Effect of supratentorial space-occupying lesions on regional intracranial pressure and local cerebral blood flow: an experimental study in baboons¹

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SYNOPSIS Cortical blood flow and epidural intracranial pressure have been measured in the two supratentorial compartments of the intracranial space in experimental baboons during the acute expansion of a parieto-occipital epidural balloon. Differential pressures between the two halves of the supratentorial space have been found, and these have been associated with evidence that flow has fallen more quickly in the hemisphere most compressed. The evidence points to a more rapid exhaustion of the autoregulatory capacity in the hemisphere subjected to greater compression, a fall in perfusion pressure to below critical autoregulatory levels occurring slightly before that in the opposite hemisphere, and the establishment of a differential flow pattern for a short time during a critical phase of compression. The displacements induced by inflation of the parieto-occipital balloon have been described.

The relationship between the failure of function of nervous tissue and the development of a compressing lesion is of primary interest to the neurosurgeon. Investigation of the pathophysiological processes involved in this relationship has been stimulated increasingly in recent years by development of techniques for the measurement of cerebral blood flow in a regional (Lassen *et al.*, 1963; Høedt-Rasmussen *et al.*, 1966; Høedt-Rasmussen, 1967) or a focal manner (Aukland *et al.*, 1964; Aukland, 1965), and by the accumulation of data on intracranial pressure obtained either in the clinic using a central cerebrospinal fluid (CSF) space measurement (Lundberg, 1960) or using transducers inserted into the subdural (Hulme and Cooper, 1966; Tindall *et al.*, 1972) or epidural space (Jacobson and Rothballe, 1967; Dorsch *et al.*, 1971; Sundbärg and Nornes, 1972; Symon *et al.*, 1972). It has be-

come clear that the type of neurological dysfunction resulting from a space-occupying lesion is critically dependent not only on the site of the lesion but on the rapidity of its growth. To some extent this is a reflection of the rate at which the lesion crosses the flat or accommodating part of the pressure/volume curve (Langfitt, 1969), but it is only by the accumulation of data acquired by modern methods that a meaningful interpretation of the relationships between circulatory depression secondary to pressure, neurological dysfunction secondary to circulatory impairment, and the origin of tissue shifts within the brain can begin.

The present work was an attempt to relate pressure and flow events occurring in response to rapidly inflated epidural expanding lesions in primates.

METHODS

Six baboons (*Papio cynocephalus* or *Papio nubius*) of either sex, in the weight range 10-15 kg, were used in these experiments. After tranquillization with phencyclidine, they were anaesthetized with a sleep dose of thiopentone, followed by intravenous α

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chloralose (60 mg/kg), intubated, and respiration maintained with a Starling pump after immobilization with gallamine triethiodide (1 mg/kg repeated as necessary). End-tidal CO_2 was continuously monitored with a Beckman gas analyser (model LB1) by sampling from the endotracheal tube. Blood pressure was recorded by a P23G Statham arterial gauge from a femoro-aortic catheter, central venous pressure recorded by a P23V Statham gauge from the superior vena cava via one femoral vein, and a second femoro-aortic catheter introduced for intermittent sampling of arterial blood for analysis in the micro-Astrup apparatus for pH, pCO_2 , and pO_2 . The respirator volume was adjusted to maintain a normal arterial pCO_2 between 35 and 45 mmHg, and pure oxygen used as the inhalational gas. The animals were then positioned in a Narishige stereotactic apparatus (model SN3) and twist drill holes in the skull made to enable placement of fine platinum electrodes (Symon *et al.*, 1973) in putamen and white matter on both sides, and in frontal and parietal cortex bilaterally. The reference electrode for the hydrogen system was placed subcutaneously in the interscapular region. Four extradural pressure gauges (Dorsch *et al.*, 1971) were placed through 12 mm trephine holes in both frontal and parietal zones, and a further 12 mm trephine hole made in the postparieto-occipital zone on the right side. The transducers were held in place with acrylic, and an extradural balloon was introduced to lie in the parieto-occipital zone near the occipital pole of the right hemisphere through the parieto-occipital trephine hole, the dura mater having been stripped. This defect was then closed with acrylic.

