

Cerebral blood flow during cardiopulmonary bypass in man: effect of arterial filtration

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ABSTRACT Cerebral blood flow was recorded in 39 patients undergoing cardiac surgery by intra-arterial injection of xenon 133. There were three subgroups of patients: 10 patients had a 20 micron arterial filter (Johnson) and 11 a 40 micron filter (Pall), and 18 had no arterial filtration. All patients had a 40 micron (Pall) filter in the coronary suction line. Significant changes in cerebral blood flow occurred during extracorporeal circulation ($p < 0.0001$). For all patients cerebral blood flow increased from a resting prebypass level of 30 to 46 and 57 ml/100 g a minute during initial and stable hypothermic extracorporeal circulation respectively. Both measurements were obtained at 26°C and the recordings were made on average 12 and 55 minutes after the extracorporeal circulation was started. During rewarming cerebral blood flow increased to 64, 53, 41, and 36 ml/g a minute at 31°, 33°, 35°, and 37°C respectively, and when measured four and 16 minutes on average after bypass it was 44 and 41 ml/100 g a minute. This general brain hyperperfusion was noticed in all patients with a high enough mean blood pressure to produce hyperaemia. Interposing 20 and 40 micron arterial filters reduced cerebral blood flow but did not prevent this hyperaemia. The cerebral autoregulation, which maintains a constant cerebral blood flow within wide limits of perfusion pressures, was not affected by arterial filtration. The lower limit of blood pressure at which a further reduction in blood pressure was followed by a reduction in cerebral blood flow was around 60 mm Hg in all three groups.

Currently postoperative mortality is of little use as a measure of the quality of cardiac surgery, as mortality rates are generally low, despite strikingly different perfusion techniques. A new index of the quality of surgery is emerging, based on psychometric analysis of the extent to which complex mental functioning is preserved in the early postoperative period, combined with more quantitative methods, such as analysis of spinal fluid intracellular markers¹⁻³ and measurements of cerebral blood flow during and after cardiac surgery.⁴⁻⁸

In our earlier studies of cerebral blood flow during cardiac surgery we found a consistent hyperperfusion of the brain during cardiopulmonary bypass⁶⁻⁸ and a diffusely reduced regional cerebral blood flow after surgery,⁵ the most reasonable explanation being a

diffuse microvascular blockage of microembolic origin.

Filtration of the blood returned from the coronary suction line has become widely accepted, but the beneficial effect of arterial line filters is still questioned. The introduction of refined techniques for detecting microemboli present in the arterial line and in the carotid arteries have suggested that the incidence of potentially hazardous microemboli during conventional cardiopulmonary bypass is much greater than previously realised. Since the size of microemboli that would be safe cannot be defined, it seems reasonable to reduce the quantity as much as possible.

The present study was designed to determine whether arterial filtration could prevent the abnormal brain hyperperfusion usually noted in our patients during bypass.

Methods

The results and their interpretation are based on a study of 39 unselected adult patients undergoing open

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Table 1 General and perioperative data (means (SE) [range]) on the patients having arterial filtration and the control patients with no filter

	Filter groups		Controls
	20 µm filter	40 µm filter	
Number of patients	10	11	18
Age (y)	53.2 (2.6) [40–65]	49.5 (4.5) [27–69]	56.4 (2.4) [40–72]
Perfusion time (min)	146 (12) [107–209]	95 (15) [60–235]	119 (10) [72–205]
Aortic cross clamping (min)	83 (8) [46–130]	65 (12) [30–171]	73 (7) [22–142]
Duration of hypotension during bypass (min)			
< 40 mm Hg	4 (2) [0–15]	9 (3) [0–25]	8 (2) [0–38]
< 50 mm Hg	22 (6) [0–65]	26 (4) [10–50]	29 (4) [0–77]
Preoperative mean arterial blood pressure (mm Hg)	103 (7) [81–135]	94 (5) [67–123]	97 (3) [73–120]
Haemolysis at end of bypass (µmol/l)	Not measured	11 (2) [2–28]	16 (3) [2–49]

heart surgery. All patients had a 40 micron filter (Pall) in the cardiectomy suction line. In 21 patients arterial filtration was used: a 20 micron (Johnson) filter in 10 patients and a 40 micron (Pall) filter in 11 patients; 18 patients with no arterial filtration served as controls. A total of 670 measurements of cerebral blood flow with associated variables were obtained: 201 measurements in the group with a 20 micron filter, 180 in the group with a 40 micron filter, and 289 in the control group. The experimental protocol was approved by the chairman of the department of cardiothoracic surgery. Informed consent for the study was obtained from all patients before the study.

