Cerebral blood flow after surgery for recent subarachnoid haemorrhage

J MERORY, D J THOMAS, P R D HUMPHREY, G H DU BOULAY,
JOHN MARSHALL, R W ROSS RUSSELL, LINDSAY SYMON, E ZILKHA

From the Institute of Neurology, National Hospital for Nervous Diseases, London

SUMMARY 243 measurements of cerebral blood flow by a noninvasive ^{133}Xe clearance technique have been made in 45 patients undergoing surgery for a recently ruptured cerebral aneurysm. Two groups of patients have been defined by the presence or absence of a postoperative rise in cerebral blood flow which showed a significant correlation with level of consciousness after operation.

When Walton¹ wrote his classical monograph on subarachnoid haemorrhage he reported a mortality of 45% during the first hospital admission following a bleed. Since that time a great deal has been done to improve the prognosis for those patients in whom the haemorrhage arises from a ruptured aneurysm. This improvement owes much to better angiography (in particular to magnification techniques), to the introduction of the dissecting microscope² which permits better visualisation of the aneurysm through a smaller operative field, and to the development of the Scoville clip which is gently released on to the neck of the aneurysm instead of requiring to be positioned by pressure. Important also has been the recognition of the decisive influence of the clinical status of the patient prior to surgery³⁻⁴ and the timing of operations upon the outcome.

Despite these advances which have enabled a mortality as low as 1.6% to be achieved in suitable patients operated upon within days of their first bleed^{1, 6} there remain two important groups which continue to pose a challenge. The first consists of those whose clinical condition from the outset makes them in general an unacceptable operative risk (Hunt and Hess⁴ Grades 4 and 5). The second comprises those who preoperative clinical condition is good, who undergo seemingly uneventful surgery, initially follow a satisfactory postoperative course and then suddenly or gradually develop either a focal deficit, a general depression of consciousness or both. This latter group provided the stimulus for the present

study of cerebral blood flow.

In order to discover what might be happening in these patients it is necessary first to have a clear picture of the day to day variations in cerebral blood flow after uneventful aneurysm surgery. This is not easy to discern because of the multiplicity of factors such as preoperative clinical status, site of aneurysm and timing and type of surgery which profoundly influence the course of events. There is in addition the question of vasospasm.

That narrowing of large cerebral arteries can be illustrated angiographically following subarachnoid haemorrhage is beyond doubt. There is moreover evidence from animal experiments that vasoconstriction develops in two phases, one immediately and one which is maximal between three and eight days after the bleed, as shown for instance by Brawley *et al*⁷ and Tanabe *et al*⁸ in dogs, Svendgaard *et al*⁹ in rabbits and Simeone *et al*¹⁰ in rhesus monkeys.

Evidence from human clinical studies is less satisfactory. From the early days when angiography was carried out within the first 24 hours after a bleed, it has been known that very severe and widespread vasoconstriction is present in a small proportion of patients.¹¹⁻¹³ What is less certain is to what extent the delayed vasoconstriction which may be demonstrated some days later¹⁴ is the same phenomenon as the biphasic vasoconstriction seen in animal experiments or to what extent it may be caused in part by further small bleeds. This vasoconstriction reaches its maximum between three and eight days after the haemorrhage and has usually subsided by the end of the second week.¹⁵ Severe generalised vasoconstriction is associated with poor clinical status, but less extensive milder vasoconstriction gives little indication of clinical status.

Address for reprint requests: Professor J Marshall, University Department of Clinical Neurology, The National Hospital, Queen Square, London WC1N 3BG.

Accepted 15 August 1979

The introduction of isotope clearance methods of measuring cerebral blood flow (CBF) raised hopes that a close relationship between CBF and clinical status and prognosis might be demonstrable. This has in general been found to be so¹⁶⁻²⁰ though reports to the contrary have appeared.²¹ Some authors have even concluded that low flow may simply reflect reduced metabolic demand and may not in itself be a bad sign.²²

Elucidation of the problem has until recently been handicapped by the fact that measurement of CBF by the ¹³³Xe clearance technique necessitated injection into the internal carotid artery, severely limiting the number of measurements which could be made in any one patient. Symon *et al*¹⁸ and Heilbrun *et al*²² were only able to perform one preoperative and one postoperative study in one and three cases respectively. Bergvall *et al*¹⁵ studied 21 cases before and after operation but only two had two postoperative measurements. Grubb *et al*²³ using ¹⁵O examined 11 patients before and after operation obtaining one postoperative measurement in nine and two measurements in two patients.

