Raised intracranial pressure and cerebral blood flow

4. Intracranial pressure gradients and regional cerebral blood flow

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SYNOPSIS Intracranial pressure was raised by expansion of a supratentorial subdural balloon in anaesthetized baboons. Pressures were measured at several sites, both supratentorial and infratentorial, and cerebral blood flow was measured in each cerebral hemisphere separately. Pressures recorded from the right and left lateral ventricles corresponded closely throughout. Highly significant correlations were also obtained between the pressures in the right and left subdural spaces and the mean intraventricular pressure. There was, thus, no evidence of intracompartmental pressure gradients within the supratentorial space. Pressure gradients did, however, develop between the supratentorial and infratentorial compartments in the majority of experiments, although the level of supratentorial pressure at which this occurred, varied. Despite the presence of a large mass lesion over the right cerebral hemisphere, no significant differences developed between levels of cerebral blood flow in the two hemispheres, although flow in the right hemisphere remained consistently slightly lower than that in the left after the balloon was inserted.

In previous studies cerebral blood flow was examined in different types of experimental intracranial hypertension and the pattern of blood flow changes shown to vary with the method of increasing intracranial pressure (Johnston *et al.*, 1972, 1973). Attempts to relate blood flow to either intracranial pressure or cerebral perfusion pressure depend, however, on the assumption that both pressure and blood flow are relatively constant, at least within the major intracranial compartments. Doubt has recently been cast on this assumption by experimental studies showing substantial intracompartmental pressure gradients in states of raised intracranial pressure (Weinstein *et al.*, 1968; Brock *et al.*, 1972). It has been suggested that significant regional variations in blood flow may result from such gradients.

Whether or not significant intracompartmental pressure gradients exist in states of raised intracranial pressure is clearly of considerable importance when attempting to establish quantitative correlations between raised intracranial pressure and its various secondary effects such as reduction of cerebral blood flow. No less is it of

importance to the clinician who may be basing decisions of patient management on measurement of intracranial pressure from a single point in the neuraxis. The aim of the present study was to examine the profile of pressure changes occurring in the supratentorial and infratentorial compartments during progressive expansion of a supratentorial subdural balloon. The observed pressure changes were correlated with changes in cerebral blood flow in each of the cerebral hemispheres.

METHODS

Eight baboons, weighing between 8.5 and 15 kg, were used. Anaesthesia was induced with phencyclidine hydrochloride (10 mg intramuscularly) and thiopentone sodium (60 mg intramuscularly) and maintained with phencyclidine hydrochloride and a nitrous oxide/oxygen mixture. The animals were paralysed with suxamethonium chloride and ventilation controlled using a Starling pump delivering a tidal volume which was adjusted according to arterial blood gas and end tidal CO₂ levels. The animal's temperature was maintained using a heating lamp and a continuous intravenous infusion of 0.9% saline was given.

Intracranial pressure was raised by expansion of a small balloon placed subdurally over the parietal region of the right cerebral hemisphere, through a burr hole. Fluid was added to the balloon intermittently, at approximately 30 minute intervals, sufficient to raise the intracranial pressure by 10–20 mmHg on each occasion. Measurements were continued until blood flow ceased or fell to negligible levels.

The following parameters were measured.

INTRACRANIAL PRESSURES 1. *Ventricular fluid pressures (VFP)* were measured from both right (R) and left (L) lateral ventricles by means of polyethylene cannulae placed in the frontal horns of each ventricle via twist drill holes on the coronal suture, 1 cm lateral to the bregma.

2. *Subdural pressures (SDP)* were measured from the subdural space over the lateral aspect of both right (R) and left (L) cerebral hemispheres, using fluid-filled polyethylene catheters inserted through laterally placed burr holes. The dural incisions were made just large enough to admit the catheters and were closed, with a purse-string suture, around the catheters.

3. *Cisterna magna pressure (CMP)* was measured using a polyethylene cannula inserted into the cisterna magna by puncture of the atlanto-occipital membrane under direct vision.

All pressures were measured using strain gauge transducers. The cranial defects were sealed with dental cement.

