake would likely be minimal and not of sufficient magnitude to explain our results.

Significant hypotension may reduce volatile anesthetic requirements.[2] While we measured a significant change in mean arterial pressure from 83 to 69 mmHg (table 4), the latter level is above that which would likely be associated with reductions in MAC.[2]

With respect to acid-base disturbances, in the seven animals for which we have complete data sets (table 5), there was no significant difference in arterial pH or P_{CO_2} pre- *versus* postbypass and while there was a statistically significant reduction in arterial P_{O_2} (443–386 mmHg), this is unlikely to be clinically significant.

To determine whether dead-space ventilation could be the explanation for our results, we examined the stability of enflurane MAC determinations over time (group 3). There was a significant difference in the gradient between inspired and expired enflurane concentrations at the beginning of the experiment when compared with the values obtained at the end (0.15 ± 0.05 *vs* $0.06 \pm 0.05\%$; $P < 0.05$). This suggests that indeed at the beginning of the experiment there was contamination of the end-tidal concentration by inspired anesthetic from areas of the lung ventilated but not perfused *i.e.*, dead space.[11] As the duration of anesthesia progressed, the gradient decreased suggesting that as saturation of tissues was occurring, there was reduced uptake of the anesthetic and dead-space contribution declined. This could lead to a falsely elevated MAC determination for the pre-CPB determination and a more accurate MAC determination in the post-CPB period. Unfortunately, gradients were not measured in the animals undergoing CPB. However, the stability of MAC determinations in group 3 (table 6) over time argues against this being a major factor in our results. While dead-space ventilation may have contributed to the variability we observed in MAC reduction, we believe it cannot be the entire explanation.

Of the remaining factors known to affect MAC,[12] none apply to this experimental situation. We therefore conclude that CPB itself is responsible for some of the alteration in enflurane requirements.

Reasons why CPB may alter enflurane requirements for anesthesia are purely speculative at this point. CPB is known to activate the complement system with disruption of cellular integrity.[13–16] Perhaps this disruption of mem-

TABLE 7. Changes in Hemodynamic Parameters Over Time during Five Sequential Determinations of Enflurane MAC in Six Dogs

Parameter	Control MAC*	MAC 2†	MAC 3‡	MAC 4§	MAC 5¶
Heart rate (beats per min)	115 ± 7	112 ± 7	114 ± 3	112 ± 8	112 ± 7
Mean systemic arterial pressure (mmHg)	97 ± 12	94 ± 9	92 ± 9	88 ± 6	88 ± 10
Mean pulmonary arterial pressure (mmHg)	9 ± 1	8 ± 3	8 ± 2	9 ± 2	9 ± 2
Right atrial pressure (mmHg)	2 ± 1	2 ± 1	2 ± 1	2 ± 1	2 ± 1
Pulmonary artery occlusion pressure (mmHg)	3 ± 1	3 ± 1	3 ± 2	4 ± 2	5 ± 2
Cardiac output (l/min)	2.8 ± 0.7	3.2 ± 0.8	3.5 ± 0.8	3.6 ± 0.8	4.0 ± 0.7
Systemic vascular resistance (dyne·s^{-1}·cm^{-5})	2898 ± 677	2428 ± 766	2194 ± 548	2035 ± 545	1761 ± 522**
Pulmonary vascular resistance (dyne·s^{-1}·cm^{-5})	157 ± 54	123 ± 50	118 ± 54	103 ± 37	83 ± 25

Each value represents the mean ± SD determination for the six dogs at any particular determination of MAC.

* Value for the hemodynamic parameter listed in column 1 measured following the first determination of enflurane MAC at 1.95 ± 1.02 h from the start of the experiment.

† Value for the hemodynamic parameter listed in column 1 measured following the second determination of enflurane MAC at 3.65 ± 1.28 h.

‡ Value for the hemodynamic parameter listed in column 1 measured following the third determination of enflurane MAC at 5.50 ± 1.49 h.

§ Value for the hemodynamic parameter listed in column 1 measured following the fourth determination of enflurane MAC at 7.12 ± 1.54 h.

¶ Value for the hemodynamic parameter listed in column 1 measured following the fifth and last determination of enflurane MAC at 8.55 ± 1.60 h.

** $P < 0.05$ *versus* control MAC.

branes and cellular swelling in some way alters the central nervous system sensitivity to volatile anesthetic agents. Microaggregates are commonly found in blood during CPB.[17–21] In this regard, our deliberate use of a variety of bubble oxygenators and failure to employ in line arterial filtration may be significant. Perhaps diffuse microvascular occlusion is responsible for altered anesthetic requirements by reducing flow to areas of the brain most sensitive to volatile anesthetics. The inconsistency of this insult might explain some of the variability in the results from this study. Clearly more investigation is required. Questions arise from this study with respect to the etiology of the reduction in anesthetic requirements; the specificity for enflurane alone; the time course; and whether interaction with other central nervous system depressants may further reduce enflurane anesthetic requirements.

We caution against the straightforward application of these results to humans. While the mean reduction in enflurane requirements due to CPB was significant, there was a large variability with a range of 4–59%. Until the mechanism whereby CPB reduces enflurane requirements for anesthesia is further elucidated, a cautious approach to the supplementation of anesthesia during CPB is indicated.

We conclude that requirements for enflurane anesthesia following normothermic CPB may be reduced. However, the degree of reduction is highly variable. This may be one explanation for our clinical observation of a reduced requirement for anesthesia following CPB.

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