The development of the intravenous or inhalation method of administration of ¹³³Xe has made possible repeated CBF measurements in individual patients. Weir *et al*²⁴ using this technique made 76 measurements of CBF in 32 patients, 23 of whom had preoperative and postoperative studies. There appeared to be a postoperative rise in CBF, but as pCO₂ was not measured the results are difficult to interpret. The present study was undertaken to define in detail the day to day variations in CBF following surgery and in particular to discover whether they could be related to the postoperative clinical condition and course of the patient.

Patients and methods

243 preoperative and postoperative CBF measurements were performed on 45 patients admitted acutely to the National Hospitals for Nervous Diseases following subarachnoid haemorrhage subsequently proven by angiography to be from a cerebral aneurysm. The decision to operate was based on clinical grounds and not on the CBF data.

CBF was measured by a modification of the non-invasive ¹³³Xe clearance technique described by Obrist *et al*,²⁵ details of which are reported elsewhere.²⁶ In brief, 5 to 7 mCi ¹³³Xe were injected into a dorsal vein of a hand. The clearance of isotope from the brain was monitored for 11.5 minutes by three sodium iodide detectors of 25 mm diameter on each side of the skull. A seventh detector placed over a wide bore tube leading from a face mask monitored the expired ¹³³Xe. The head and expired ¹³³Xe curves

were displayed visually and analysed by computer. The measurement of CBF used throughout this study was the mean of the fast clearing component of the six clearance curves.

pCO₂ was estimated on blood obtained from a vein on the dorsum of a hand which had been previously warmed to a skin temperature of 35°C. This has been shown to give a reliable measure of arterial pCO₂ but not of pO₂.²⁶⁻²⁷ Blood pressure (BP) was measured using a standard sphygmomanometer cuff on the arm.

The clinical status of the patient was specifically recorded for the purpose of the study with particular attention to level of consciousness, evidence of focal lesions of the cerebral hemispheres and signs of brain stem disturbance.

Results

There were 17 male patients with a mean age of 47 years (SD 12.4; range 18-62) and 28 females, mean age 45 years (SD 10.4; range 23-63). The clinical status of the patients graded according to Hunt and Hess⁴ and the mean preoperative CBF of the patients in each grade is given in table 1. Although the CBF in group III was lower than in groups I and II the difference was not significant ($p > 0.1$) nor was there any significant difference between the pCO₂ and BP between any of the groups.

The time course of the mean CBF changes for the 45 patients preoperatively and for the first seven postoperative days is presented in table 2. This shows a postoperative rise in CBF particularly on the first postoperative day. The preoperative CBF of 55.2 ml/100 g/min was compared with the CBF of 62.6 ml/100 g/min on the first postoperative day by a paired 't' test; the increase was found to be significant at the 1 per cent level. This was not due to a difference in either pCO₂ or BP.

Inspection of the temporal profile of CBF in individual patients however showed that the postoperative first day rise was absent in 16 cases. In two of these the preoperative and postoperative CBF levels were the same whilst in the remaining 14 there was an appreciable fall. The postoperative rise in CBF among the 29 patients in whom it was present ranged from 7 to 155 per cent above the pre-

Table 1 Preoperative clinical status and cerebral blood flow

Grade (Hunt & Hess 1968)	No of patients	Mean CBF (SD) ml/100 g/min	Mean arterial pressure mm Hg (SD)	pCO ₂ torr mm Hg (SD)
I	10	59.5 (18.6)	91.1 (12.4)	35.4 (5.2)
II	14	59.2 (18.7)	101.4 (15.9)	34.6 (5.2)
III	19	50.8 (15.6)	98.3 (14.9)	34.1 (3.6)
IV	2	46.7 (—)	106.5 (—)	34.3 (—)

Table 2 Time course of cerebral blood flow after surgery

	Preoperative	Postoperative day						
		1	2	3	4	5	6	7
No of studies	45	45	29	35	29	19	21	20
CBF ml/100 g/min	55.2 (17.5)	62.6 (16.9)	55.9 (13.3)	58.5 (19.1)	60.5 (18.11)	53.9 (13.7)	55.8 (15.6)	55.4 (19.2)
pCO ₂ torr	34.6 (4.4)	34.4 (3.9)	35.7 (3.7)	34.5 (4.0)	36.7 (3.7)	37.3 (4.4)	36.5 (4.5)	37.4 (3.7)
Mean arterial BP mm Hg	98.0 (15.5)	96.8 (13.7)	99.7 (15.6)	101.7 (14.8)	95.1 (14.5)	100.1 (18.1)	103.9 (16.1)	96.5 (14.5)

Means ($\pm$ 1 SD) are shown

operative level. The absolute levels of CBF in the two groups are contrasted in table 3 and the figure.