The transducers used were similar to those previously used (Corne *et al.*, 1968) with two major modifications. The construction of the present gauges was entirely coplanar, the tip of the sensing arm being on the same plane as the outer and sensitive part of the body, thus eliminating any influence of dural tension (Dorsch and Symon, 1972; Majors *et al.*, 1972). In these gauges also, metal foil rather than semiconductor gauges were used, so that full bridge configuration within the gauge could be employed, with resulting improvement in sensitivity and drift. A spinal needle was introduced into the cisterna magna and connected with a Statham P23 BB pressure transducer for recording of CSF pressure. After a few minutes had been allowed for pressures to stabilize, the extradural pressures were calibrated against cisternal pressure as an extra check, although extradural pressure could be obtained by the substitution of current deflection in a previously made *in vitro* calibration graph. Extradural pressure calibrated in this way correlated well with cisternal pressure measured at the same time

FIG. 1. A comparison of cisternal (x) and extradural (y) pressures in a baboon. Extradural pressures in this graph are predicted from the preliminary *in vitro* calibration of the transducer, and the 95% confidence limits are shown.

(Fig. 1), providing that accurate coplanar placement of the extradural transducer was ensured and excessive dural indentation avoided. As a check, therefore, intracranial pressure was in each case raised by between 30 and 50 mmHg by the inhalation of CO_2 , and deflection of extradural recordings plotted against simultaneous cisternal pressure measurements during both the rising and falling phases of intracranial pressure. A graph of deflection of extradural pressure against intracranial pressure was then made for use during the latter part of the experiment (Fig. 2). This CO_2 calibration was combined with control and test episodes of hydrogen inhalation, 7%–10% hydrogen being introduced into the endotracheal tube for three to four minutes per saturation (Pasztor *et al.*, 1973). Hydrogen clearance was measured for the 10 minutes after the discontinuance of each hydrogen inhalation. Cisternal recording was maintained for as long as possible, but invariably failed in the course of the experiment with the prolapse of the cerebellar tonsils usually at an intracranial pressure exceeding 70 mmHg.

The balloon inflated at a constant rate of 0.2 ml/min by a Palmer slow infusion pump, which ran continuously from the start of inflation of the balloon except during episodes of hydrogen clearance, when, in order to avoid irregularities in the intracranial pressure and to minimize systemic blood pressure reactions, the inflation of the balloon was

FIG. 2. In vivo calibration of the output of the extradural transducer (expressed as millimetres of pen deflection on a Beckman type R recorder) plotted against cisternal pressure in mmHg. A high degree of correlation is evident ($P < 0.001$).

maintained intermittently to keep the raised level of intracranial pressure at a constant level during hydrogen clearance. Escape of fluid from the balloon was not possible in the course of the experiment.

The outputs of the intracranial pressure transducers and of the systemic blood pressure and CVP monitors were displayed on a Beckman type R polygraph, the outputs of the hydrogen electrodes being

recorded on a Rikadenki 4-channel slow recorder (model B4021), each recorder channel sampling two electrodes alternately. The pupillary reactions were recorded by direct examination in the course of a balloon inflation. When inflation of the balloon had been pursued to high levels and very slow clearance was being obtained from both hemispheres, the experiment was terminated in one of two ways. In the first, hyperaemia was induced by suddenly deflating the balloon, and the effect recorded by a further episode of hydrogen clearance (Symon *et al.*, 1973). The balloon was then reinflated with exactly the same volume and the animal killed. In the second, the balloon remained inflated and the animal was killed. Finally, in all experiments, the head of the animal was removed and fixed with the extradural balloon *in situ* after removal of transducers and electrodes, so that shifts induced by the extradural lesion and mass depression of the occipitoparietal cortex could be examined at leisure.