STUDY GROUP AND MEASUREMENTS

Table 1 summarises the general data and perioperative information for all patients. There were 21 men and 18 women with a mean age of 54 years. The operative procedures were: aortic valve replacement in 17, mi-

tral valve replacement in 11, coronary artery bypass grafting in 10, and mitral valve replacement with coronary artery bypass grafting in one patient. None of the patients had any history or clinical evidence of cerebral vascular disease.

A baseline measurement was obtained between sternotomy and extracorporeal circulation. The next two measurements were obtained during the initial and the stable phases of hyperthermic extracorporeal circulation, 12 and 55 minutes on average after its initiation. During the rewarming phase of extracorporeal circulation measurements were obtained at 31°, 33°, 35°, and 37°C. Final measurements were obtained twice after the end of the extracorporeal circulation, on average four and 16 minutes after it had finished.

ANAESTHESIA

The patients were premedicated with 5–10 mg of mor-

Table 2 Cerebral blood flow and associated measurements (mean (SE)) in 10 patients with a 20 micron arterial filter obtained before, during, and after extracorporeal circulation (ECC)

	<i>Before ECC</i>	<i>During ECC</i>						<i>After ECC</i>		<i>Kruskal-Wallis analysis of variance (p)</i>
		<i>Hypothermia</i>		<i>Rewarming</i>						
<i>Flow:</i>		<i>1</i>	<i>2</i>	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>	<i>1</i>	<i>2</i>	
Cerebral blood flow* corrected for Pco ₂ (ml/100 g per min)	29 (1.5)	49 (3.7)	54 (2.8)	56 (6.9)	31 (6.0)	32 (5.5)	32 (2.5)	44 (6.6)	35 (6.8)	< 0.0001
Mean arterial pressure (mm Hg)	70 (2.1)	55 (2.9)	61 (1.4)	72 (3.3)	70 (2.9)	65 (2.9)	57 (1.6)	60 (3.8)	58 (2.3)	< 0.0001
Carbon dioxide tension (mm Hg)	39.7 (1.1)	33.5 (0.8)	42.1 (0.8)	52.6 (2.2)	53.7 (4.0)	56.7 (3.5)	58.1 (2.2)	53.2 (8.3)	62.1 (7.0)	< 0.0001
Packed cell volume	0.37 (0.01)	0.24 (0.01)	0.24 (0.01)	0.25 (0.02)	0.27 (0.02)	0.25 (0.02)	0.23 (0.01)	0.28 (0.01)	0.25 (0.01)	< 0.0001
Temperature (°C)†	35.8 (0.1)	24.0 (0.7)	24.2 (0.3)	28.8 (0.7)	33.5 (0.2)	35.3 (0.2)	37.0 (0.2)	36.5 (0.3)	36.4 (0.3)	< 0.0001
Measurement time before, during, and after ECC (min)	– 13 (1.7)	14 (1.4)	53 (2.5)	80 (6.6)	85 (4.7)	98 (5.6)	131 (5.7)	4 (0.7)	17 (2.2)	

*Cerebral blood flow has been corrected to a carbon dioxide tension of 40 mm Hg, 1 mm Hg giving about a 3% change in cerebral blood flow.^{6,10}

†See p 390 for details.

Conversion: Traditional to SI units—Carbon dioxide tension: 1 mm Hg ≈ 0.133 kPa.

Table 3 Cerebral blood flow and associated measurements (mean (SE)) in 11 patients with a 40 micron arterial filter obtained before, during, and after extracorporeal circulation (ECC)

	<i>Before ECC</i>	<i>During ECC</i>								<i>Kruskal-Wallis analysis of variance (p)</i>
		<i>Hypothermia</i>		<i>Rewarming</i>				<i>After ECC</i>		
<i>Flow:</i>		<i>1</i>	<i>2</i>	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>	<i>1</i>	<i>2</i>	
Cerebral blood flow* corrected for Pco ₂ (ml/100 g per min)	31 (2.1)	46 (4.0)	60 (5.2)	56 (6.8)	46 (5.0)	36 (4.0)	41 (4.7)	40 (3.3)	37 (6.4)	< 0.0001
Mean arterial pressure (mm Hg)	75 (2.8)	47 (1.9)	53 (1.9)	61 (3.4)	58 (4.5)	53 (4.9)	52 (2.7)	63 (4.1)	65 (2.9)	< 0.0001
Carbon dioxide tension (mm Hg)	35.9 (0.8)	34.0 (0.8)	42.1 (1.0)	48.8 (1.0)	50.5 (1.4)	53.4 (1.1)	51.9 (1.8)	46.5 (1.0)	48.5 (1.3)	< 0.0001
Packed cell volume	0.39 (0.01)	0.24 (0.01)	0.24 (0.01)	0.25 (0.01)	0.25 (0.01)	0.26 (0.01)	0.26 (0.01)	0.27 (0.01)	0.27 (0.01)	< 0.0001
Temperature (°C)†	36.5 (0.1)	26.9 (0.7)	26.5 (0.3)	30.1 (0.4)	32.7 (0.3)	35.0 (0.2)	36.6 (0.1)	36.2 (0.1)	35.8 (0.1)	< 0.0001
Measurement time before, during, and after ECC (min)	−7 (1.0)	9 (0.9)	54 (7.0)	66 (15.3)	70 (12.8)	86 (15.6)	87 (11.1)	4 (0.6)	13 (1.5)	

*See first footnote to table 2.