The possibility that the group with and without a postoperative rise in CBF differed in their level of pCO₂, BP (which would affect CBF if autoregulation were damaged) or venous haematocrit (VH) was considered, the relevant data being presented in table 3. Comparing them on a day by day basis there was no significant difference between the two

groups in pCO₂ or BP. The VH was significantly lower preoperatively in the group with a postoperative rise in CBF ($p < 0.05$ unpaired 't' test); it was also lower on the first and second postoperative days. However the difference between the preoperative and first postoperative VH was the same in both groups hence could not have accounted for the rise in CBF in one group and the fall in the other.

The CBF value used throughout the study was the mean of the fast clearing component (Ff) recorded by each of the six detectors. Because the proportion of fast to total flow varies both in normal brain with change in pCO₂ and under pathological conditions, the possibility that the differences in Ff between the two groups was the result of a difference in the fraction clearing at the fast rate (Fr) was examined. The results (table 4) show no significant difference on any day between the groups ($p > 0.1$).

The relationship of the presence or absence of a postoperative rise in CBF to the preoperative clinical status and CBF of the patients is presented in table 5. 51% of those with a postoperative CBF rise were in Grades III and IV against 37% of those without a rise. The preoperative CBF of 50.6 ml/100 g/min in the group of patients with a postoperative rise was significantly lower than the preoperative measurement of 63.4 ml/100 g/min in the group without a postoperative rise (unpaired 't' test $p < 0.02$). As table 5 shows the main contribution to this difference was by the patients in Grade I

Figure Pre and postoperative cerebral blood flow in 29 patients with postoperative rise (solid line) and 16 patients without (broken line).

Table 3 CBF, pCO₂, mean arterial BP, VH and (SD) in groups with and without postoperative rise in CBF

	<i>Preoperative</i>	<i>Postoperative day</i>						
		<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>	<i>5</i>	<i>6</i>	<i>7</i>
<i>With postoperative rise in CBF</i>								
No of studies	29	29	20	24	20	11	15	15
CBF ml/100 g/min	50.6† (15.3)	67.0† (16.9)	56.9 (12.4)	60.3 (14.4)	58.4 (14.1)	59.5 (15.0)	56.6 (15.7)	54.9 (21.7)
pCO ₂ torr	35.1 (3.6)	34.4 (3.9)	36.9 (3.7)	35.0 (4.1)	36.7 (4.0)	38.0 (4.4)	36.9 (4.1)	36.8 (3.6)
Mean arterial BP mm Hg	97.2 (17.0)	96.7 (14.3)	100.4 (17.4)	101.2 (15.2)	97.1 (15.0)	97.7 (17.4)	98.4 (13.9)	95.6 (13.0)
Haematocrit	0.413*(0.043)	0.351†(0.051)	0.344*(0.040)	0.360 (0.037)	0.342 (0.034)	0.354 (0.036)	0.357 (0.037)	0.370 (0.051)
<i>Without postoperative rise in CBR</i>								
No of studies	16	16	9	11	9	8	6	5
CBF ml/100 g/min	63.4†(18.5)	54.0†(13.6)	53.9 (15.8)	54.6 (13.3)	65.2 (25.3)	46.3 (7.1)	53.9 (17.0)	57.2 (10.7)
pCO ₂ torr	33.6 (5.6)	35.0 (3.9)	33.2 (3.1)	33.6 (3.5)	36.6 (3.0)	36.6 (4.7)	36.1 (5.6)	39.6 (3.0)
Mean arterial BP mm Hg	99.2 (12.9)	96.6 (12.7)	98.0 (11.4)	102.8 (14.5)	91.0 (13.2)	99.0 (10.7)	107.1 (20.4)	99.0 (19.7)
Haematocrit	0.440*(0.032)	0.385†(0.031)	0.379*(0.048)	0.356 (0.033)	0.358 (0.041)	0.403 (0.089)	0.387 (0.025)	0.392 (0.022)