CEREBRAL BLOOD FLOW (CBF) Simultaneous measurements of blood flow in each of the cerebral hemispheres were carried out, at intervals, using the ^{133}Xe clearance method. The proximal stumps of both (R) and (L) lingual arteries were cannulated after ligation of both external carotid arteries just beyond the carotid bifurcation. Simultaneous slug injections of ^{133}Xe were given and the rate of

clearance of gamma activity from each hemisphere monitored using two, $\frac{1}{2}$ in. sodium iodide crystal detectors placed, in parallel, in the occipital area and collimated to define each cerebral hemisphere with no more than 5% 'cross-talk'. Cerebral blood flow was calculated from the initial slope and from the height to area ratio of the clearance curves.

OTHER PARAMETERS 1. *Arterial blood pressure* was monitored continuously from a polyethylene catheter inserted into the abdominal aorta via the (L) femoral artery.

2. *Arterial $p\text{O}_2$, $p\text{CO}_2$, and pH* were estimated at frequent intervals, as were sagittal sinus $p\text{O}_2$ and pH, using direct reading electrodes (Radiometer).

FIG. 1. *Right and left intraventricular pressures. Data from all eight experiments.*

TABLE 1
MEAN CONTROL VALUES FOR ALL MEASURED PARAMETERS, BEFORE AND AFTER BALLOON INSERTION

Control	Mean intraventricular pressure (mmHg)		Mean subdural pressure (mmHg)		Cisterna magna pressure (mmHg)	Cerebral hemisphere blood flow (ml/100 g/min)	
	Right	Left	Right	Left		Right	Left
Before balloon insertion	7.8	7.3	4.1	5.6	5.2	43.3	39.7
After balloon insertion	10.0	10.1	8.9	10.8	9.2	39.8	41.7

3. *End-tidal CO₂* was continuously monitored using an infra-red analyser (Capnograph).

4. *Venous Hb and PCV* were estimated at frequent intervals.

RESULTS

INTRACRANIAL PRESSURES 1. *Intraventricular pressures* Mean control values are shown in Table 1. The correlation between the two intraventricular pressures remained very close as intracranial pressure was increased (Fig. 1, see Table 2). The correlation coefficient was 0.996, and the regression line did not differ significantly from the line of identity. The close correspondence between the two pressures was seen both with the transient changes in pressure occurring at the time of each addition of fluid to the balloon and during the sustained increase in pressure throughout the period of each experiment. In particular, with the transient pressure changes, there was no detectable time lag in the rise of the two pressures and the magnitude of the changes corresponded closely.

2. *Subdural pressures* Mean values, before and after balloon insertion, are shown in Table 1. The overall correspondence between each of the subdural pressures and the mean intraventricular pressures is shown in Figs 2a and 2b and that between the two subdural pressures in Fig. 3.

The correlations between the two subdural pressures and between each of the subdural pressures and the mean intraventricular pressure, with increasing intracranial pressure, were less good than that between the two intraventricular pressures but they were, nevertheless, highly significant.

The correlation coefficient between the (R) subdural pressure and the mean intraventricular pressure was 0.91 for the full series of experiments (Table 2). In six of the eight experiments there was, in fact, very close correspondence between these two pressures. This applied both to the timing and magnitude of the transient pressure increases with each addition of fluid to the balloon, and to the overall increase in pressure. In the remaining two experiments, however, the (R) subdural pressure increased only slightly with increasing intraventricular pressure. The

FIG. 2. Correspondence between mean intraventricular pressure and (a) right subdural pressure, (b) left subdural pressure. Data from all eight experiments.

FIG. 3. Correspondence between right and left subdural pressures. Data from all eight experiments.

pressure increases at the time of each balloon expansion, continued to occur simultaneously but there was a variable discrepancy in magnitude between the (R) subdural pressure and the mean intraventricular pressure in these two experiments. In both cases, there was, however, considerable difficulty in maintaining a satisfactory recording from the (R) subdural catheter.