†See p 390 for details.

Conversion: Traditional to SI units—Carbon dioxide tension: 1 mm Hg \approx 0.133 kPa.

phine or 10–15 mg of diazepam plus scopolamine 0.2–0.4 mg given intramuscularly. General anesthesia was started with thiopental 2–4 mg/kg intravenously. Pancuronium and suxamethonium were given intravenously for muscle relaxation. The patients received 1.5% enflurane in pure oxygen as volatile anaesthetic which was stopped at the time of bypass. During the extracorporeal circulation anesthesia was maintained with fentanyl 5–10 μ g/10 kg intravenously and with 0.3–0.6 mg of scopolamine intravenously. Rewarming was usually facilitated with chlorpromazine at a dose of up to 0.5 mg/kg.

CARDIOPULMONARY BYPASS

The extracorporeal technique consisted of a Rygg-Kyvsgaard heart-lung machine with a bubble oxygenator. A 40 micron filter (Pall) was used in the cardiectomy suction line in all patients. Arterial filtration was used in 21 patients: a 20 micron filter (Johnson) in 10 patients and a 40 micron filter (Pall) in 11 patients. The filters were continuously bled into the venous line with a flow rate of about 100 ml/min. The priming was Ringer's lactate, 2.0–2.5 l. During extracorporeal circulation the extracorporeal flow rate was maintained at 1.8–2.4 l/min per m². The ex-

Table 4 Cerebral blood flow and associated measurements (mean (SE)) in 18 control patients without an arterial filter obtained before, during, and after extracorporeal circulation (ECC)

	<i>Before ECC</i>	<i>During ECC</i>								<i>Kruskal-Wallis analysis of variance (p)</i>
		<i>Hypothermia</i>		<i>Rewarming</i>				<i>After ECC</i>		
<i>Flow:</i>		<i>1</i>	<i>2</i>	<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>	<i>1</i>	<i>2</i>	
Cerebral blood flow* corrected for Pco ₂ (ml/100 g per min)	33 (2.3)	44 (2.7)	57 (3.2)	72 (5.7)	65 (4.9)	49 (3.6)	38 (2.8)	47 (3.3)	49 (6.0)	< 0.0001
Mean arterial pressure (mm Hg)	77 (2.6)	49 (2.4)	58 (1.9)	65 (3.5)	62 (2.6)	57 (2.2)	51 (1.9)	63 (2.8)	67 (3.2)	< 0.0001
Carbon dioxide tension (mm Hg)	35.2 (1.0)	34.0 (1.0)	40.4 (0.8)	43.8 (1.1)	45.0 (1.2)	49.0 (1.4)	50.6 (1.1)	42.2 (1.4)	36.2 (1.3)	< 0.0001
Packed cell volume	0.37 (0.01)	0.25 (0.01)	0.25 (0.01)	0.24 (0.01)	0.25 (0.01)	0.25 (0.01)	0.25 (0.01)	0.25 (0.01)	0.27 (0.01)	< 0.0001
Temperature (°C)†	36.2 (0.1)	27.2 (0.5)	26.8 (0.3)	30.1 (0.3)	32.7 (0.2)	35.2 (0.1)	37.2 (0.1)	36.6 (0.1)	36.2 (0.1)	< 0.0001
Measurement time before, during, and after ECC (min)	−13 (1.6)	13 (1.1)	57 (4.1)	69 (7.7)	74 (6.3)	81 (7.0)	105 (5.0)	4 (0.5)	18 (1.9)	

*See first footnote to table 2.

†See p 390 for details.

Conversion: Traditional to SI units—Carbon dioxide tension: 1 mm Hg \approx 0.133 kPa.

