Regional cerebrovascular responses to acute ischaemia in normocapnia and hypercapnia

An experimental study in baboons

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SUMMARY Arterial and venous pressures have been measured in the cortical circulation of baboons. Arterial perfusion pressure was found to be relatively lower in hypercapnia than in normocapnia, while venous pressure was higher in hypercapnia than normocapnia. In hypercapnia, during middle cerebral occlusion, the arteriovenous pressure differences virtually disappeared and evidence of collateral inflow to the ischaemic zone was absent. Reactive hyperaemia after middle cerebral occlusion was reduced or abolished in hypercapnia. The significance of these findings in relation to treatment of ischaemic vascular disease with CO₂ is discussed.

Evaluation of treatment of the stroke syndrome continues to form a major part of the work of neurological departments all over the world. To the neurosurgeon, similarly, reduction in blood supply to areas of brain, associated with subarachnoid haemorrhage or occurring at or after operation, remains a major problem. There has been concern in recent years with clinical and experimental analyses of therapeutic methods which, either acutely or in a more chronic situation, might be expected to improve the circulation of areas of the brain deprived of their normal blood supply.

The cerebral circulation has been known for many years to respond to the inhalation of carbon dioxide by vasodilatation (Gibbs, F. A., Gibbs, E. L., and Lennox, 1936; Forbes, 1940; Schmidt, Kety, and Pennes, 1945), and for this reason inhalation of carbon dioxide has been regarded as a powerful therapeutic tool in the treatment of cerebrovascular disease (Hegedus and Shackelford, 1965; Meyer and Gilroy, 1968). Meyer, Sawada, Kitamura, and Toyoda (1968) have produced evidence, in a careful analysis of the chronic stroke syndrome, that the cerebral metabolic rate for oxygen and glucose is increased by inhalation of CO₂ in chronic stroke cases. With the advent of regional methods of determination of cerebral blood flow, however (Lassen, Høedt-Rasmussen, Sørensen, Skinhøj, Cronqvist, Bodforss, and Ingvar, 1963; Høedt-Rasmussen,

Sveinsdottir, and Lassen, 1966), evidence has accumulated that the usual response to CO₂ (increase in blood flow) may not occur in areas of brain deprived of their normal blood supply. In these circumstances, indeed, CO₂ inhalation may produce a regional reduction in cerebral blood flow, and this concept has been crystallized in recent years as 'the intracerebral steal syndrome' (Brawley, Strandness, and Kelly, 1967; Symon, 1968; Wüllenweber, 1968).

The present study was designed to analyse the effects of hypercapnia on the vascular reactivity and response to vascular occlusion within the middle cerebral field of the experimental primate and, by comparison with findings at normocapnic levels, to determine whether carbon dioxide improved or made worse the reaction of the bed to vascular occlusion. This paper reports the effect of hypercapnia on arterial and venous pressure within the occluded middle cerebral field, and the influence of hypercapnia on the phenomenon of reactive hyperaemia. Further data concerned with the effect of hypercapnia on venous oxygen tension, arteriovenous pCO₂ difference, and regional pH will be presented in detail subsequently.

METHODS

Ten adult baboons (*Papio nubius* or *Papio cynocephalus*), unselected as to age and sex, were used. The animals were intubated under phencyclidine sedation, supplemented if necessary by light halothane anaesthesia, and anaesthesia maintained by the intravenous administration of alpha

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chloralose 60 mg/kg. The animals were immobilized with intravenous gallamine triethiodide 1 mg/kg repeated as necessary, and ventilation maintained by means of a Starling pump (Palmer Instruments, Ltd.). The stroke volume of the pump was adjusted to produce a normal arterial $p\text{CO}_2$ between 35 and 45 mm Hg. Where hypercapnia was to be induced, a mixture of 6% CO_2 and air replaced the air at the inlet of the Starling pump and the arterial $p\text{CO}_2$ of the animal was thereby raised to between 60 and 80 mm Hg. Values of over 55 mm Hg. were accepted as hypercapnic for the purposes of the study. Arterial blood pressure was continuously monitored by femoro-aortic catheter connected to a P23 Gb Statham strain gauge, and end-tidal CO_2 continuously monitored by a Beckman infra-red gas analyzer.

Pial arterial pressure was measured from a parietal branch of the middle cerebral artery by microscopic catheterization as previously described (Symon, 1967), and regional middle cerebral venous pressure obtained by catheterization of a tributary middle cerebral vein emerging from the cortex and converging upon the vein of Labbé (Fig. 1). This is a fairly constant feature of the baboon. Details of this technique are described elsewhere (Symon, 1970).