The correlation coefficient between the (L) subdural pressure and the mean intraventricular pressure was 0.94 (Table 2). With the (L) subdural pressure there was less variation than with the (R) subdural pressure, and overall increases in pressure corresponded well with the increases

in mean intraventricular pressure in seven of the eight experiments. Similarly, the transient induced changes in intraventricular pressure at the time of each addition of fluid to the balloon, were closely mirrored, both in timing and magnitude, by changes in the (L) subdural pressure. In one experiment, however, no satisfactory recording could be obtained from the (L) subdural catheter, while in the two experiments in which the (R) subdural pressure did not correspond closely with the intraventricular pressure the (L) subdural pressure also tended to lag slightly behind the intraventricular pressure. The correlation coefficient for the two subdural pressures throughout the eight experiments was 0.96 (Table 2).

FIG. 4. Correspondence between cisterna magna pressure and mean intraventricular pressure. Data from all eight experiments.

TABLE 2
CORRELATIONS BETWEEN MEASURED SUPRATENTORIAL PRESSURES

Variables	Regression equation	Correlation coefficient r	Student's t	Probability P	Standard error of estimate of y S_y	Number of paired observations n
RVFP and LVFP	$y = 0.99x + 0.94$	0.996	83	≤ 0.001	2.49	55
RSDP and LSDP	$y = 0.89x - 1.5$	0.96	21	≤ 0.001	7.86	45
RSDP and VFP	$y = 0.84x - 1.42$	0.91	16	≤ 0.001	10.7	54
LSDP and VFP	$y = 0.91 - 0.1$	0.94	18	≤ 0.001	9.95	47

RVFP: right ventricular fluid pressure. RSDP: right subdural pressure. VFP: mean ventricular fluid pressure. LVFP: left ventricular fluid pressure. LSDP: left subdural pressure.

FIG. 5. Mean right and left cerebral hemisphere blood flow levels, with increasing mean intraventricular pressure.

3. *Cisterna magna pressure* Mean values before and after balloon insertion are shown in Table 1. The overall correspondence between cisterna magna pressure and mean intraventricular pressure for all eight experiments is summarized in Fig. 4. The correspondence between the two pressures was, in fact, quite variable. In six of the eight experiments cisterna magna pressure rose in conjunction with the mean intraventricular pressure during the initial stages of increasing intracranial pressure but, beyond a certain level, further increases in supratentorial pressure were no longer reflected by similar increases in infratentorial pressure and a progressive intercompartmental gradient developed. The level at which the apparent block occurred varied: in four

animals at a supratentorial pressure of approximately 30 mmHg and in two animals at a supratentorial pressure of approximately 60 mmHg. In the two remaining animals the cisterna magna pressure continued to rise with increasing supratentorial pressure and no gradient developed. In these two experiments, however, the maximum intracranial pressures reached were low, 35, and 64 mmHg respectively.

Before the development of an intercompartmental block in six animals and throughout in the remaining two animals, the time course and magnitude of the increases in cisterna magna pressure with each addition of fluid to the balloon corresponded closely with the changes occurring in the supratentorial pressures. After a

TABLE 3

MEAN RIGHT AND LEFT CEREBRAL HEMISPHERE BLOOD FLOW VALUES FOR 25 MM HG RANGES OF INTRACRANIAL PRESSURE

	VFP < 25 mmHg		VFP 25-50 mmHg		VFP 50-75 mmHg		VFP > 75 mmHg	
	Right	Left	Right	Left	Right	Left	Right	Left
Mean CBF (ml/100 g/min)	42.1	42.3	34.8	39.0	19.4	25.1	17.4	20.4
Standard deviation	14.1	14.1	6.9	10.6	12.1	13.4	10.7	14.8
Paired observations (no.)	29		10		9		5	
t	0.0989		2.1948		2.0578		0.8485	
P	> 0.9		> 0.05		> 0.05		> 0.9	

VFP: mean ventricular fluid pressure. CBF: cerebral blood flow.

block had developed, however, further increases in supratentorial pressure produced only minimal changes in cisterna magna pressure.

4. Blood pressure All eight animals showed transient increases in blood pressure, with each addition of fluid to the balloon. Only three of these animals showed a sustained increase in blood pressure with progressive intracranial hypertension and even in these animals, the magnitude of the increase was much less than that seen with cisterna magna infusion in a previous series of experiments (Johnston *et al.*, 1972).