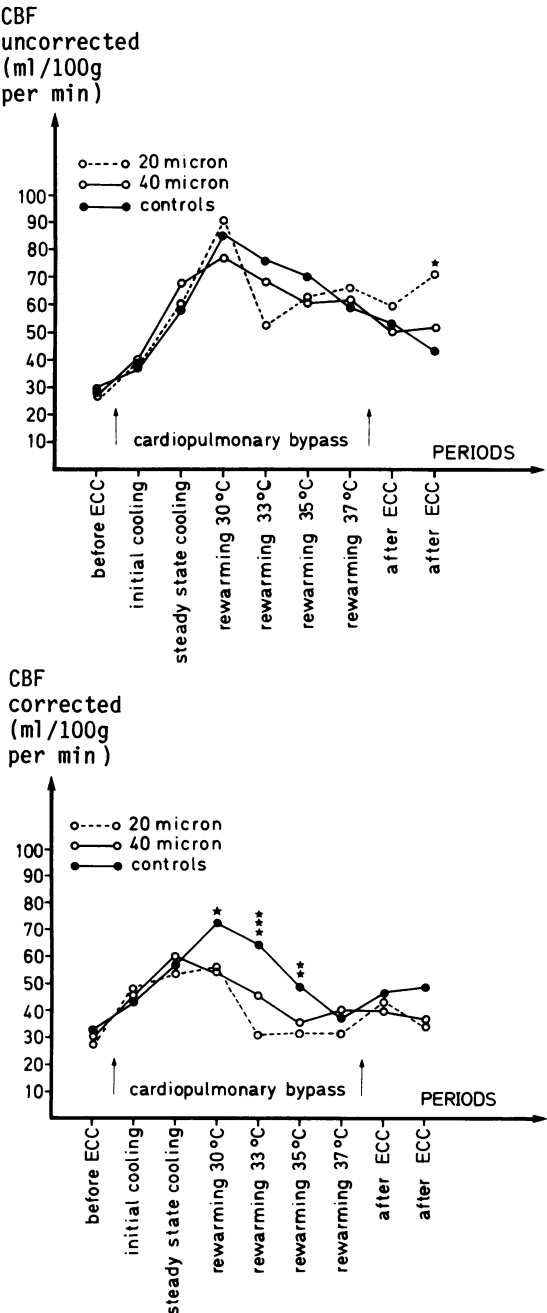


Fig 1 Cerebral blood flow (CBF) measured during nine periods of cardiac surgery: before bypass, twice during hypothermic bypass, four times during the rewarming procedure, and twice after bypass. (a) Uncorrected cerebral blood flow; (b) cerebral blood flow corrected to a carbon dioxide tension of 40 mm Hg (5.3 kPa). Significance: *** $p < 0.002$; ** $p < 0.01$; $p < 0.05$. ECC—extracorporeal circulation.

tracorporeal circulation was started with gradually increasing flow, full flow being established within the first minute. Bretschneider's or St Thomas' cardioplegic solution, at 4°C, was infused into the aortic root just after aorta had been cross clamped. Cooling was induced until an oesophageal temperature of 28–30°C was reached and the temperature was kept at this level during the cardiac repair. Carbon dioxide was added to the oxygenator to give a concentration of 5% until steady state hypothermia had been reached, and then reduced to 3%. During rewarming the temperature gradient between the oxygenator and the patient was not allowed to exceed 12°C. Table 1 summarises data on the patients for the bypass period.

CEREBRAL BLOOD FLOW

Cerebral blood flow was measured with the xenon 133 intra-arterial injection method^{9,10} modified for studies in man during open heart surgery.⁶ This method allows rapid repetitive measurement of cerebral blood flow. ^{133}Xe was injected into the right common or the internal carotid artery and the clearance of ^{133}Xe was followed by a single 2.5 cm NaI crystal positioned over the right parietal region. Cerebral blood flow (CBF) was calculated by the initial slope method,¹⁰ the formula being $\text{CBF} = -\lambda \cdot \ln 10 \cdot D_0 \cdot 100$ (ml/100g per minute), where the blood-brain partition coefficient for grey matter, λ , is 0.87 ml/g and

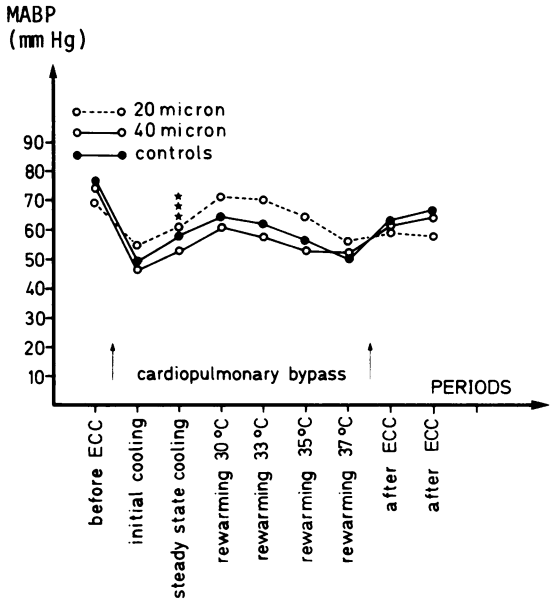


Fig 2 Mean arterial blood pressure (MABP) changes during the nine measurement periods of cardiac surgery in the three groups of patients. Significance: *** $p < 0.002$; ECC—extracorporeal circulation.