INTRACRANIAL PRESSURE MEASUREMENTS The data for intracranial pressure measurements, taken during the course of gradually increasing pressure induced by inflation of the extradural balloon, are shown in Table 1 for the four transducers in the six experiments. For the purpose of analysis, four points during the evolution of the experiment have been chosen. The first of these was when the cisternal reference external transducer recorded a pressure of 10 mmHg. This was usually slightly into the experiment from baseline but constituted a handy point of

TABLE 1
INTRACRANIAL PRESSURE DATA*

ICP level		Experiments						Mean	SD	Hemisphere		P
		1	2	3	4	5	6			Mean	SD	
Cisternal pressure 10 mmHg	L anterior	9.0	10.0	5.0	8.5	6.0	8.0	7.75	1.89	8.83	2.14	> 0.05
	L posterior	9.5	13.0	6.5	10.0	9.0	6.0	9.00	2.55			
	R anterior	6.5	9.5	6.0	10.0	9.0	8.0	8.17	1.63			
	R posterior	16.0	11.0	5.0	12.0	19.0	11.5	12.42	4.78			
Left posterior extradural pressure 30 mmHg	L anterior	39.5	40.0	29.5	27.5	28.6	27.0	32.02	6.05	31.01	4.04	< 0.01
	L posterior	30.0	30.0	30.0	30.0	30.0	30.0	30.00	0.00			
	R anterior	37.5	48.0	28.0	39.0	30.0	32.5	35.83	7.31			
	R posterior	52.0	55.0	37.5	43.0	37.6	33.0	43.02	8.77			
Left posterior extradural pressure 70 mmHg	L anterior	65.0	79.7	67.5	75.0	57.0	70.0	69.03	7.92	69.52	5.14	< 0.001
	L posterior	70.0	70.0	70.0	70.0	70.0	70.0	70.00	0.00			
	R anterior	91.0	81.0	71.0	78.6	58.0	92.0	78.60	12.82			
	R posterior	91.0	96.0	77.5	88.0	82.7	95.0	88.37	7.20			
Peak level left posterior extradural pressure	L anterior	83.0	132.0	190.0	80.0	80.0	153.0	119.67	46.26	120.25	39.85	< 0.01
	L posterior	86.0	113.0	189.0	84.0	104.0	149.0	120.83	40.88			
	R anterior	104.0	127.0	197.0	100.0	86.0	192.0	134.33	48.46			
	R posterior	116.0	164.0	207.0	160.0	113.0	200.0	160.00				

* Extradural pressure in mmHg.

reference. It was thereafter unsatisfactory to use the cisternal reference, since this pressure recording invariably failed at some stage during the development of the experiment. The left posterior transducer, that is, the one furthest away from the balloon on the opposite side of the falx, was thereafter chosen as the reference. Another comparison was made when this reference transducer recorded a level of 30 mmHg, again at 70 mmHg, and finally when the intracranial pressures had reached their peak and blood flows were very low or absent.

Early in the development of the experiment, with the cisternal pressures recording 10 mmHg, there was no significant difference between the recordings from the four transducer sites considered individually. The right posterior transducer anterior to the area of the balloon insertion usually recorded slightly higher values than the rest, the mean being 12.42 mmHg compared with the other means of 9 mmHg for the left posterior, 7.75 mmHg for the left anterior and 8.17 for the right anterior, but these differences were not significant. The hemispherical mean pressures at basal level, 8.83 mmHg (SD ± 2.14) for the left hemisphere, and 10.30 mmHg (SD ± 3.89) for the right hemisphere, were also not significantly different.