CEREBRAL BLOOD FLOW Mean values for each cerebral hemisphere, before and after insertion of the balloon are shown in Table 1. In all eight experiments cerebral blood flow was maintained around control levels during the initial phases of raised intracranial pressure (range 40–70 mmHg). As the pressure was further increased blood flow fell progressively. The overall relationship between cerebral blood flow and both cerebral perfusion pressure and intracranial pressure was, therefore, similar to that described in the earlier experiments (Johnston *et al.*, 1973).

There was no significant difference between the blood flow in the two hemispheres during control measurements, either before or after balloon insertion. Before balloon insertion, however, mean values for right hemisphere flows were slightly higher than for left hemisphere flows whereas after balloon insertion this was reversed. As the intracranial pressure was progressively increased the values for left hemisphere flow remained consistently slightly higher than for right hemisphere flow, although the difference remained slight, even at the more extreme levels of intracranial hypertension (Fig. 5). When corresponding values of blood flow for the two cerebral hemispheres were compared for various ranges of intracranial pressure, using the paired *t* test, there was no significant difference between the two sides (Table 3).

DISCUSSION

The present results clearly show an intercompartmental pressure gradient, between supratentorial and infratentorial compartments, will

develop when intracranial pressure is progressively increased due to a focal expanding mass. No definite intracompartmental pressure gradients, within the supratentorial compartment, were, however, seen. There was an extremely close correspondence between the intraventricular pressure from the two hemispheres at all times and a relatively close correspondence between the pressure measured from the subdural spaces over the convexities of both cerebral hemispheres. Measurements of cerebral blood flow from each hemisphere during progressive intracranial hypertension showed a consistently slightly lower flow in the hemisphere on the side of the lesion. The differences were, however, small and statistically insignificant and did not increase with increasing intracranial pressure.

The existence of intercompartmental pressure gradients in states of raised intracranial pressure is well documented (von Bergmann, 1885; Smyth and Henderson, 1938; Kaufmann and Clark, 1970). Such gradients may occur at two sites; between supratentorial and infratentorial compartments across the tentorium cerebelli and between infratentorial and spinal compartments across the foramen magnum. The development of these gradients seems to depend on obliteration of the subarachnoid spaces at the sites, by displacement of brain tissue. If the subarachnoid space can be reconstituted then the gradients may be reversed (Langfitt *et al.*, 1964). It is important in this respect to distinguish cause and effect in that it is the displacement of brain tissue which gives rise to these sustained intercompartmental gradients rather than *vice versa*.

The situation is much less clear when intracompartmental pressure gradients are considered. There are now several reports of the development of such gradients within the supratentorial compartment during raised intracranial pressure (Weinstein *et al.*, 1968; Brock *et al.*, 1972). The nature of the gradient appears to depend critically on the sites of measurement of pressures. Thus, in one study, where raised intracranial pressure followed an embolic lesion of one cerebral hemisphere a considerable pressure difference between the two sides was noted when extradural pressures were measured over the two hemispheres. The magnitude, and even the direction of these gradients was, however, quite variable (Brock *et al.*, 1972). Such pressure

differences may simply reflect the variable transmission of pressure across the dura mater, due to the particular physical properties of that membrane and its attachment to the cranium. Other measurements, in man, at relatively low levels of intracranial pressure, have also shown that extradural pressures do not correlate exactly with intraventricular pressures (Coroneos *et al.*, 1972). Further, experimental studies have shown that when extradural pressures are raised by the addition of fluid to the extradural space the pressure within the space is transmitted to the underlying subarachnoid space in a variable manner (Langfitt *et al.*, 1964). The demonstration of intracompartmental pressure gradients based on measurements of extradural pressures may, therefore, be misleading.

In contrast, an increase in intracranial pressure due to the addition of fluid to the subarachnoid space is freely transmitted throughout that space, provided it is patent. Similarly, it is probable that when intracranial pressure is raised by any means there is an immediate equalization of pressure throughout the subarachnoid space. The variability in the subdural pressures in the present study may reflect destruction of the subarachnoid space at the time of catheter insertion, particularly as those experiments in which there was greatest variability were those in which leakage of CSF occurred around the point of catheter insertion. Further, when the ventricular CSF is in free communication with the subarachnoid CSF, pressure will be uniform throughout the whole fluid system, in accordance with Pascall's law (Weinstein *et al.*, 1968).