D_0 is the initial slope (the first 10–40 s) of a logarithmic recording of the clearance curve.

Mean arterial blood pressure, packed cell volume, carbon dioxide tension (PCO_2), oxygen tension (PO_2), and temperatures (oesophagus, rectum, arterial line) were measured each time cerebral blood flow was measured. The blood gases were measured at 37°C (ABL4 Radiometer, Copenhagen) and corrected to the relevant temperature.

TEMPERATURE

We have previously measured temperatures in the rectum, oesophagus, rhinopharynx, tympanic membrane, arterial line, and the bulb of the internal jugular vein. From these measurements, using the temperature in the bulb of the jugular vein as a reference we concluded that the best routine estimate of the brain temperature is the mean of the oesophagus and the arterial line temperatures. The second best choice is the oesophageal temperature. The temperature is not crucial in this study, however, and when temperature is mentioned it refers either to rectal temperature (before extracorporeal circulation), the mean of the arterial and the oesophageal temperatures (during the procedure), or oesophageal temperature (after extracorporeal circulation).

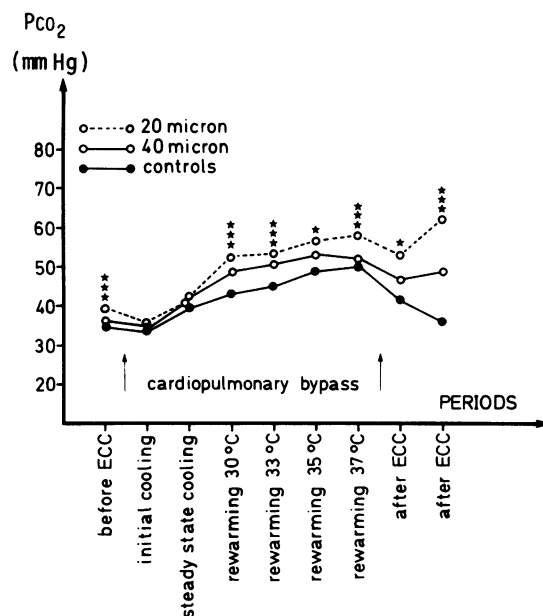


Fig 3 Plasma carbon dioxide tension (PCO_2) corrected to the actual temperature during the nine measurement periods of cardiac surgery in the three groups of patients.

Significance: *** $p < 0.0002$; * $p < 0.05$.

ECC—extracorporeal circulation. Conversion: Traditional to SI units— PCO_2 : 1 mm Hg \approx 0.133 kPa.

STATISTICS

Owing to a skew distribution non-parametric statistics were preferred.¹¹ Analysis of variance within and between the groups was performed with Kruskal-Wallis rank test. The significance level was $p < 0.05$.

Results

During extracorporeal circulation significant changes in cerebral blood flow occurred in all the patients studied ($p < 0.0001$). Mean cerebral blood flow for the whole group ($n = 39$) increased from 30 ml/100 g a minute before bypass to 46 and 57 ml/100 g a minute during the initial and stable hypothermic phases respectively. During the rewarming procedure cerebral blood flow was 64, 53, 41, and 36 ml/100 g a minute at 31°, 33°, 35°, and 37°C. Four and 16 minutes after extracorporeal circulation had ended cerebral blood flow was 44 and 41 ml/100 g a minute. The corresponding values for the three subgroups are presented in tables 2–4 and figures 1–3.

Interposing arterial filters only slightly modified the hyperperfusion during extracorporeal circulation. Correcting cerebral blood flow for changes in PCO_2 to a standard PCO_2 of 40 mm Hg (5.3 kPa) showed that the hyperaemia was to some extent prevented during the rewarming procedure at 30°, 33°, and 35°C ($p < 0.05$, < 0.002 , and < 0.01 respectively), the smallest filter pore size (20 micron) being most efficient (fig 1). The same trend towards a lower cerebral blood flow was noted when cerebral blood flow was not corrected for changes in PCO_2 (fig 1a). When the 21

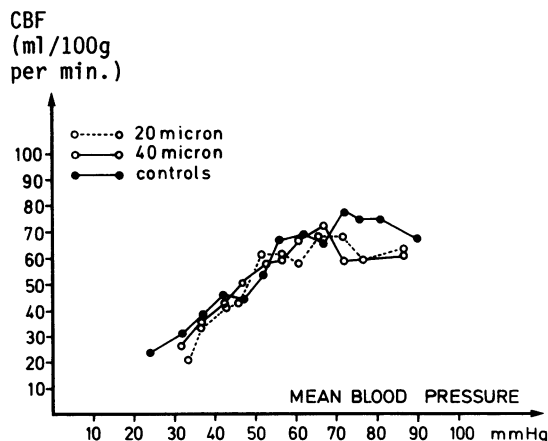


Fig 4 Cerebral autoregulation for cerebral blood flow (CBF) and mean arterial blood pressure (MABP): measurements obtained during and after cardiac surgery in the three groups of patients. Only cerebral blood flow measurements obtained after bypass was started are included to avoid the abrupt change in packed cell volume at the start of bypass.