By the time the left posterior or reference transducer had reached 30 mmHg, the difference between the right and left-sided transducer pressures had reached significant levels, the right-sided mean being 39.43 mmHg (SD ± 8.2) and the left-sided mean 31.01 mmHg (SD ± 4.0). The difference between the two was significant ($P < 0.01$). As the intracranial pressure continued to rise, reaching the left posterior reference of 70 mmHg, differences between the two sides increased. Thus, the mean left-sided extradural pressure of 69.52 mmHg (SD ± 5.1) and the mean right-sided pressure of 83.49 mmHg (SD ± 10.7) were significantly different at the $P < 0.001$ level. As pressures approached peak values and clearance levels declined, there remained significantly different pressure levels on the two sides: mean left-sided pressure of 120.25 mmHg (SD ± 39.9) comparing with mean right-sided pressure of 147.17 mmHg (SD ± 42.5), with $P < 0.01$. It is interesting that, though the right posterior transducer invariably recorded higher pressure than the others, the scatter of the data meant that a statistically significant gradient between this and the others could not be obtained. It did not prevent the clear demonstration, however, that the pressures in the supratentorial compartment on the side of the balloon became significantly higher than those on the opposite side of the falx.

In one experiment (P.F.B. 3), the position of the balloon was slightly different from the other five;

what was intended as a strictly parieto-occipital placement on the right side developed in the course of the experiment into a mainly right-sided placement, with some extension across the midline behind the sagittal sinus. The figures for this experiment, which are included in the general table, are of interest in that the differences between the right-sided transducers and the left-sided transducers are somewhat lower than in the other experiments.

EFFECTS OF EXTRADURAL EXPANDING LESION ON BLOOD FLOW The effect of the gradually expanding extradural lesion in the right parieto-occipital zone on blood flow in the two halves of the supratentorial compartment is summarized in Table 2. Although

TABLE 2
FLOW DATA

Experiment	ICP level (LPE-D transducer) (flow in ml/100 g/min)							
	10 mmHg		30 mmHg		70 mmHg		Peak	
	Left	Right	Left	Right	Left	Right	Left	Right
1	80.6	99.0	69.3	75.3	83.4	83.4	11.0	6.9
2	75.3	57.7	63.0	57.7	26.6	3.4	8.7	2.3
3	73.8	76.0	80.6	84.9	77.0	73.8	15.4	10.0
4	99.0	73.8	86.6	69.3	86.6	57.7	71.7	49.0
5	63.0	76.2	86.6	53.3	69.3	46.2	33.0	10.0
6	69.3	86.6	78.7	57.7	78.7	69.3	31.5	23.3
Mean	76.8	78.2	77.5	66.4	69.6	55.6	28.6	17.8
SD	12.4	13.8	9.5	12.3	22.3	28.7	23.5	17.3
P	>0.05		>0.05		<0.05		<0.05	

anterior and posterior cortical hydrogen electrodes were placed in both hemispheres, anterior placements only have been used in the comparison of the cortical blood flows in the current table, since the right posterior electrode failed in a sufficiently large number of instances to prevent meaningful analysis of the data. Deep electrode placements will be analysed in a later paper. Values for cortical blood flow were values from the fast component unless a monoexponential curve was obtained, when the mean blood flow gave values similar to that of the fast component (Pasztor *et al.*, 1973). The initial values in the two hemispheres were similar, a mean flow of 76.8 ml/100 g/min (SD ± 12.4) for the left hemisphere and 78.2 ml/100 g/min (SD ± 13.8) for the right hemisphere being obtained. At an intracranial pressure of 30 mmHg, although the hemispherical blood flow on the right had fallen to 66.4 ml/100 g/min (SD ± 12.3), this was neither signifi-

cantly different from the control value nor from the left hemispherical value of 77.5 ml/100 g/min (SD $\pm$ 9.5). By the time the intracranial pressure had reached 70 mmHg, blood flow in both hemispheres had shown a slight fall, the left to 69.6 ml/100 g/min (SD $\pm$ 22.3) and the right to 55.6 ml/100 g/min (SD $\pm$ 28.7). The difference between the left hemispherical blood flow at 70 mmHg and control was still not significant, but a significant difference at the 5% level had appeared between the right and left hemispheres, and the right hemisphere had now significantly lower blood flow than its own control values, again at the 5% level. At peak level of intracranial pressure, when the clearance on the right hemisphere had reached very low levels, an average mean blood flow on the right of 17.8 ml/100 g/min (SD $\pm$ 17.3) had been reached. Blood flow in the left hemisphere had by now also declined to a mean of 28.6 ml/100 g/min (SD $\pm$ 23.5), significantly different at the $P < 0.05$ level from the flow in the right. In both instances also, there was a highly significant difference ($P < 0.01$) between the peak blood flow in the two hemispheres and control levels on each side.