FIG. 1. Schematic diagram of the lateral surface of the baboon hemisphere to show the catheter placements.

In all experiments, the ipsilateral carotid artery in the neck was exposed and an encircling ligature placed round it to facilitate temporary occlusion during the experiment. The carotid sinus was not exposed and the sinus nerve was left intact.

The height of all strain gauges was adjusted so that the centre of the gauge was level with the centre of the mid-thoracic spine with the animal on its side, this being taken as approximately the level of the right atrium. The precautions necessary to ensure adequate continuous recording from these catheters and calibration of the arterial gauges are described elsewhere (Symon, 1967).

The venous gauge was calibrated against a saline column in a saline-filled system.

The middle cerebral artery was approached for occlusion by a subtemporal route, freed of its arachnoid coverings in the medial part of the Sylvian fissure, and temporarily occluded by a light spring clip, as previously described (Symon, Ishikawa, and Meyer, 1963). During the course of the experiments, a control occlusion, in normocapnic circumstances, was made first, followed by an occlusion in hypercapnia. A third occlusion in normocapnia was then made to ensure that the differences between normocapnia and hypercapnia were not those of sequential occlusions. Provided the animal's condition remained good and normal reactivity to carotid occlusion and to CO_2 remained, the cycle was repeated. The results in each animal therefore represent the mean of several normocapnic occlusions, compared with at least two occlusions under hypercapnia. Before each test situation, the response of the vascular bed to occlusion of the ipsilateral carotid artery was assessed to ensure that there was evidence of dilatation of the vascular bed to reduced input perfusion pressure, and the reaction of the bed to brief inhalation of 3% CO_2 was also assessed to ensure that reactivity to CO_2 was present. Without these safeguards, the functional integrity of vascular preparations can be extremely difficult to assess and the results may be of little value.

RESULTS

VENOUS AND ARTERIAL PRESSURE IN MIDDLE CEREBRAL FIELD DURING OCCLUSION IN NORMOCAPNIC AND HYPERCAPNIC CIRCUMSTANCES In the 10 animals, the mean pial arterial pressure in normocapnic circumstances was 85.3 mm Hg ($\text{SD} \pm 6.8$), representing a value of some 80% ($\text{SD} \pm 11.6$) of mean arterial blood pressure.

Increase in arterial $p\text{CO}_2$ to more than 55 mm Hg—the level chosen as 'hypercapnia'—caused a significant increase in systemic arterial pressure ($P < 0.001$). The absolute level of mean cerebral arterial pressure in hypercapnic circumstances was 83.3 mm Hg ($\text{SD} \pm 6.7$), which is not significantly different from the figure in normocapnia, but, if the cerebral arterial blood pressure is expressed as a percentage of the systemic pressure, the hypercapnic figure of 72% ($\text{SD} \pm 7.9$) is significantly lower than the figure in normocapnic circumstances ($P < 0.01$) (Table 1).

When the middle cerebral artery was occluded in normocapnia, the level of middle cerebral arterial pressure fell to 17.8 mm Hg ($\text{SD} \pm 3.7$), without significant change in systemic blood pressure, the ratio of cerebral arterial to systemic pressure then being 16.8% ($\text{SD} \pm 4.7$). Occlusion in hypercapnia produced an even lower figure for middle cerebral arterial pressure, the mean in the 10 animals being 13.7 mm Hg ($\text{SD} \pm 3.9$), again without significant change in systemic blood pressure (Table 1). Middle