Unpaired t test between groups for that day * $p < 0.05$ † $p < 0.02$

Table 4 Proportion (Fr) of total CBF represented by fast clearing component

	<i>Preoperative</i>	<i>Postoperative day</i>						
		<i>1</i>	<i>2</i>	<i>3</i>	<i>4</i>	<i>5</i>	<i>6</i>	<i>7</i>
<i>With postoperative rise in CBF</i>								
No of studies	29	29	20	24	20	11	15	15
CBF ml/100 g/min	50.6 (15.3)	67.0 (16.9)	56.9 (12.4)	60.3 (14.4)	58.4 (14.1)	59.5 (15.0)	56.6 (15.7)	54.9 (21.7)
Fr	69.1 (8.9)	65.0 (8.4)	62.3 (7.5)	63.1 (9.3)	64.1 (8.1)	64.4 (7.4)	65.8 (10.7)	67.2 (8.8)
<i>Without postoperative rise in CBF</i>								
No of studies	16	16	9	11	9	8	6	5
CBF ml/100 g/min	63.4 (18.5)	54.0 (13.6)	53.9 (15.8)	54.6 (13.3)	65.2 (25.3)	46.3 (7.1)	53.9 (17.0)	57.2 (10.7)
Fr	68.6 (6.6)	62.8 (7.6)	66.5 (7.4)	64.4 (8.4)	69.9 (7.0)	62.7 (7.2)	64.1 (10.6)	64.9 (5.6)

Means ($\pm$ 1SD) as shown

preoperatively.

The degree and duration of induced hypotension during surgery may have affected postoperative CBF; accordingly the group with and without a postoperative rise were examined for any difference in this respect. In the group with a postoperative rise in CBF the mean value for the lowest level of systolic BP during surgery was 74 mm Hg (SD 9.6) which was maintained for a mean time of 44 (SD 37) min; the mean of the total time during which the BP was below 100 mm Hg was 98 min (SD 46). The values for the group without a postoperative rise in CBF were 71 mm Hg (SD 9.3), 29 min (SD 26) and 106 min (SD 57) respectively. None of these differ significantly.

A number of other factors which might have influenced the results were examined. The time from the bleed to the operation was 12.1 days (SD 7.4) in the group with a postoperative rise in CBF against 9.4 days (SD 4.1) in the group without; the difference is not significant. Likewise the interval between the angiogram and the preoperative CBF was not significantly different, being respectively 2.7 days (SD 2.6) and 1.2 days (SD 1.9) in the group with and without a postoperative CBF rise.

A previous history of hypertension was obtained from four of the 29 patients with a postoperative rise in CBF and from two of the 16 without. A haematoma was present in 4 of the former group and one of the latter.

There was no difference in the management of the patients in the two groups with regard to the anaesthetic regime and preoperative and postoperative drug therapy; one patient from each group was given an infusion of metaraminol to elevate blood pressure but this was not until the third and fifth postoperative days. All patients were given infusions of low molecular weight dextran postoperatively, with two exceptions in the group with a postoperative rise in CBF who were given dextrose only. In none of the patients was drainage of cerebrospinal fluid performed.

Finally the presence or absence of a postoperative rise in CBF was correlated with the patients' level of consciousness after surgery, the results being given in table 6. This shows a striking difference between the two groups; 24 of the 29 patients with a postoperative rise in CBF were alert on the first postoperative day against only 4 of the 16 without a rise. Chi squared test shows this difference to be highly significant ($\chi^2 = 12.28$ $p < 0.0005$).

Table 6 CBF and level of consciousness on first postoperative day

Clinical condition	With postoperative rise in CBF	Without postoperative rise in CBF	Total
Alert	24	4	28
Drowsy	5	12	17
Total	29	16	45

 $\chi^2 = 12.28$ $p < 0.0005$

Table 5 Preoperative clinical status and CBF in patients with and without a postoperative CBF rise

