Experimental Study of Patterns of Brain Distortion and Ischemia Produced by an Intracranial Mass*

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Expanding intracranial masses can cause neuronal dysfunction by several possible mechanisms. A rapidly expanding mass lesion may produce vascular compression and ischemia of brain tissue adjacent to the lesion. Brain substance remote from the mass also can be rendered ischemic because of the particular vulnerability of its blood supply to distortion and compression. A notable example is compression of the posterior cerebral artery against the edge of the tentorium. A third mechanism to be considered is alteration of the electrical and chemical properties of neurons by distortion of their architectural arrangement. This is particularly pertinent in evaluating the significance of brainstem displacement and distortion.

The purposes of the present investigation were to study displacement and distortion of the brain and intracranial vascular compression produced by acute expansion of an extracerebral balloon, and to correlate these effects with pressure measurements from various intracranial compartments. Particular attention was directed to gross morphological changes in the brain stem.

Experimental Methods

Experiments were performed in adult cats and rhesus monkeys anesthetized with intravenous pentobarbital (Diabutal, 30 mg/kg). Twelve cats were used to study transmission of pressure through the brain. The animals were placed in a stereotaxic headholder, and small recording balloons were inserted into the cerebral hemispheres. Each balloon was injected with a small volume of water (0.2–0.4 ml). Baseline pressures varied among the recording balloons, so adjustments in volume were made until pressures in all balloons rose equally in response to injection of saline into the cisterna magna. Pressure differences recorded with subsequent inflations of an extracerebral injection balloon were considered to be valid if a cisternal injection at the end of the experiment produced an equal rise in pressure among recording balloons.

Three monkeys were used to compare communication of pressure from the supratentorial space to the brain stem and to the posterior fossa basal cisterns. A recording balloon and a catheter were placed in opposite cerebellopontine cisterns. The balloon pressure was considered a measurement of brain-stem tissue pressure. A subdural catheter and a subdural balloon in the supratentorial space recorded cerebrospinal fluid and brain tissue pressures respectively. All pressures were measured with Sanborn transducers and recorded on an 8-channel Sanborn polygraph.

Fifty-one cats were used to assess patterns of displacement, distortion, and ischemia of the brain during rapid expansion of an extracerebral subdural balloon. Evans Blue dye (3%, 5 ml/kg) was injected into the femoral vein immediately following completion of the balloon injection. The distribution of dye permitted estimation of regional ischemia in the brain. Intracranial pressure was measured from a subdural balloon over the cerebral hemisphere contralateral to the injection balloon. The position of the recording balloon was the same in all animals, and the injection and recording balloons were accurately placed in the anteroposterior stereotaxic plane. The cats' heads were frozen in liquid nitrogen at 15 seconds, 2½ minutes, or 5 minutes after dye injection. The heads were then sectioned in coronal and mid-sagittal planes with a bandsaw and photographed with Kodacolor-X color negative film. The black and white prints used for illustration were made with yellow and magenta filters.

In 10 animals 3 mm samples of frozen tissue were fixed in very cold, 10% formaldehyde

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solution for 10 to 14 days. The tissue was then sectioned on a microtome in 200 \( \mu \) sections and stained by the benzidine procedure for hemoglobin.\(^8\)

**Results**

**Communication of Pressure Within the Brain.** Expansion of an intracerebral balloon sufficient to raise the pressure adjacent to the balloon to approximately 100 mm Hg in 20 seconds results in a significant difference in pressure across the brain. Figure 1 is a diagram of intracerebral balloon pressures at various distances from the injection balloon in six animals at the end of injection. The maximum difference recorded was 35 mm Hg. Figure 2 illustrates an equal rise in intracerebral balloon pressures in response to injection of saline into the cisterna magna, and the difference in pressure across the brain that accompanies expansion of a supratentorial balloon.

In Fig. 3, pressures were recorded from a balloon and a catheter in the posterior fossa, and from a supratentorial subdural catheter and balloon. Intracranial pressure was increased by gradual expansion of a second supratentorial subdural balloon. Pressure was readily transmitted from the cerebral hemispheres to the posterior fossa balloon adjacent to the brain stem at a time when obstruction of the subarachnoid pathways at the tentorial incisura prevented free communication of fluid pressure to the basal cisterns surrounding the brain stem.