A critical question, as yet unresolved, is the extent to which pressure within the subarachnoid space represents pressure within the brain tissue and related to this, the extent to which an increase in pressure within the brain substance is transmitted to the rest of the brain and to the subarachnoid and ventricular CSF. With expansion of an intracerebral balloon Weinstein *et al.* (1968) found that pressure gradients did develop across brain tissue, although the physical characteristics of balloons as pressure measuring devices in this situation leave something to be desired. On the other hand, a sudden increase in pressure due to mechanical trauma was found to occur equally throughout the supratentorial

compartment, although differences were noted between supratentorial and infratentorial pressures. It would be of considerable interest to know whether differences of pressure exist between non-communicating fluid collections within the cerebral hemispheres under conditions of raised intracranial pressure. Where shift of intracranial contents occurs, there must be, or have been, a pressure differential, although this may only have been transient and dissipated by the redistribution of the intracranial contents. Clearly, however, much remains to be learned about intracompartmental pressure gradients and the physical properties of the intracranial contents which determine their nature.

Measurements of cerebral blood flow, in the present study, showed that, after insertion of the subdural balloon, the flow in the hemisphere on the side of the balloon was consistently slightly less than that in the contralateral hemisphere. The differences between the two sides, were, however, slight and insignificant. Further, the difference did not increase with increasing intracranial pressure even to the extreme levels of pressure. Estimations of blood flow were, however, delayed for at least several minutes after each addition of fluid to the balloon—that is, until conditions had become relatively stable. This may mean that transient flow changes related to acute increases in the size of the mass, of the type demonstrated by Weinstein *et al.* (1968), were overlooked. Such transient flow changes may be related to the transient pressure gradients discussed above and their dissipation through the brain tissue. The correspondence of the blood flow values from the two sides was also reflected in the cerebral perfusion pressure/cerebral blood flow relationship for each hemisphere. There was no evidence to suggest disturbance of autoregulation limited to the side of the lesion, due to the effects of local compression (Brock *et al.*, 1972).

These findings, both with regard to intracranial pressure and blood flow, are of importance to the clinician measuring intracranial pressure. It is clear that within each intracranial compartment measurement of pressure from one of the fluid containing spaces, subarachnoid or intraventricular, is a valid measurement and refers to the overall intracompartmental pressure irrespective of the site of the lesion. From

such measurements it is, therefore, possible to draw conclusions about the level of intracranial pressure and its general effects such as reduction of cerebral blood flow, if the characteristics of the particular relationship are adequately defined. Whether clinical measurement of pressure from different compartments simultaneously has anything to offer in terms of patient management is uncertain (Kaufmann and Clark, 1970).

In conclusion, it is apparent that the intercommunicating fluid system comprising the ventricular and subarachnoid CSF acts to distribute evenly and rapidly the intracranial pressure, even at extreme levels of pressure. When this system is blocked, however, sustained pressure gradients may develop, this applying, within the limits of the present data, to intercompartmental gradients. With sudden increases in intracranial pressure, such as that due to rapid expansion of an intracerebral mass, transient pressure gradients may develop across brain tissue which are dissipated by redistribution of the intracranial contents and communication with the fluid-containing spaces. There is, in fact, no good clinical or experimental evidence for the existence of sustained intracompartmental pressure gradients. Reservation must be made, however, with regard to extradural masses or pressures, as these would appear to be influenced by the physical properties of the dura mater and its attachment to the cranium. With an increase in intracranial pressure from any cause, cerebral blood flow is related to the level of intracranial pressure, although the characteristics of this relationship clearly depend on the nature of the increase in intracranial pressure (Johnston *et al.*, 1972, 1973). In the present study, however, there was no difference in the changes in blood flow with increasing intracranial pressure between the cerebral hemisphere on the side of the lesion and the contralateral hemisphere. The clinician measuring pressure

from one point in one intracranial compartment may, therefore, feel secure in drawing conclusions (from his measurements), as to the generalized effects of raised intracranial pressure, at least within that particular compartment.

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