Grade Hunt & Hess 1968	With postoperative CBF rise				Without postoperative CBF rise			
	No of patients	Mean CBF (SD) ml/100 g/min	Mean arterial BP mm Hg (SD)	pCO ₂ torr (SD)	No of patients	Mean CBF (SD) ml/100 g/min	Mean arterial BP mm Hg (SD)	pCO ₂ torr (SD)
I	7	52.0* (13.8)	90.0 (11.5)	37.4* (3.7)	3	76.9* (18.2)	93.7 (16.7)	30.8* (6.0)
II	7	53.4 (16.3)	103.5 (20.2)	36.8 (3.9)	7	65.0 (20.2)	99.7 (12.5)	32.5 (5.7)
III	13	48.9 (16.2)	96.8 (15.9)	33.1 (2.4)	6	54.8 (14.4)	101.5 (13.4)	36.3 (4.9)
IV	2	46.7 (—)	106.5 (33.2)	34.3 (2.5)	0	—	—	—
Total	29	50.5 (15.3)	—	—	16	63.4 (18.5)	—	—

*t test between group with and without postoperative rise $p < 0.02$

PATIENTS WITH A POSTOPERATIVE RISE IN CBF

As a rise in CBF after surgery appeared to be associated with alertness on the first postoperative day, it was of interest to seek reasons why five of the patients in this group were drowsy. The first of these (No 260) was a poor risk being in grade IV preoperatively with a CBF of 31.3 ml/100 g/min. She had left posterior communicating and middle cerebral aneurysms, both of which were clipped. She remained in coma after operation despite CBF measurements around 68 ml/100 g/min until her death five months later. A postoperative CT scan showed intraventricular haemorrhage and extensive infarction. The second patient (No 423) who had a left posterior communicating aneurysm was in Grade I preoperatively. She had a preoperative CBF of 55 ml/100 g/min and a first postoperative day flow of 70 ml/100 g/min at which time she was however slightly drowsy. On the fourth day CBF was 59 ml/100 g/min. Later that day she developed a right faciobrachial weakness, dysphasia and hemianopia. A CT scan showed only mild hydrocephalus with no evidence of a focal lesion. The mean CBF on the following day was 71 ml. She made a considerable degree of recovery being left with only mild weakness of the right upper limb. The third patient (No 352) had an anterior communicating aneurysm adequate occlusion of which involved some narrowing of the left (*sic*) anterior cerebral artery. The patient, in grade I preoperatively with a CBF of 40 ml/100 g/min, was drowsy on the first postoperative day with mean CBF of 45 ml/100 g/min. On day 5 the patient (who was left-handed) became increasingly obtunded with a mild left (*sic*) hemiparesis and dysphasia. The mean CBF was 45 ml/100 g/min and angiography showed that the right anterior cerebral artery filled retrogradely from middle cerebral collateral vessels. CT scan showed a right anterior low density lesion. Elevation of systemic blood pressure by metaraminol infusion for several days resulted in a rise in CBF and a resolution of the drowsiness and focal neurological deficit. The patient went on to make a full and satisfactory recovery. The fourth patient (No 146) because of drowsiness was in Grade III preoperatively though without focal deficit; the CBF was 47 ml/100 g/min. The patient had an anterior communicating aneurysm which filled from the right. The operation was uneventful but on the first postoperative day he was still drowsy but had in addition a mild left hemiparesis; he had a mean CBF of 50 ml/100 g/min. His condition deteriorated and on the third postoperative day a right sided extradural haematoma was evacuated, following which he improved. The fifth patient (No 308) was in Grade III preoperatively because of his level of consciousness; he had a CBF of 27 ml/100 g/min. An anterior com-

municating aneurysm was clipped during which procedure it was necessary to occlude both anterior cerebral arteries for 10 minutes. Postoperatively he was still drowsy with a CBF of 34.5 ml/100 g/min. He then developed a right hemiplegia and dysphasia. CBF during the first seven postoperative days fluctuated between 30 and 51 ml/100 g/min. He subsequently developed akinetic mutism and died two months later.

Thus of the five patients who despite a postoperative rise in CBF were drowsy on the first postoperative day four subsequently developed a focal neurological deficit. The one who died (No 260) was a poor risk being in Grade IV preoperatively and remained in coma postoperatively until she died. Of the four who developed a focal deficit one had a postoperative extradural haematoma, two had interference with blood flow through the anterior cerebral arteries during surgery and in only one was there no readily detectable reason for the focal deficit. However two other patients in this group had the anterior communicating artery clipped without any untoward effects.

PATIENTS WITHOUT A POSTOPERATIVE RISE IN CBF

Of the 16 patients who did not have a rise in CBF after surgery only four were alert on the first postoperative day, their mean CBF being 70 ml/100 g/min. The absence of a rise in these four was probably due to the fact that their mean preoperative CBF of 85 ml/100 g/min was already high for patients with recent subarachnoid haemorrhage.