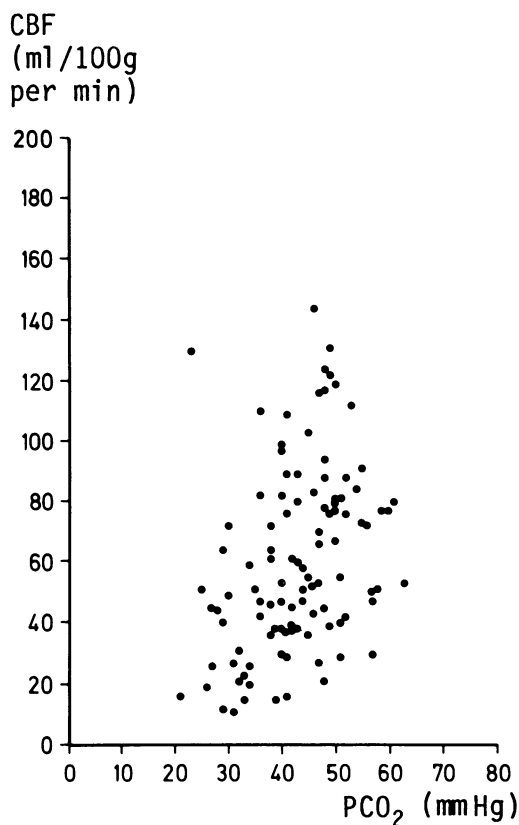


Fig 5 Plasma carbon dioxide tension (PCO_2) in relation to cerebral blood flow (CBF) before, during, and after cardiopulmonary bypass.

patients having 20 or 40 micron arterial filters were compared with the 18 controls during the rewarming period at 33° and 35°C, the cerebral blood flow was lowest in the patients with filters (62 and 73 ml/100 g a minute; $p < 0.05$). The total number of cerebral blood flow measurements with associated measurements during the period of bypass was 37 for both groups. The other measurements for the filter and the control group were: mean arterial blood pressure 60 and 60 mm Hg (8 kPa), PCO_2 53.3 and 47.1 mm Hg (7.1 and 6.3 kPa), packed cell volume 0.25 and 0.25, and temperature 34.1° and 34.0°C. There is a notable difference in PCO_2 between the groups (fig 3). Any correction will accentuate the difference in cerebral blood flow, being lowest in the patients with arterial filtration (fig 1b). The general trend, however, despite arterial filtration, was for all patients to show the same tendency towards hyperperfusion during extracorporeal circulation.

The cerebral autoregulation, reflecting the re-

lationship between cerebral blood flow and mean arterial blood pressure during and after extracorporeal circulation was the same for all three groups (fig 4). Reducing mean arterial blood pressure below 55–60 mm Hg was followed by a fall in cerebral blood flow, the lower limit of autoregulation being exceeded.

Carbon dioxide tension (fig 5) was an important determinant of cerebral blood flow ($p < 0.001$).

Discussion

Operations with extracorporeal circulation cause impairment of intellectual function.^{3 12–25} This probably reflects cerebral injuries that are mostly reversible, but signs of permanent injuries do occur.^{1–3 5 26} The earlier and more extensively the patients have been tested, the higher has been the incidence and severity of the observed deficits.^{12 13}

Emboli from valve calcification and intracardiac air are commonly detected in the carotid artery when the left ventricle begins to eject,²⁷ but exposure to extracorporeal circulation is probably the most important operative risk factor. Microembolisation, the duration of perfusion, hypotension during perfusion, and PCO_2 also seem to be of aetiological importance in the postoperative encephalopathic syndrome that follows most cardiac operations.^{5 12 28}

The potential dangers of extracorporeal circulation are important because of the increasing number of valve and coronary artery bypass operations. In the United States coronary bypass grafting is now as commonplace as hysterectomy and appendectomy,²⁹ so there is no room for complacency until the optimal bypass technique has been evolved.