TABLE 1

CEREBRAL ARTERIAL PRESSURE IN MIDDLE CEREBRAL OCCLUSION (MM HG): NORMOCAPNIC AND HYPERCAPNIC

Exp. no.	Normocapnic						Hypercapnic					
	Pre-occlusion			Occlusion			Pre-occlusion			Occlusion		
	(SBP)	(MCP)	(%)	(SBP)	(MCP)	(%)	(SBP)	(MCP)	(%)	(SBP)	(MCP)	(%)
1	86	80	93	98	22	22	100	74	74	109	15	14
2	100	78	78	110	12	11	112	72	64.3	102	8	7
3	135	85	63	141	12	9	156	88	66	153	9	6
4	110	102	93	102	22	21	102	83	81	102	9	9
5	134	82	61	130	16	12	154	84	55	154	18	12
6	88	82	93	92	17	18	100	77	77	100	16	16
7	106	88	83	95	21	22	115	90	78	120	18	15
8	104	85	82	100	19	19	118	87	74	120	15	13
9	110	82	75	105	20	19	120	90	75	125	17	14
10	114	89	78	110	17	15	115	88	76	110	12	11
Mean	107.9	85.3	79.9	108.3	17.8	16.8	119.2	83.3	72.0	121.3	13.7	11.7
SD	±14.5	±6.8	±11.6	±15.7	±3.7	±4.7	±20.2	±6.7	±7.9	±18.8	±3.9	±3.4
P values	◆ N.S. ◆			◆ N.S. ◆			◆ N.S. ◆			◆ N.S. ◆		
	◆			◆			◆			◆		
				<0.01			<0.01			<0.001		

cerebral pressure then constituted 11.7% of systemic pressure (SD ± 3.4). The cerebral arterial pressure after occlusion was significantly lower, therefore, in hypercapnic circumstances, both in absolute terms and as a percentage of systemic blood pressure (*P* < 0.001).

In normocapnia, the resting venous pressure in the middle cerebral veins was found to be 193.6 mm H₂O (SD ± 32.4). Raising the CO₂ tension greatly increased the cerebral venous pressure (mean value, 318.8 mm H₂O, SD ± 42.9). With middle cerebral occlusion, the venous pressure remained notably

higher in the hypercapnic animals; thus in hypercapnia the venous pressure was 183 mm H₂O (SD ± 27.2), while in the normocapnic animals it was 130 mm H₂O (SD ± 30), a difference significant at the *P* < 0.001 level. Expressed as a percentage of the resting venous pressure level, however, the venous pressure within the hypercapnic middle cerebral bed after occlusion of the middle cerebral artery was significantly lower (58.1%, SD ± 4.92) than the normocapnic (67.0%, SD ± 6.3, *P* < 0.01) (Table 2).

It is interesting that, though the fall in the

TABLE 2

CORTICAL VENOUS PRESSURE IMMEDIATELY AND 30 SECONDS AFTER MCA OCCLUSION: NORMOCAPNIA AND HYPERCAPNIA

Expt. no.	Control mmH ₂ O values		Immediate occlusion values				Occlusion and 30 seconds			
	N/Cap. mmH ₂ O	H/Cap. mmH ₂ O	N/Cap.		H/Cap.		N/Cap.		H/Cap.	
			mmH ₂ O	% control	mmH ₂ O	% control	mmH ₂ O	% control	mmH ₂ O	% control
1	196	366	131	66.8	197	53.7	134	210	210	57.3
2	181	313	114	63.0	165	52.7	129	71.3	127	54.6
3	199	381	112	56.3	204	53.5	118	59.3	193	50.7
4	264	350	208	78.8	230	65.7	212	80.3	226	64.6
5	140	302	105	72.8	182	60.1	116	83.1	194	64.3
6	171	244	119	69.7	160	65.6	129	75.3	157	64.2
7	204	276	126	61.8	143	51.8	107	52.9	145	52.5
8	193	365	122	63.4	213	58.4	134	69.4	206	56.4
9	174	285	117	67.0	172	60.3	124	71.2	174	61.0
10	214	286	151	70.4	164	57.4	163	76.2	172	60.2
Mean	193.6	318.8	130	67.0	183	58.1	136.6	70.7	184	58.5
SD	±32.39	±42.91	±30.0	±6.34	±27.2	±4.92	±30.4	±9.13	±25.3	±5.05
P values	◆ <0.001 ◆		◆ <0.001 ◆		◆ <0.05 ◆		◆ <0.001 ◆		◆ N.S. ◆	

hypercapnic venous pressure produced by occlusion was significantly greater, the hypercapnic venous pressure still remained higher than the normocapnic. When this is compared with the much lower arterial perfusion pressure, it becomes clear that the driving pressure for the forward movement of blood in the occluded vascular bed must be appreciably lower in circumstances of hypercapnia, as will be discussed subsequently.