EFFECTS OF EXTRADURAL SPACE OCCUPATION ON PERFUSION PRESSURE Perfusion pressure was calculated as the difference between mean systemic blood

corresponded to 10 mmHg level from the cisternal pressure transducer and represents the same point as extradural pressure records at this level in Table 1. As intracranial pressure rose to 30 mmHg, measured from the left posterior transducer, perfusion pressure on the right side of the head fell to 97.3 mmHg (SD $\pm$ 21.3), while that on the left remained unchanged at 103.2 mmHg (SD $\pm$ 18.1). This was already a significant deviation from normal on the right side ($P < 0.05$) and there was a significant difference between the two hemispheres again at the 5% level. By the time the intracranial pressure at the left posterior transducer had risen to 70 mmHg, a wider gap in available perfusion pressure had appeared. On the right, perfusion pressure had fallen to 58.4 (SD $\pm$ 19.7) and that on the left had also fallen to 70.3 mmHg (SD $\pm$ 21.9). Differences between the two hemispheres were now significant at $P < 0.01$, and both were significantly different from the resting level ($P < 0.01$). As peak intracranial pressure was reached, perfusion pressure levels of 16 mmHg (SD $\pm$ 9.7) were obtained from the right hemisphere, and 37.2 mmHg (SD $\pm$ 12.2) for the left, the differences again remaining significant at the $P < 0.01$ level.

EVIDENCE OF INTRACRANIAL SHIFTS DURING PARIETO-OCCIPITAL BALLOON INFLATION The shift induced by the expanded balloon was checked in each instance by fixation of the head after the death of the animal, the balloon being inflated at the time. There were minor differences in the extent of intracranial shifts produced, largely dependent upon minor variations in the siting of the extradural lesion, but in only one of the experiments were these differences of any significance. This was in experiment P.F.B. 3, in which the balloon had crossed the sagittal sinus and produced a lesser extradural expansion in the left hemisphere. As a result of this, the midline shift induced in this experiment was slightly less than in the other experiments, but basic characteristics were otherwise the same.

Typical displacements are shown in Figs 3 to 5, taken from the same experiment (P.F.B. 1). The balloon, whose volume was between 6 and 8 ml fully inflated, induced great depression in the posterior parietal and occipital regions centred just in front of the lunate sulcus, not crossing the midline, clearly not obstructing the sagittal sinus, and producing a conspicuous herniation of the posterior part of the hippocampal gyrus and the associated temporal lobe through the posterior part of the tentorial hiatus (Fig. 4). In some experiments, a lesser contralateral herniation was also observable at this point. As shown in Fig. 5, in addition to the foraminal hernia, appreciable herniation of the posterior part of the cingulate gyrus beneath the falx

TABLE 3
PERFUSION PRESSURE DATA

Experiment	ICP level (LPE-D transducer) (perfusion pressure in mmHg)							
	10 mmHg		30 mmHg		70 mmHg		Peak	
	Left	Right	Left	Right	Left	Right	Left	Right
1	96	94	86	76	105	82	45	20
2	91	91	93	91	87	77.5	51	22
3	101	100	125	120	57	43	18	9
4	106	106	84	73	50	38	44	26
5	126	126	122	123	71	68	28	20
6	98	97	109	101	52	42	37	0
Mean	103.0	102.3	103.2	97.3	70.3	58.4	37.3	16.2
SD	12.33	12.69	18.06	21.32	21.94	19.68	12.25	9.72
P	> 0.05		< 0.05		< 0.01		< 0.01	

pressure and average supratentorial compartment pressure on each side, the mean of anterior and posterior extradural pressures being used to calculate each average supratentorial compartment pressure at any given time (Table 3). The initial perfusion pressure was similar on the two sides of the head, being 102.3 mmHg (SD $\pm$ 12.7) on the right, and 103 mmHg (SD $\pm$ 12.3) on the left. This basal level