**Displacement, Distortion, and Vascular Compression.** Rapid expansion of an extra-cerebral subdural balloon caused cessation of blood flow in cerebral tissue subjacent to the balloon and also in remote regions of the brain.

\[\text{Pressure in mm Hg. Time between triangles 1 minute.}\]

![Diagram of intracerebral balloon pressures](image1.png)

![Changes in pressure recorded in left parietal (LPB) and right frontal (RFB) balloons in response to injection of saline into the cisterna magna (dark arrows) and expansion of a third intracerebral balloon (light arrows). With the latter injections a difference in pressure of approximately 25 mm Hg was produced.](image2.png)

![A supratentorial balloon had been expanded gradually until a difference in pressure had been created between the supratentorial space and the posterior fossa. Pressures were recorded from a catheter in the supratentorial subarachnoid space (ST-csf), a supratentorial subdural balloon (ST-bal), a catheter in a posterior fossa cistern (PF-csf), and a posterior fossa balloon (PF-bal). This illustration demonstrates full communication of pressure from the supratentorial space to the posterior fossa balloon with only minimal communication of pressure to the subarachnoid space surrounding the brainstem.](image3.png)
Experimental Intracranial Expanding Mass 515

Fig. 4. Left: Brain subjacent to the subdural injection balloon (Position A-15) fails to fill with Evans Blue dye indicating cessation of cerebral blood flow in this region. Volume of injection 1.3 ml. ICP 55 mm Hg and systemic arterial pressure (SAP) 150/80 at the time of sacrifice. Right: Inflation of the balloon (A 15) with 1 ml water in 1 minute to an ICP of 85 mm Hg. SAP was 145/105. Much of the brain is ischemic with preservation of flow to deep structures only. Note, however, ischemia of the hypothalamus.

brain. In Fig. 4 (left), the crescent-shaped region of brain beneath the balloon failed to fill with Evans Blue dye, indicating total ischemia. In the animal illustrated in Fig. 4 (right) the difference between the intracranial and the systemic arterial pressures was less. Ischemia was more widespread throughout the brain with relative sparing of basal ganglia and medial temporal structures. The hypothalamus also failed to fill with dye.

Transtentorial herniation and caudal displacement of the brain stem also occurred during expansion of the supratentorial subdural balloon. Figure 5 (left) shows the normal relationship of brain stem structures to the bony tentorium in the cat. The dorsal surface of the inferior colliculus is 1 mm caudal to the center of the edge of the tentorium. In Fig. 5 (right) the balloon was inflated with 1 ml water in 1 minute, and the animal was immediately sacrificed. The inferior colliculus was displaced caudally 8 mm, and a portion of the occipital lobe and the splenium of the corpus callosum had herniated beneath the tentorium. The cerebellum was distorted, and the cerebellar tonsils had herniated into the upper portion of the spinal canal. The hypothalamus was compressed against the dorsal sellae, and particularly striking was the flattening and distortion of the brain stem. The distortion is due to the fact that the dorsal surface of the brain stem was displaced caudally more than its ventral surface.

The degree of brain stem displacement and transtentorial herniation was related to the volume and rate of injection of the balloon, but the location of the balloon was also an important factor. In two of the animals

Fig. 5. Left: Sagittal section of head of normal cat showing position of tentorial incisura (dots) and the inferior colliculus (arrow). Right: Expansion of subdural balloon (A 11) to an intracranial pressure of 80 mm Hg in 1 minute with 1 ml water. Note herniation of occipital lobe and marked caudal displacement of the tectum. The brain stem and cerebellum are distorted.
illustrated in Fig. 6 (upper and lower left) the balloons were in the frontal and parietal regions respectively. The balloon was injected with 1 ml water in 1 minute in both animals. The volume of ischemic brain adjacent to the balloon was approximately the same, but the caudal displacement of the inferior colliculus was twice as great with the parietal balloon. At the completion of the balloon injection in the animal illustrated at the top right, there was almost total brain ischemia. Only the cerebellum was spared. This nearly complete abolition of blood flow was due to the fact that intracranial pressure at the end of injection equaled the diastolic pressure. The size of a mass required to produce local brain ischemia in the posterior fossa is smaller than in the supratentorial compartment, because the space available to accommodate the mass is less in the posterior fossa (lower right).