After middle cerebral occlusion in the baboon, as in the rhesus monkey (Symon, 1967), there was little evidence of recovery of arterial blood pressure over the period of 30 seconds used as a test occlusion. However, in the normocapnic venous pressure, there was perceptible elevation of venous pressure within 30 seconds. This took the form of a gradual rise, presumably from the arrival of blood in the occluded bed from collateral vessels. Thus, at 30 seconds, the percentage of the resting level had increased from 67 at the time of occlusion to 70.7 (SD $\pm$ 9.1), a difference significant at the $P < 0.01$ level. In the hypercapnic occlusions, however, such a rise in pressure did not occur, venous pressure remaining, as arterial pressure, virtually unchanged over the

period of 30 second occlusion. Thus, at the end of 30 seconds in the 10 animals, the mean middle cerebral venous pressure was some 58.5% of resting pressure (SD $\pm$ 5.1), not significantly different from the level at the time of occlusion of 58.1% ($P > 0.05$) (Table 2).

ABOLITION OF REACTIVE HYPERAEMIA BY HYPERCAPNIA After the release of temporary middle cerebral occlusion, while the arterial record commonly showed diminution in pulse pressure and slow recovery of mean arterial pressure, due to the presence of post-traumatic arterial spasm, the venous tracing from the normocapnic vascular bed showed a great overswing, both in venous pressure and in venous pulsation over a period of three to four minutes, corresponding to a phase of reactive hyperaemia. The extent of this hyperaemia may be assessed by comparing arterial and venous pulse heights (Symon, 1969), the transmission of pulse in the vascular bed being then regarded as an index of the state of the regional peripheral resistance. Data pertaining to pre- and post-occlusion pressure and pulse levels are contained in Table 3. It will be seen

TABLE 3

MEAN ARTERIAL AND VENOUS PRESSURE, PULSE PRESSURE AND 'PULSE INDEX' BEFORE AND AFTER MIDDLE CEREBRAL OCCLUSION: NORMOCAPNIA AND HYPERCAPNIA

Expt. no.	Pial arterial pressure (mm Hg)				Pial venous pressure (mm Hg)					
	Mean pressure		Pulse pressure		Mean pressure		Pulse pressure		Pulse index	
	Before	After	Before	After	Before	After	Before	After	Before	After
A. Normocapnia										
1	80	64	17	10	204	287	21	47	1.7	4.7
2	72	80	29	25	233	335	48	40	1.7	5.6
3	85	50	16	7	170	234	11	19	0.7	2.7
4	102	66	22	14	264	336	28	40	1.3	2.9
5	82	36	11	11	150	235	5	15	0.5	1.4
6	82	60	4	3	128	243	4	14	1.0	4.7
7	88	74	13	9	154	294	12	24	0.9	2.7
8	85	65	12	8	185	295	15	55	1.3	6.9
9	82	70	15	10	178	310	21	60	1.4	6.0
10	89	75	17	12	204	325	28	84	1.7	7.0
Mean	85.3	65.0	15.6	10.9	187	289	19.3	49.8	1.2	4.5
SD	±6.8	±10.7	±6.7	±5.8	±40.7	±39.7	±13.1	±38.9	±0.4	±1.9
P values	<0.001		<0.001		<0.001		<0.01		<0.001	
B. Hypercapnia										
1	74	40	8	8	366	300	79	67	9.9	8.4
2	72	70	16	12	384	330	84	74	5.3	6.2
3	88	53	20	16	381	352	92	83	4.6	5.2
4	83	46	14	10	350	396	41	50	2.9	5.0
5	84	50	18	6	392	315	81	54	4.5	9.0
6	77	60	3	2	250	208	28	20	9.3	10.0
7	90	52	8	5	248	282	22	25	2.7	5.0
8	87	80	14	10	325	300	64	60	4.8	6.0
9	90	64	12	12	318	335	58	62	4.9	5.2
10	88	48	10	8	336	325	70	60	7.0	7.5
Mean	83.3	56.3	12.3	8.9	335	314	61.7	55.5	5.6	6.7
SD	±6.7	±12.3	±5.1	±4.0	±51.7	±49.0	±24.2	±19.8	±2.4	±1.8
P values	<0.001		<0.01		<0.01		<0.01		<0.01	

that, although in normocapnia the pial arterial pressure declined from a mean value of 85.3 mm Hg ($SD \pm 6.8$) to a value of 65.0 mm Hg ($SD \pm 10.7$), the mean pial venous pressure of 187 mm H₂O ($SD \pm 40.7$) rose immediately on the release of occlusion to a value of 289 mm H₂O ($SD \pm 39.7$). At the same time, in spite of decrease in arterial pulse height from a mean value of 15.6 mm Hg before occlusion to a value of 10.9 mm Hg ($SD \pm 5.8$), the venous pulse height rose from a pre-occlusion level of 19.3 mm H₂O ($SD \pm 13.1$) to a value immediately on release of 49.8 mm H₂O ($SD \pm 38.9$). The 'pulse index'—that is, the venous pulse height in mm H₂O divided by arterial pulse height in mm Hg—gave a value of 1.17 ($SD \pm 0.4$) before occlusion, and a value of 4.5 ($SD \pm 1.9$) after occlusion. In the hypercapnic occlusions,