Of the remaining 12 patients, all of whom were drowsy, four did badly. They were in Grade III preoperatively with a mean CBF of 42.0 ml/100 g/min (range 27-54) which is appreciably lower than the 55 ml/100 g/min for the whole series. After operation their level of consciousness was depressed for a prolonged period and, though they showed no notable focal neurological deficit, the recovery of three was marred by considerable mental impairment and one died. The mean CBF for this group on the first postoperative day was 41 ml/100 g/min.

The remaining eight drowsy patients included two who subsequently developed focal deficits. The first (No 144), who was in Grade III preoperatively with a CBF of 40.9 ml/100 g/min, had an uncomplicated operation for a left posterior communicating aneurysm. Her CBF on the first postoperative day was only 39 ml/100 g/min. On the fourth day she developed a right hemiparesis and dysphasia. Mean CBF was 57 ml/100 g/min. CT scan showed diffuse swelling of the left hemisphere. The hemiparesis improved but some dysphasia persisted. The second patient (No 120) who was in Grade II preoperatively with a CBF of 42 ml/100 g/min had a giant right

posterior communicating aneurysm. Operation was technically difficult and involved dissection of the anterior chroidal artery from the fundus of the aneurysm and temporary occlusion of the middle cerebral and distal carotid arteries for four minutes. The posterior communicating artery was occluded by the clip on the neck of the aneurysm. CBF on the first postoperative day was 30 ml/100 g/min and mild pyramidal signs on the left were evident. On the third day he became more drowsy and developed a frank hemiparesis which was abolished by elevating the systemic blood pressure with intravenous metaraminol thereby raising the CBF to 49 ml/100 g/min. For several days the focal deficit fluctuated in relation to the level of systemic blood pressure, the paresis returning as blood pressure fell. Later it was possible to discontinue metaraminol and the patient went on to make a full recovery. Postoperative angiography showed no filling of the right anterior choroïdal artery and CT scan at the time of fluctuating paresis showed a right capsular low density area which resolved with the resolution of the paresis.

In summary in this group of 16 patients without a postoperative increase in CBF the four who were alert postoperatively already had a very high preoperative flow. Of the 12 who were drowsy four did badly; the remaining eight recovered but two of these developed focal neurological deficits, one with diffuse swelling of the hemisphere, the other after temporary occlusion of the internal carotid artery during surgery. In two other patients among the eight, the internal carotid artery was occluded temporarily without the development of focal deficit.

Discussion

This study is the first to provide data on daily measurements of CBF in individual patients during the first week following aneurysm surgery. It has shown that the measurement of cerebral perfusion by a noninvasive technique following surgery for ruptured cerebral aneurysm may provide useful information about the relationship between CBF and the clinical state of the patient. The situation revealed is complex, but certain generalisations seem justified.

In patients of satisfactory clinical status whose preoperative CBF is not high, surgery carried out during the first week after rupture of an aneurysm may be followed by an increase in postoperative CBF, this being most marked on the first postoperative day. This postoperative increase in CBF is usually associated with a satisfactory clinical status, the patient being alert on the first postoperative day and making an uneventful recovery. Patients with a postoperative increase in CBF who are not alert have either been poor risks preoperatively or been subject

to difficulties during surgery.

Absence of a postoperative rise in CBF is not invariably a bad prognostic sign but certainly indicates the need to determine the cause. The preoperative flow may already have been high as was the case in four of the patients in this series, all of whom were alert postoperatively. A high preoperative flow must be distinguished from luxury perfusion. In the latter case the patients preoperative clinical condition is likely to have been so poor that he would not have been considered for surgery at that time. A patient in good clinical condition whose CBF is high is suitable for surgery but then may not show a postoperative rise in CBF.

Absence of a postoperative rise in CBF without a high preoperative level is associated with drowsiness and seems to have implications for prognosis. Four of the twelve patients, though without focal deficits, made a poor recovery remaining mentally impaired; one died subsequently. The remainder made a gradual but complete recovery except for a persisting neurological abnormality in one.

The development of late focal neurological complications seemed not to be related to the presence or absence of the generalised postoperative rise in CBF. They occurred in both groups; three out of the seven were related to operative difficulty which had necessitated interruption of blood flow through an artery for a time. However in two other cases clipping of the anterior communicating artery was without complication. Although operative difficulties may be important the level of CBF cannot be ignored in management. Autoregulation and vasoreactivity to CO₂ were not formally tested, but the experience in the two patients in whom raising the blood pressure by drugs produced an increase in CBF and reduction in the degree of focal neurological deficit indicates that autoregulation was impaired and that elevation of the blood pressure was beneficial.

