Experimental Intracranial Hypertension and Papilledema in the Monkey*

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The purpose of the present experiments was to attempt to develop a reliable method of producing sustained cerebral compression and increased intracranial pressure in the monkey together with a simple technique for recording the intracranial pressure over long periods of time without loss of cerebrospinal fluid. The technique to be described has been successful in this regard and has provided a means for producing many of the neurological manifestations of an expanding intracranial mass, including papilledema, paralysis of the extraocular nerves, visual loss, and paralysis of the extremities. It also has provided an experimental means for studying the reaction of the brain to gradual compression and the transmission of pressure within the intracranial space.

Method

Rhesus monkeys were used in all experiments. An expanding intracranial mass was produced by insertion of a fine-thread steel bolt into a trephine hole in the skull (Fig. 1), followed by periodic injections of Pantopaque† into the extradural space. A hole is drilled in the center of the head of the bolt and tapped. A 2nd hole is drilled through the center of the shank to within 1/16 in. of the bottom and a 3rd hole is placed perpendicular to this through the shank. In the head of the bolt is inserted a gasket which is held in place by a machined cap with a hole in the center for insertion of the injecting needle. A gasket is placed over the shank flush with the lower surface of the head of the bolt. The bolt, which is self-tapping, is then screwed into place with a nut driver. The gasket is compressed between the head of the bolt and the skull forming a water-tight seal.

Fig. 1. Diagram of injection bolt. Cross section on right; side and top views on left. Complete description in text.

Following insertion of the injection bolt measurements of control pressure are obtained. A needle attached by a 3-way stopcock and catheter to a Sanborn transducer and polygraph is inserted through the diaphragm in the head of the bolt. Since the base of the shank is intact the dura mater cannot be penetrated. The amplitude of the pulsations on the polygraph record is adequate to provide assurance that a true pressure is being recorded. One to 1.5 cc. Pantopaque then are injected unilaterally into the extradural space through the side arm of the stopcock or through a separate injecting needle inserted into the bolt beside the recording needle. The latter method permits continuous recording of the pressure during injection.

Roentgenograms are obtained to delineate the size and distribution of the Pantopaque (Fig. 2) and to be certain that none has leaked into the subarachnoid space through an unsuspected tear in the dura mater. Extradural pressure recordings are then carried out at frequent intervals and additional Pantopaque is added as required to maintain intracranial hypertension. The neurological status of the animal is evaluated and recorded on film, and the optic disks are visualized and photographed with a funduscope camera. Initially it was assumed that the pressure in the extradural space on the side of the injection of

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† Iopendylate; Standard X-ray Co., Chicago, Illinois.
Pantopaque was an accurate measurement of the intracranial subarachnoid pressure, but this is not always correct. For this reason bilateral injection bolts are now inserted in each experiment (Fig. 3).

Following death of the animal the intracranial vessels are perfused with saline, formalin, and frequently latex. The brain is removed, allowed to fix in 10 per cent formalin for 3 weeks, and examined by frozen-section technique. All 5th and 6th sections are stained with luxol blue and the Spielmeyer technique for myelin.

**Results**

The results are based on experiments performed upon 21 monkeys. In 7 monkeys an injection bolt was inserted on 1 side only, and in the remaining 14 animals injection bolts were inserted bilaterally because of the demonstration that the extradural pressure on the side of injection may not be an accurate measure of the subarachnoid pressure. However, it has been shown that the contralateral extradural pressure is virtually identical to the subarachnoid pressure over the cerebral hemisphere. Therefore, measurements of intracranial pressure are cited only for those animals with bilateral injection bolts and unilateral injections of Pantopaque, in which the extradural pressure was recorded contralateral to the injected side.

In this latter series there were 9 monkeys, in all of which increased intracranial pressure developed.

Several patterns were observed in the response of intracranial pressure. In some animals injection of 1 cc. Pantopaque into the extradural space on the day of operation was followed by a sustained rise in intracranial pressure, resulting in death of the animal in 2 to 9 days. In others, daily injections were required to maintain the pressure at hypertensive levels. In monkey ML51, illustrated in Fig. 4, control pressure was 6 mm. Hg, and after a transient rise in pressure with injec-