although the pattern of arterial response, reduction in mean pressure and in pulse pressure after the release of occlusion was not dissimilar from the normocapnic, the mean venous pressure of 335 mm H₂O ($SD \pm 5.17$) before occlusion showed no hyperaemic rise as in the normocapnic, the post-occlusion level being 314 mm H₂O ($SD \pm 49.0$). Indeed, this is a fall significant at the $P < 0.01$ level. Venous pulse likewise fell, from the pre-occlusion level of 61.7 mm H₂O ($SD \pm 24.2$) to a post-release level of 55.5 mm H₂O ($SD \pm 19.8$), the level of this significance being $P < 0.01$. 'Pulse index', though significantly increased ($P < 0.01$), was much less increased than in normocapnic circumstances.

It is therefore clear that the haemodynamic manifestations of reactive hyperaemia after tempor-

FIG. 2. Experimental record to show the effects of hypercapnia on reactive hyperaemia. ETCO₂, end-tidal CO₂ concentration; MCVP, middle cerebral venous pressure (the elevation before the point of middle cerebral occlusion is due to direct pressure on the cortex in retraction and control levels are more properly taken before this); MCAP, middle cerebral arterial pressure; SBP, systemic blood pressure. The arterial pCO₂ was estimated at the points shown from systemic arterial blood. The length of the occlusion was 30 seconds, and the record has been broken during and following occlusion to avoid excessive width in the figure.

ary middle cerebral occlusion are reduced or abolished by hypercapnia. The findings are illustrated in the experimental record shown in Fig. 2.

DISCUSSION

The results reported above showed significant differences in intravascular pressures between normocapnic and hypercapnic animals. Certain adaptive phenomena during and after occlusion did not appear as effective when arterial $p\text{CO}_2$ was raised.

The level of arterial blood pressure in the pial network in the intact circulation showed no absolute change with the induction of hypercapnia, despite the fact that the systemic blood pressure was significantly elevated. In previous experiments (Symon, 1967), pial arterial pressure remained a fairly constant fraction of systemic arterial blood pressure within the normal physiological ranges of systemic blood pressure, except under the influence of raised arterial $p\text{CO}_2$. It is possible that vasodilatation of resistance vessels distal to the point of measurement in the pia mater could, in hypercapnia, siphon blood so rapidly from the pial network that, despite increased systemic blood pressure, intravascular pressure at this level remained constant. Alternatively, vasoconstriction of delivery vessels in the neck (internal carotid), under the influence of central sympathetic discharges produced by hypercapnia, might act as some form or fraction of an autoregulatory mechanism preventing elevated systemic blood pressure from being communicated to the pial level. The vessels in the neck are known to constrict under the influence of sympathetic stimulation (Mchedlishvili, 1968). Both these hypotheses indicate some independence of response of the proximal and distal cerebral vessels and imply that the regulatory responses of the CNS vasculature are not homogeneous, as has already been suggested in asphyxia (Mchedlishvili, Ormotsadze, Nikolaishvili, and Baramidze, 1967).

Cerebral arterial pressure distal to middle cerebral occlusion was appreciably lower in hypercapnia. This is in agreement with findings previously reported in dogs (Symon, 1963; Brawley *et al.*, 1967) with middle cerebral occlusion, and in baboons with partial occlusion from traumatic arterial spasm (Symon, 1967b). During middle cerebral occlusion, pressure measurements in the pia mater are from an area separate from that portion of the circulation known to be under vasomotor control (the neck vessels), and reduction in intravascular pressure can be explained only by change in vascular reactivity in areas distal to the occlusion. A possible explanation would be that the occluded bed, already dilated from the fall in intravascular pressure under

the influence of the Bayliss phenomenon (Bayliss, 1902), is further dilated by raised CO_2 tension, and, with inflow limited to collateral vessels, increased capacity in the bed produces a fall in intravascular pressure reflected back to the arterial point of measurement. Alternatively, however, the elevated arterial $p\text{CO}_2$ may produce actual reduction of collateral inflow and hence reduce intravascular arterial pressure in the ischaemic zone. This might be due to vasodilatation in the normal brain to CO_2 exceeding dilatation in the already partially adapted ischaemic zone, with the result that flow from normal to abnormal areas is reduced—the basis of the intracerebral steal phenomenon suggested by Brawley *et al.* (1967).