In those animals in which the cerebrovascular architecture was assessed by intravascular staining, an attempt was made to correlate patterns of vascular collapse with cerebral blood flow in brain surrounding the balloon. In Fig. 7, brain subjacent to the balloon failed to fill with dye. The vascular architecture of gray and white matter in regions remote from the balloon and in areas of vascular stasis beneath the balloon is illustrated. Immediately subjacent to the balloon (B) complete collapse of the large surface and perforating vessels was evident. In contrast, many small vessels were patent but were reduced in number compared to the opposite hemisphere. Thus, small vessels remained patent in brain made ischemic by inflow or outflow obstruction.

After completion of a balloon injection, the brain tends to adapt to the expanded mass until equilibrium is established within the intracranial space. This was evident from a comparison of the volume of ischemia adjacent to the balloon and the degree of caudal displacement of the brain stem in cats sacrificed at different times following completion of the injection. When the animal was sacrificed as quickly as possible, the ischemic lesion was large, and moderate displacement of the brain stem was present (Fig. 8 top left). In a cat sacrificed 2½ minutes after completion of the injection, herniation through the incisura and displacement of the tectum was
greater, and the volume of ischemic brain adjacent to the balloon was diminished (Fig. 8 lower left). Five minutes after completion of the injection the inferior colliculus was displaced 10 mm caudal to the tentorium, and only a small portion of brain remained ischemic (Fig. 8 top right).

Mean arterial pressures were equal in the cats illustrated in the top left and lower right photographs in Fig. 8. Intracranial pressure was elevated to the same level in an equal period of time in both animals, by balloon inflation (top left) and by injection of saline into the cisterna magna (lower right). Neither ischemia nor brain stem displacement was present in the latter animal. These observations emphasized the importance of the specific cause of increased intracranial pressure in any given situation. The pathological effects of diffuse intracranial hypertension were much less profound than those produced by a rapidly expanding mass.

During gradual expansion of an intracranial balloon over a period of several hours, cerebrospinal fluid was expressed from the subarachnoid space and cisterns. This created more space for the brain to accommodate to the balloon, and distortion and displacement were less. In Fig. 9 (top photographs) the balloon was expanded to a volume of 1 ml in 3 hours. Intracranial pressure was minimally elevated, and there was little distortion of the brain. In contrast, the balloon was expanded to the same volume in 1 minute (bottom photographs); distortion, displacement, and regional ischemia were present, and the intracranial pressure was elevated to 50 mm Hg.
Discussion

When the intracranial subarachnoid pathways are patent, an increase in pressure produced by the injection of fluid into the subarachnoid spaces is communicated equally and rapidly throughout these spaces. This is an application of Pascal's law which states that a force applied to any portion of the surface of a contained volume of liquid is exerted unchanged on all other portions within the container. Furthermore, if an increase in pressure is equally transmitted throughout the cerebrospinal fluid pathways, then the pressure exerted on each unit of brain surface also is equal. Under these circumstances the brain is neither displaced nor distorted by the rise in pressure. If the brain is not distorted, a force applied will result in the generation of a uniform pressure throughout the brain. Thus, a diffuse increase in pressure in the cerebrospinal fluid spaces is transmitted equally throughout the brain, and under these conditions the entire intracranial space behaves as a fluid compartment. As long as pressure is everywhere equal within the craniospinal axis, caudal displacement of the brain does not occur, irrespective of the height of the pressure.