FIG. 3 (left) *P.F.B. no. 1. The parieto-occipital depression produced over one hemisphere by the inflation of an extradural balloon (volume 8 ml).*

FIG. 4 (right) *P.F.B. no. 1. Downward depression of the right uncus, depression of the tentorial surface of the cerebellum, and herniation of both cerebellar tonsils induced by extradural balloon inflation.*

FIG. 5. *P.F.B. no. 1. Coronal sections of the hemispheres, cerebellum, and brain-stem in an animal killed with maximal inflation of an extradural balloon in the parieto-occipital zone. The brain was fixed in situ. The references in millimetres are to distances posterior (negative distance) and anterior (positive distances) to the external auditory meatus, the point of fixation in the stereotaxic apparatus.*

was evident, and the posterior part of the thalamus, diencephalon and upper brain-stem was conspicuously deviated across the midline. The whole ventricular system was flattened and displaced to the left. The cerebellar tonsils were bilaterally herniated downwards as shown in Fig. 4, and there was no evidence of particular laterality about the posterior fossa displacements. It is interesting that in all the animals, appreciable down-curving of the tentorium had taken place, with the development of a notably concave upper surface to the cerebellum, the vermis being retained as a sharp peak.

The distortions in Figs 3–5 represent the situation in the hemisphere at the time of peak recording of intracranial pressure and blood flow, when quite demonstrable and significant differences in the supratentorial compartment pressures were evident, when perfusion pressure in the two hemispheres was significantly different, and when there was significantly lower blood flow in the right hemisphere than in the left.

DISCUSSION

It is only in recent years with the development of the Xenon clearance technique (Lassen *et al.*, 1963; Høedt-Rasmussen *et al.*, 1966; Høedt-Rasmussen, 1967) and its use in man that the wide variations in regional cerebral blood flow from one area of brain to the next have been appreciated. A study of regional changes in the much smaller primate brain has been less easy to obtain in absolute terms, since the collimation of the Xenon clearance technique makes multiple regional recording difficult, and since the continuous recording methods of heat clearance are difficult to quantitate. The development of the hydrogen clearance technique by Aukland and his associates (Aukland *et al.*, 1964; Aukland, 1965), and its modification in our laboratory (Pasztor *et al.*, 1973; Symon *et al.*, 1973) have enabled us to record blood flow in discrete areas of the primate hemisphere and to compare supratentorial cortical flow between one hemisphere and the other without any possibility of contamination either from extracerebral sources or from grey matter of the opposite side or deep grey matter in the same hemisphere.

While developments in blood flow methodology have reached the stage of fairly widespread acceptance, measurement of intracranial pressures in the various portions of the intracranial

space has had less wide documentation and debate continues as to how far the various techniques of measurements may yield comparable results. Several groups have presented data (Dorsch and Symon, 1972; Majors *et al.*, 1972; Sundbärg and Nornes, 1972; Tindall *et al.*, 1972) to show that in conditions of low and moderate intracranial pressure, extradural pressure and central CSF space pressure (cisternal or ventricular) yield identical recordings, but that in circumstances of high intracranial pressure extradural recording with a coplanar device will yield consistently higher pressures, indicating that it is at this stage measuring a component of actual tissue pressure transmitted from the brain held under tension by the elastic pia mater itself. To discuss the potential of coplanar measurements for dynamic deformation analysis in the brain would be outside the scope of this paper, but has been initiated in the work of Schettini *et al.* (1971), who were the first to point out the extreme importance of coplanarity in such pressure recordings. The extradural transducer made and used in our laboratory enables recordings to be made with ease at four points in the baboon skull; further miniaturization of the transducer might enable more recordings to be made, but in the present study a four-point placement was sufficient to demonstrate beyond equivocation the development of differential pressures between the supratentorial compartments with a posterior parieto-occipital extradural expanding lesion.