EMBOLI

The general pattern of cerebral blood flow during operation was constant for all patients whether arterial filtration was used or not. The second measurement obtained during initial cooling (an average of 12 minutes after the onset of extracorporeal circulation) showed an increase in cerebral blood flow matching the haemodilution, but given the hypothermic state (26°C) it was too high. The further increase during steady state hypothermia and the rewarming procedure was unexpected (fig 1). Although it is difficult to point to a single factor as the main cause of the perioperative brain hyperperfusion and the postoperative encephalopathic syndrome, cerebral microembolisation probably plays the leading part, the hyperaemia being a reaction to a prior diffuse hypoperfusion.^{5 6}

Blood circulating through a pump oxygenator system during cardiopulmonary bypass carries many embolising particles, most of which originate from the

coronary suction line.³⁰⁻³² Lipid and other aspirated material account for some of the particles detected in the cardiectomy return blood, but platelet aggregates probably constitute the major portion by volume of the particulate microemboli.³² Gaseous microemboli are probably also important in the pathogenesis of brain hyperperfusion. Inevitably saturated liquids degas and form gaseous microemboli when temperatures increase, owing to a reduced solubility. This aspect of extracorporeal circulation is particularly important at the onset of bypass, particularly if nitrous oxide has been continued until perfusion begins.³³ Defoaming is never complete and the small bubbles are carried by liquid flow into the arterial line before they can rise to the surface of the arterial reservoir. The smaller diameter bubbles are more likely to be trapped because buoyancy is directly related to size. The capability of the arterial line filter to trap gas bubbles may be the main advantage of using the filter in that position. We had no Doppler assessment of the number of emboli; but undoubtedly 20 and 40 micron arterial filters remove many circulating emboli, although there are still particles and bubbles left in the perfusate.³⁰

The number of microemboli detected in the perfusate may correlate poorly with the severity of the postoperative central nervous system dysfunction because of the diverse ability of different microemboli to obstruct the vascular bed of the brain. Reducing the quantity as much as possible, however, would seem reasonable.

In experimental and clinical studies arterial filtration prevented the formation of emboli,^{30 34-36} improved the clinical outcome and neuropsychometric scores after operation,^{16 18 19 22 25} reduced the incidence of emboli in neuropathological investigations,³⁷⁻⁴² and prevented structural changes in the brain.^{1 26}

There is some blood trauma with filters of small pore size,⁴³ so the inclusion of a 40 micron filter has become popular.^{25 39 43 44} Despite the use of micro-porous filters in the extracorporeal circulation unit, however, there are still many microaggregates and gaseous microemboli left in the perfusate.³⁰ Arterial line filters do not replace the coronary suction filter, because if they serve as the only filter they will not be adequate.³⁰

It is impossible to define the safe filter pore size, but the experimental work by Prosenz⁴⁵ showed that plastic microspheres smaller than 7 microns pass freely through the cerebral capillary bed, whereas those of 7-14 microns are sometimes trapped. Microspheres of 14-74 microns pass only if arteriovenous shunts have been opened in response to hypoxia. This and other experimental investigations suggest that the smallest filter pore size should be used. Our mea-

surements of cerebral blood flow support but do not clinch this suggestion.

EFFECT OF ARTERIAL FILTRATION

On the basis of cerebral blood flow data corrected to a standard PCO₂ of 40 mm Hg (5.3 kPa),^{6 10} arterial filters significantly reduced the hyperaemia during the rewarming procedure at 30°, 33°, and 35°C (fig 1b) but did not completely prevent it. The significant reduction in cerebral blood flow could be fortuitous. The same trend was, however, noted in the uncorrected data (fig 1a) and cerebral blood flow does undoubtedly respond to changes in PCO₂. Owing to individual differences in the relationship between cerebral blood flow and PCO₂, resulting change in cerebral blood flow may be 2-4% per 1 mm Hg (0.13 kPa) change in PCO₂, but any correction will accentuate the existing difference between the filter groups and the control group (fig 1 and tables 2-4).

The significant reduction in cerebral blood flow occurred during the rewarming period, whereas no difference was noticed during the earlier cooling period. This could reflect differences in the amount of solid and gaseous particles constituting the population of emboli in the perfusate. The filters are more efficient at removing gaseous particles, which are known to increase during the rewarming procedure, but our data are not conclusive.

The effect on cerebral blood flow induced by procaine in the cardioplegic solutions also has to be considered. The effect is transient, however, and is noticed only during hypothermic bypass, just after the infusion of the cardioplegic solution.⁸

Given that arterial filters of 20 or 40 microns slightly reduced cerebral blood flow but did not prevent brain hyperaemia and filters of even smaller pore size would probably result in too much blood trauma, some other measure is needed to reduce cerebral blood flow. Management of PCO₂ could be a simple way of doing this, and hence appreciably reduce the amount of emboli which could be trapped in the brain capillaries.¹²

CARBON DIOXIDE TENSION

Manipulation of PCO₂ causes considerable changes in cerebral blood flow as hypercapnia produces vasodilation with increased flow and hypocapnia causes vasoconstriction with decreased flow (fig 5). The sensitivity to changes in PCO₂ in our patients was within the normal range.¹⁰ The considerable scatter in figure 5 was mostly due to variations in blood pressure, which has a known modulating effect on the relationship between cerebral blood flow and PCO₂.⁴⁶ In this series of patients we added carbon dioxide to the oxygenator. As carbon dioxide is a potent vasodilator, however, and consequently impairs the cere-

bral autoregulation, we do not add it to the oxygenator any longer. In addition to the resulting beneficial effect on the cerebral autoregulation, a reduced PCO_2 and hence a lower cerebral blood flow has the advantage that the number of circulating emboli entering the brain is considerably reduced.