In previous experiments we have found that pressure in an extradural collection of fluid could be raised to very high values with only minimal communication of pressure to the intradural space. This occurs because the dura is an elastic membrane that resists distension and thereby resists transmission of pressure beyond it. Cairns expressed the opinion that intracranial pressure produced by a tumor may be greater in the brain adjacent to the tumor than in more remote portions of the intracranial space. He attributed this to cerebral structures such as arteries that are not readily displaced by the tumor. Cairns was stating the concept that the brain contains elastic materials that resist distortion and displacement and cause the establishment of differences in pressure within the brain. Holbourn discussed further the relationship of intracranial pressure, as hydrostatic pressure in a fluid-filled container, to a different kind of force, namely stress applied to an elastic substance.

* An elastic substance is one that resists deformation in response to an applied stress and returns to its original shape and position when the stress is removed. Steel is highly elastic. Materials that are easily deformed and do not regain their original shape are termed plastic. The term “pressure” should be used only in a hydrostatic system. The generation and transmission of forces in elastic materials are expressed as “stress-strain” relationships. However, at the risk of oversimplification, pressure is used herein to describe forces within both the brain and intracranial fluid compartments.
In evaluating the pressure phenomena that accompany expansion of an intracranial mass, one should consider both the increase in pressure that occurs within brain adjacent to the mass and the diffuse rise in intracranial pressure produced by an increase in intracranial volume. This raises the issue whether pressure recorded from the cerebral subarachnoid space or a lateral ventricle is an accurate measurement of pressure throughout the supratentorial compartment. The present data show that the difference in pressure across the brain created by rapid expansion of an intracranial balloon is relatively small. These observations, plus measurements of brain elasticity with a special stress-strain recording instrument (unpublished observations), demonstrate that the brain is far more plastic than elastic. Thus, it is unlikely that a significant difference in pressure exists between nerve tissue surrounding a slowly expanding lesion and remote portions of the brain. However, tissue pressure measurements in chronic animals or in patients with space-occupying masses are required to prove this point. Measurements of brain tissue pressure with the present technique are subject to considerable error. Dynamics in the region of the recording balloon may be altered by hemorrhage and by tissue swelling around the balloon. Also, if the balloon is not spherical, tension in a portion of its wall may contribute to the pressure recorded. Guyton has criticized methods of recording interstitial pressure in other organs and introduced an ingenious device for measuring pressure in the extracellular space. This has not been applied to the study of brain pressure.
Further evidence for a low modulus of elasticity of brain is the rapidity with which brainstem displacement and transtentorial herniation occur during acute expansion of a mass. The tectum was displaced caudally 10 mm within a few minutes from the beginning of the injection. In engineering terms this movement is described as "plastic creep," and the brain continues to move away from the region of maximum force (the balloon) until those forces tending to displace the tissue are counter-balanced by the elastic properties of the brain tending to resist further deformation.

Evaluation of the significance of the elastic and plastic properties of nervous tissue must take into account the rigid container that bounds the brain. As a mass expands within the intracranial space, the volume of the mass is accommodated by displacement of cerebrospinal fluid, presumably into blood vessels and caudal subarachnoid pathways. Also, caudal brain stem displacement and transtentorial herniation reduce the volume of brain in the supratentorial compartment. The normal blood volume of the brain is so small, it is doubtful that blood acts as a significant buffer. If the mass expands slowly, the volume displaced may equal the volume added, and intracranial pressure measured from fluid compartments does not change. When the volume of the mass exceeds the displaced volume of cerebrospinal fluid, intracranial pressure rises, and this pressure is freely and nearly instantaneously transmitted throughout the intracranial space. Thus, two pressure components are developed by the expanding mass. If expansion is very rapid, the pressure in the brain adjacent to the mass may exceed the pressure in distant parts of the intracranial space, but this difference in pressure is dissipated by the plastic properties of nerve tissue. The second component is the diffuse rise in intracranial tension which is the increase in pressure that must occur if the volume within a filled, rigid container is increased. According to Pascal's law, this pressure is freely transmitted throughout the container.