The cause of the postoperative rise in CBF remains to be elucidated. It would have been of interest to relate the presence or absence of a rise in CBF to the level of intracranial pressure (ICP). Fearnside and Adams²⁸ measured ICP postoperatively and found that the level of pressure was inversely correlated with clinical status. Raised pressure might impede blood flow sufficiently to account for the absence of the postoperative rise in CBF and the poorer clinical status of the patients. It was not felt to be practical to measure ICP routinely in these patients who were already being subjected to daily measurements of CBF albeit by a noninvasive technique and so the relationship of CBF to ICP in the series must remain speculative.

The postoperative rise in CBF is unlikely to be the result of temporary vasoparalysis as this would not

be in keeping with the good clinical condition and alertness of the majority of the patients. A more satisfactory explanation is that the vascular tree has retained its reactivity and that the rise in CBF is a hyperaemic response to the period of hypotension employed during the operative treatment of these patients. On this hypothesis the absence of a post-operative rise in CBF despite a similar degree and duration of hypotension may indicate some impairment of responsiveness of the cerebral vessels. Thus, despite the higher preoperative level of CBF, the impaired responsiveness of the cerebral vessels might prevent the adjustment of flow to metabolic needs and so contribute to the drowsy state of the majority of the patients in the group and the generalised cerebral damage suffered by four. Although the group was not more prone to late focal neurological complications than the group with a postoperative rise in CBF (such complications sometimes being related to operative difficulties), the fact that four suffered diffuse cerebral impairment suggests that a study should be undertaken of the effect of cautiously raising the blood pressure in such patients whilst observing its effect on CBF and state of consciousness.

The development of noninvasive techniques for the measurement of CBF promises to be a valuable tool in the study of those cases of subarachnoid haemorrhage and aneurysmal surgery who do not do well. A single measurement is unlikely to be helpful, but serial measurements correlated with clinical status, CT scanning and taken in conjunction with the information provided by the preoperative angiogram and the experience at operation may well ultimately facilitate the postoperative management of these patients.

The work was supported by an MRC Project Grant and John Merory by a grant from the Brain Research Trust. We thank Mr Norman Grant, Professor Valentine Logue, Mr DGT Thomas and Mr LS Walsh for permission to study cases under their care, Professor Peter Armitage for statistical advice, Miss Sheila Redmond for technical assistance and Miss Beryl Laatz for secretarial assistance.

References

- 1 Walton JN. *Subarachnoid haemorrhage*. Edinburgh: E & S Livingstone Ltd, 1956.
- 2 Krayenbuhl HA, Yasargil MG, Flamm ES, Tew JM. Microsurgical treatment of intracranial saccular aneurysms. *J Neurosurg* 1972; **37**:678-86.
- 3 Botterell EH, Loughheed WM, Scott JW, Vanderwater SL. Hypothermia and interruption of carotid and cerebral circulation in the surgical management of intracranial aneurysms. *J Neurosurg* 1956; **13**:1-42.