Venous pressure in hemispheric veins was found significantly higher at elevated arterial $p\text{CO}_2$ levels with the circulation intact, and evidence of vasodilatation was present in the increased ratio of venous to arterial pulse heights (Symon, 1969). The lack of increase in occluded venous pressure in the 30 seconds after occlusion in hypercapnia, contrasting with the recovery evident in normocapnia, and the absence of reactive hyperaemia after release of occlusion in hypercapnia, admits of two possible explanations. It might be that raised arterial $p\text{CO}_2$ so dilated collateral channels that significant ischaemia was not produced in the zone distal to middle cerebral occlusion; there would then be no stimulus to collateral vasodilatation and therefore no modification of venous pressure over the 30 seconds after occlusion, and no accumulation of metabolites to invoke post-ischaemic hyperaemia. Regional studies of $p\text{O}_2$, $p\text{CO}_2$, and pH, however, during and after occlusion show that significant ischaemia does indeed occur in the hypercapnic animal after middle cerebral occlusion, and abnormality of venous effluent gas tensions persists into the post-occlusive phase in the hypercapnic very much longer in the absence of reactive hyperaemia (Symon, 1968). Further, although absolute levels of venous pressure remained higher in hypercapnia, which might suggest relatively less ischaemia, there was a significantly greater fall from the preceding level in hypercapnia, indicating not less, but rather greater, disturbance in circulatory dynamics under conditions of raised arterial $p\text{CO}_2$. The alternative explanation which therefore appears more likely, again assumes a finite adaptive capacity, or vasodilator reactivity, within the cerebral circulation. Raised arterial $p\text{CO}_2$ more potently evokes dilatation than change in intravascular pressure. Both, however, compete for the same reactive capacity. Thus, when an area already hypercapnic becomes ischaemic, the adaptive processes, both within the ischaemic zone and in the collateral circulation adjoining it, already partially

evoked by the primary stimulus, are incapable of the same extent of response to modify the evoked ischaemia as in normocapnia. The effect of hypercapnia is therefore detrimental to the ischaemic zone. The same mechanism seems likely where hypercapnia succeeds ischaemia, as in the clinical situation where hypercapnia is used as an adjunct to stroke therapy or in other forms of vascular insufficiency in neurological practice. It would seem that, in the circumstances of acute occlusion at least, induced hypercapnia is more likely to be harmful than of help.

The raised venous pressure noted in hypercapnic ischaemic zones is associated with pial arterial pressures considerably lower than in normocapnia. As a result, circumstances are peculiarly adverse to continued forward circulation through the capillaries of an ischaemic zone. The calculation shown in Table 4 indicates that the pressure differential available in the ischaemic zone for forward flow of blood from artery to vein under hypercapnic conditions, is extremely small. The source of the high ischaemic zone venous pressure is clearly communication with surrounding cerebral venous beds where the high non-ischaemic venous pressure of hypercapnia remains.

TABLE 4
CALCULATION OF 'DRIVING PRESSURE' IN
NORMOCAPNIC AND HYPERCAPNIC OCCLUSIONS

Exp no.	Occlusion pressures (mm Hg)			
	Normocapnia		Hypercapnia	
	Arterial	Venous	Arterial	Venous
1	22	9.6	15	14.5
2	12	8.4	8	12.1
3	12	8.2	9	15.0
4	22	15.3	9	17.0
5	16	7.7	18	13.4
6	17	8.8	16	11.8
7	21	9.3	18	10.5
8	19	9.0	15	15.7
9	20	8.6	17	12.6
10	17	11.1	12	12.1
Mean	17.8	9.6	13.7	13.4
SD	±3.7	±2.2	±3.9	±2.0

The pathophysiological basis for reduction of ischaemic zone perfusion under the influence of raised arterial $p\text{CO}_2$ (the 'intracerebral steal' phenomenon) is therefore shown to be: (1) reduced ischaemic zone arterial pressure; (2) raised ischaemic zone venous pressure with reduced arteriovenous pressure difference; (3) failure of the adaptive response of the collateral circulation, which, already dilated by the primary stimulus either ischaemic or hypercapnic, finds the normal cerebral vasculature

surrounding the ischaemic area less able to provide the differential head of pressure necessary to secure influx of collateral blood into the ischaemic zone itself.

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