The critical rate of lesion expansion, 0.2 ml per minute, was chosen somewhat arbitrarily to produce the complete evolution of critically raised pressure within a comfortably measurable experimental time, but falls well within the limits demonstrated by Nakatani and Ommaya (1972) who showed that the development of the typical Cushing response was dependent upon the rate of expansion of an epidural balloon above a critical rate which they found to be 0.02 ml per minute in the rhesus monkey. More gradual expansion led to prolongation of the experiment, but if expansion rates were cut down to below 0.02 ml. per minute, Nakatani and Ommaya demonstrated that differential pressures between supratentorial and infratentorial compartments did not develop, and the vasopressor response could not be elicited. Our present work demonstrates

that in the non-compressed hemisphere there is no evidence of dissociation between anterior and posterior pressures, but (although the data are not statistically conclusive) they do suggest that the differential pressure develops in the supratentorial compartment between the posterior and anterior portions of the compartment as the pressure increases. It seems probable, therefore, that the transmission of pressure is from the immediate area of the balloon through the normal hemisphere, then beneath the falx, and diffusely into the opposite hemisphere. Our data suggest that differential pressures are most easily obtained with rapid rates of expansion, again agreeing with the observations of Nakatani and Ommaya (1973). The differential pressures demonstrated in our experiments were associated with shifts which would be regarded as typical of a rapidly expanding supratentorial mass in man: subfalcine herniation, ipsilateral uncal herniation, and, to a lesser extent, contralateral uncal herniation, and bilateral foraminal impaction of the tonsils. The fact that these shifts were in our animals invariably associated with Cushing responses, and with dilatation of the ipsilateral pupil initially, leads us strongly to suppose that the origin of the Cushing response is deformation of the upper brain-stem. Nakatani and Ommaya's observation that very slow rates of expansion of an extradural balloon led to the disappearance both of the Cushing response and of differential pressures between supratentorial and infratentorial compartment is, we feel, strong evidence in this regard also.

A certain volume of work has been presented in recent years (Johnston and Rowan, 1974) which has failed to demonstrate differential pressures between the supratentorial compartments with experimental balloon inflation, and suggesting that the Cushing response has its origin in some central neurogenic mechanism as yet undetermined. It seems, however, beyond doubt that the recording of central CSF space pressure made in such experiments is invariably that of mean intracranial pressure, since, as long as the CSF spaces are in continuity one with the other, the pressures will be instantaneously equalized by fluid transmission. It is possible also that the profound collapse of the ventricular systems, as illustrated for example in Fig. 5, means that at such high levels of intracranial pressure satisfac-

tory pressure recording from a fluid transmission system will never be practicable. In this respect, our experiences support this conclusion; the cisternal pressure invariably failed when tonsillar herniation began. It is also probable that the methodology employed in the work of Johnston *et al.* (1972), with regard to blood flow analysis, is unsuitable for the determination of differential blood flow. The use of even accurately collimated Xenon probes cannot exclude contamination from the opposite hemisphere and even from the base of the skull, and, since the differential flows in our own series were difficult to demonstrate at the 5% level, we suggest that the additional scatter introduced into the data by such contamination when the Xenon method was employed would make statistically significant differences very difficult to find.

The effect of the expansion of the balloon immediately beneath a Xenon collimator, as in the Glasgow studies, must also cause concern about changes in count rate. If, for example, a posteriorly placed collimator is trained on the post-parietal region and the balloon is subsequently inflated beneath this collimator to a volume of 10–14 ml saline (Johnston *et al.* 1973), the count rate of this detector will decline substantially since the tissue to which it is mainly reactive has been displaced outside the area of maximum sensitivity of the detector. The reliability and significance of flows estimated using this detector will then be questionable compared with those obtained from a comparably placed contralateral probe.