J Merory, D J Thomas, P R D Humphrey et al

- 4 Hunt WE, Hess RM. Surgical risk related to the time of intervention in the repair of intracranial aneurysms. *J Neurosurg* 1968; **28**:14-20.
- 5 Alvord EC, Loeser JD, Bailey WL, Copass MK. Subarachnoid haemorrhage due to ruptured aneurysms. A simple method of estimating prognosis. *Arch Neurol* 1972; **27**:273-84.
- 6 Symon L. Disordered cerebrovascular physiology in aneurysmal subarachnoid haemorrhage. *Acta Neurochir* 1978; **41**:7-22.
- 7 Brawley BW, Strandness DE Jr, Kelly WA. The biphasic response of cerebral vasospasm in experimental subarachnoid haemorrhage. *J Neurosurg* 1968; **28**:1-8.
- 8 Tanabe Y, Sakatark K, Yamada H, Ho T, Takada M. Cerebral vasospasm and ultrastructural changes in cerebral arterial wall. *J Neurosurg* 1978; **49**:229-38.
- 9 Svenggaard NA, Edvinsson L, Olin T, Owman VL, Saline CL. On the Pathophysiology of cerebral vasospasm: transmitter changes in perivascular sympathetic nerves and increased pial artery sensitivity to norepinephrine and serotonin. In: Owman C, Edvinsson C, eds. *Neurogenic control of the brain circulation*. Oxford: Pergamon Press, 1977; 143-52.
- 10 Simeone FA, Trepper PJ, Brown DJ. Cerebral blood flow evaluation of prolonged experimental vasospasm. *J Neurosurg* 1972; **37**:302-11.
- 11 Fletcher TM, Taveras JM, Pool JL. Cerebral vasospasm in angiography for intracranial aneurysms. *Arch Neurol* 1959; **1**:38-47.
- 12 du Boulay G. Distribution of spasm in the intracranial arteries after subarachnoid haemorrhage. *Acta Radiol [Diagn]* 1963; **1**:257-66.
- 13 Allcock JM, Drake CG. Ruptured intracranial aneurysms—the role of arterial spasm. *J Neurosurg* 1965; **22**:21-9.
- 14 Kagstrom E, Greitz T, Hanson J, Galera R. Changes in cerebral blood flow after subarachnoid haemorrhage. *Proc III Int Congr Neurol Surg*. Amsterdam: Excerpta Medica ICS, 1966; 110.
- 15 Bergvall U, Steiner L, Forster DMC. Early pattern of cerebral circulatory disturbances following subarachnoid haemorrhage. *Neuroradiol* 1973; **5**:24-32.
- 16 James IM. Changes in cerebral blood flow and in systemic arterial pressure following spontaneous subarachnoid haemorrhage. *Clin Sci Mol Med* 1968; **35**:11-22.
- 17 Ferguson GG, Harper AM, Fitch W, Rowan JO, Jennett B. Cerebral blood flow measurements after spontaneous subarachnoid haemorrhage. *Eur Neurol* 1972; **8**:15-22.
- 18 Symon L, Ackerman R, Bull JWD, Du Boulay EPGH, Marshall J, Rees J, Ross Russell R. The use of the Xenon clearance method in subarachnoid haemorrhage. *Eur Neurol* 1972; **8**:8-14.

- 19 Nilsson BW. Cerebral flow in patients with subarachnoid haemorrhage studied with an intravenous isotope technique. Its clinical significance in the timing of surgery of cerebral arterial aneurysm. *Acta Neurochirurgica* 37, 33–48.
- 20 Pitts LH, MacPherson P, Wyper DJ, Jennett WB. Cerebral blood flow, angiographic cerebral vasospasm and subarachnoid haemorrhage. *Acta Neuro Scand* 1977; **56**:334–5.
- 21 Zingesser LH, Schechter MM, Dexter J, Katzman R, Scheinberg LC. On the significance of spasm associated with rupture of a cerebral aneurysm. The relationship between spasm as noted angiographically and regional blood flow determination. *Arch Neurol* 1968; **18**: 520–8.
- 22 Heilbrun NP, Olesen J, Lassen NA. Regional cerebral blood flow studies in subarachnoid haemorrhage. *J Neurosurg* 1972; **37**:36–44.
- 23 Grubb RL, Raichle ME, Eichling JO, Gado MH. Effects of subarachnoid haemorrhage on cerebral blood volume, blood flow and oxygen utilization in humans. *J Neurosurg* 1977; **46**: 446–53.
- 24 Weir B, Menon D, Overton T. Regional cerebral blood flow in patients with aneurysms: estimation by Xenon 133 inhalation. *Can J Neurol Sci* 1978; **5**:301–5.
- 25 Obrist WD, Thompson HK, Wang WS, Wilkinson WE. Regional cerebral blood flow estimated by ¹³³Xenon inhalation. *Stroke* 1975; **6**:245–56.
- 26 Thomas DJ, Zilkha E, Redmond S, du Boulay GH, Marshall J, Ross Russell R, Symon L. An intravenous ¹³³Xenon clearance technique for measuring cerebral blood flow. *J Neurol Sci* 1979; **40**:53–63.
- 27 Brooks D, Wynn V. Use of venous blood for pH and carbon dioxide studies, especially in respiratory failure and during anaesthesia. *Lancet* 1959; **1**:227–30.
- 28 Fearnside MR, Adams CBT. Abstract in Proceedings of the Society of British Neurological Surgeons meeting. *J Neurol Neurosurg Psychiatry* 1978; **41**:1052.