During expansion of a supratentorial mass, obstruction of the subarachnoid pathways at the tentorial incisura develops, and when the obstruction is complete supratentorial pressure no longer communicates with the subarachnoid space in the posterior fossa and spinal canal. In a previous report we assumed that pressure in the brain stem equals the pressure in the posterior fossa basal cisterns; that the lower brain stem, in effect, is protected from the supratentorial hypertension by the incisural obstruction. The present data demonstrate that pressure is rapidly transmitted from the cerebral hemispheres through the brain stem at a time when the posterior fossa subarachnoid pressure is unaffected. Thus, the brain stem is subjected fully to the pressure head developed within the supratentorial compartment, and, in terms of function, tissue pressure is the critical factor.

The local brain ischemia produced by rapid expansion of the balloon is due to vascular compression. The ischemia is localized because, for a brief period, the pressure in the brain adjacent to the balloon is higher than the arterial inflow pressure which is responsible for maintaining patency of the vessels. The blood vessels in the remainder of the brain fill with dye because the tissue pressure, although increased, is less than the perfusion pressure. By increasing the volume of fluid injected into the balloon or decreasing the time of injection, or by decreasing the systemic arterial pressure, the volume of ischemic brain is increased. Furthermore, vascular compression and ischemia spread in an essentially circumferential manner from the balloon. During the passage of time following completion of the injection, the volume of ischemic brain adjacent to the balloon decreases, because the initial high pressure is dissipated by movement of the brain.

Large arteries and veins were collapsed in ischemic brain adjacent to the balloon whereas many small vessels still contained blood. Ischemia of remote portions of the brain, such as the hypothalamus, probably is due to compression of surface vessels against the surrounding bone or distortion of the vascular supply to these regions. Patterns of cerebrovascular collapse caused by expansion of a mass or brain swelling have been reviewed recently.

Displacement and distortion of the brain stem in these experiments developed rapidly and were severe. The degree of displacement and herniation is a function of the volume of
Experimental Intracranial Expanding Mass

the mass and is independent of pressure in the supratentorial space. If the mass is expanded quickly displacement will occur more rapidly because of the large initial difference in pressure across the brain; but the volume of displaced brain equals the volume of the mass minus the volume of cerebrospinal fluid expressed from the intracranial space and is independent of pressure. Despite severe distortion and displacement of the brain stem, brain stem ischemia was not observed in these experiments except as a direct extension of the ischemic zone from the balloon. The injection of dye served only to determine the patency of vessels, and inadequate blood flow may have been present in many regions that filled with dye. Nevertheless, the results do demonstrate that blood vessels within the brain stem may be patent, despite severe distortion of its architecture, at a time when blood flow to the cerebral hemispheres has been abolished by diffuse vascular compression.

The functional significance of these observations has not been elucidated, because the studies were confined for the most part to gross morphological changes. A critical reduction in blood flow always leads to functional alterations but the importance of distortion of the nervous system in the absence of ischemia is not so clear. The significance of these relationships can be established only by correlation of morphological changes with regional cerebral blood flow and measurements of brain function.

Summary and Conclusions

Pressures were measured from the brain and intracranial fluid compartments during rapid expansion of intracerebral and extracerebral (subdural) balloons in cats and monkeys. A vital dye was injected at the completion of injection in order to study patterns of regional ischemia. The animals' heads were frozen in liquid nitrogen, sectioned in various planes, and photographed.

Significant pressure differences across the brain were developed by rapid inflation of an intracerebral balloon, but these were less than anticipated, and the relatively small differences in pressure are attributed to the plastic (as opposed to elastic) qualities of the brain that allow it to be easily deformed.

Brain stem displacement and distortion were seen in all animals and were a function of the volume of the injection balloon and the time of injection. When the balloon was expanded slowly, expression of cerebrospinal fluid from the supratentorial compartment permitted accommodation of a larger volume, and brain stem displacement was less.

Pressure changes generated in the supratentorial space were freely transmitted throughout the brain stem at a time when transmission of pressure to the posterior fossa subarachnoid spaces was abolished by obstruction at the tentorial incisura.

Rapid inflation of a subdural balloon not only caused ischemia of the brain adjacent to the balloon, but also in remote portions of the intracranial space, the latter probably due to the particular vulnerability of the blood supply of those regions to compression and distortion.

References