PERFUSION PRESSURE

A reduced flow rate and arterial blood pressure (< 60 mm Hg) during extracorporeal circulation have been advocated to prevent rewarming of the heart via a non-coronary collateral circulation,⁴⁷ but they were associated with a high incidence (75%) of the central nervous system dysfunction during the first week after operation. Other cardiac surgery centres regard cardiopulmonary bypass as a state of controlled shock and accept low arterial blood pressures. This policy, at least so far as the cerebral circulation is concerned, may entail a risk of brain damage.

Many papers incriminate hypotension as a major cause of dysfunction of the central nervous system. Witoszka *et al*²⁴ reported neurological abnormalities in patients with a low mean arterial blood pressure (< 45 mm Hg) during extracorporeal circulation. Javid *et al*²¹ reported neurological abnormalities in 60% if mean arterial blood pressure was lower than 50 mm Hg. Postmortem findings give additional support to the hypothesis that cerebral damage occurs at surgery and may be the result of inadequate cerebral perfusion.^{15 24 40 48 49} The most common histological manifestation was the kind of neuronal degeneration attributed to anoxia. The lesions were distributed in arterial boundary zones and were similar to the experimental lesions that follow profound hypotension.^{48 49} Boundary zone infarcts occur when there is oligoemic hypoxia due to episodes of reduced perfusion, the lesions being bilateral in nature.

The concept of autoregulation is well described and widely accepted. Our finding of the relationship between cerebral blood flow and mean arterial blood pressure during extracorporeal circulation supports the classical concept of autoregulation. The lower limit of autoregulation in our patients was reached at around 55–60 mm Hg in mean arterial blood pressure, after which a further reduction in pressure reduced cerebral blood flow. Thus we cannot recommend a perfusion pressure lower than this if cerebral ischaemia is to be avoided.

ISCHAEMIA

The possibility of an ischaemic lesion as the underlying cause of dysfunction of the central nervous system after cardiac surgery is supported by the findings of intracellular markers in cerebrospinal fluid.^{1–3} The reactive brain hyperaemia noted in our patients supports this idea. The brain, however, either is more

resistant to ischaemia than has previously been recognised or has sufficient compensatory potential to allow patients to regain full or near normal function weeks after extracorporeal circulation despite its severe early dysfunction.

Brain cells combine a high energy expenditure with a low energy reserve, and as they have only a modest capillarity an abundant supply of oxygen is needed to avoid brain ischaemia. Ischaemia may be global or regional, complete or partial. Conditions that reduce cerebral blood flow will lead to global incomplete ischaemia—for example, during hypotension or increased intracranial pressure. Regional complete ischaemia may result from embolism. In some tissues—for example, muscle—capillaries can be opened to meet the increased demands for blood flow. In brain tissue, however, no such recruitment is possible. If focal or global hypoxia is complicated by a reduced cerebral perfusion pressure the compensatory increase in cerebral blood flow is curtailed. As a result, the oxygen delivery is further compromised and the cellular energy state deteriorates.

Pronounced hypoxia can be tolerated without causing a reduction in the cerebral metabolic rate of oxygen or a major derangement in the cerebral energy state. Even arterial oxygen tensions of 20–25 mm Hg (2.7–3.3 kPa) can be tolerated if the mean arterial blood pressure is high enough to allow the reactive increase in cerebral blood flow that represents the main if not sole mechanism to prevent energy failure. Experimental manipulations that interfere with the compensatory increase in cerebral blood flow lead to energy failure at the cellular level.⁵⁰

CONCLUSION

The abnormally high cerebral blood flow during hypothermia and the early rewarming period are probably the combination of an increased PCO_2 and a diffuse microembolisation, the increase in cerebral blood flow being secondary to a prior hypoperfusion at the microcirculatory level. The formation of microemboli during cardiopulmonary bypass is unavoidable. Interposing arterial filters reduced but did not prevent the brain hyperperfusion during bypass. There are many good reasons for using arterial filters. Our data on cerebral blood flow constitute no proof, but along with other experimental and clinical studies they support the idea that arterial filtration should be used. The smaller the filter pore size the better. We would also emphasise the importance of maintaining an adequate cerebral perfusion pressure (> 55 –60 mm Hg) to prevent regional or general cerebral ischaemia.

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