The finding in the present series of experiments that blood flow did not deviate significantly from normal in either hemisphere until an intracranial pressure of over 70 mmHg had been reached is in keeping with our previous demonstration that the autoregulatory characteristics of the baboon cerebral circulation, as assessed by hydrogen clearance, will maintain normal flow to a level of intracranial pressure of this magnitude assuming normal blood pressure in the animal at the time. Indeed, a plot of data from both cortical and deep flow in the present series of experiments showed a curve of autoregulation similar to that obtained in elevation in intracranial pressure by cisternal infusion. In particular, there was no evidence of hyperaemia either in superficial or deep tissues preceding the fall of

flow induced by a rising perfusion pressure (Symon *et al.*, 1973). In the data from the experiments as a whole it was impossible to separate the curve of autoregulation for the earlier compressed hemisphere from that of the opposite side, but, as Tables 2 and 3 show, the appearance of significant differences in the flow data occurred at the 70 mmHg reference level in the left posterior transducer. At this time, the lesser compressed hemisphere retained a cortical blood flow of 69.6 ml/100 g/min, which was not significantly different from control, and perfusion pressure in this hemisphere was 70.3 mmHg, within the autoregulatory range of the circulation. On the right side, however, the hemisphere beneath the balloon had a perfusion pressure which at 58.4 mmHg is below the level at which one would expect autoregulation to extend in this preparation, and indeed blood flow in the cortex of this hemisphere had fallen to 55.6 ml/100g/min, significantly different from control values of that hemisphere at the 5% level, and from the blood flow of the opposite hemisphere at the same level of significance. From this point onwards in the experiment, both hemispheres had perfusion pressures of a level consistent with a passive pressure relationship, so that the continuing difference in flow between the two hemispheres is explicable by the higher intracranial pressure induced in the supratentorial compartment on the side of the balloon, and the correspondingly reduced perfusion pressure in that hemisphere as compared with its fellow. The supratentorial compartmental pressures at the rate of balloon expansion chosen differed by levels sufficiently great to be easily determined by an extradural pressure recording device; even so, these differences were hardly sufficient to exhaust the autoregulatory capacity of the more compressed hemisphere very much before that of the less compressed. The technique of episodic blood flow recording, therefore, may render it quite difficult to pick up depression of flow in one hemisphere significantly before the other hemisphere follows suit, and it is therefore not possible to separate curves of autoregulation for the two hemispheres. It seems that failure of autoregulation in our preparation took place in one hemisphere shortly before the 70 mmHg intracranial pressure was reached at the reference transducer, and in the other hemisphere shortly

after this point. Perhaps a more frequent recording of flow by the technique of two minute clearance might resolve this close flow matching.

It is also difficult to resolve events at or about the critical level of failure of autoregulation, in relation to the development of intracranial shifts and of medullary compression. In our own experiments, about the time when intracranial shifts were occurring, as deduced from failure of reaction and beginning of dilatation of the ipsilateral pupil, autoregulation in the ipsilateral hemisphere was beginning to fail, and short-lived Cushing responses were making their presence evident on the systemic blood pressure trace. We suggest that the transmission of the pressure wave to the opposite hemisphere thereafter resulted in a fall in contralateral hemispheric flow, with diencephalic compression and the fully developed Cushing response. Death from mid-brain compression and medullary ischaemia would follow shortly thereafter.

Experimental evidence at this time suggests that a more gradual rate of expansion of supratentorial balloons does not result in the development of such readily demonstrable differential pressures. The explanation probably lies in the astonishing viscoelastic properties of the brain, which enable it to change shape while preserving function within limits; it seems likely that this represents a further adaptive factor in the pressure flow relationship. One would suppose therefore that, with a slower rate of expansion, the failure of autoregulation and critical displacements in the brain-stem would be delayed until a much larger lesion had been accommodated. At a critical stage, however, a slight further incremental expansion might result in the rapid development of differential pressures, excessive shifts, and sudden clinical deterioration. Nevertheless, it has been shown by Dorsch and Symon (1972) and by O'Brien and Waltz (1972) that differential pressures may be recorded even with the relatively slow expansion produced by infarction of one hemisphere. The degree to which the plastic properties of the brain are capable of evening out intra-tissue pressure gradients is a subject which deserves study and which will clearly stimulate methodological advance in the near future.

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