Experimental Hydrocephalus

Part 1: A Technique for Producing Obstructive Hydrocephalus in the Monkey

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In 1914 Dandy and Blackfan demonstrated that hydrocephalus could be produced in dogs by obstructing the aqueduct of Sylvius. The observation was of fundamental importance and for many years spurred intense interest in the physiology and pathology of the ventricular system. With time, however, it became evident that several problems existed. First, the surgical techniques were complicated and were reliable only in the hands of a few. Second, the techniques failed to produce consistent results, and even when they were successful the hydrocephalus that developed was rarely advanced before 3 to 8 weeks. Third, attempts to produce hydrocephalus in species other than the dog were largely unsuccessful.

A number of investigators have suggested modifications of the original technique of Dandy and Blackfan. Unfortunately, none of these techniques provided a substantially superior experimental model, and for lack of such a model much of the early momentum in hydrocephalus research was lost.

The following report describes a new and relatively simple experimental technique for producing obstructive hydrocephalus in the monkey. The details of the technique, its reliability, and the advantages of the experimental model are discussed.

Materials and Methods

In this study we used 230 rhesus monkeys (Macaca mulatta) weighing 4 to 6 lbs and ranging in age from 1½ to 2 years. Under light Sernylan anesthesia, the animals were positioned face down in a stereotaxic head holder so as to flex the neck forward as much as possible. With strict surgical precautions, a small bilateral suboccipital craniotomy was made through a posterior midline incision (Fig. 1 left). The defects in bone and dura were made as small as possible to reduce the effects of surgical decompression. The foramen of Magendie, which is a true foramen in the monkey, was then dilated by introducing a blunt-nosed staphylorrhaphy into the cavity of the fourth ventricle (Fig. 1 right). By this maneuver, the orifice of the foramen was easily widened, and no further manipulation or retraction of the cerebellum was required.

A No. 8 Foley catheter was then introduced into the cavity of the fourth ventricle and its tip advanced to the level of the caudal aqueduct. To assure proper seating of the entire balloon within the cavity of the fourth ventricle, it was necessary to cut off the nose of the catheter so that it protruded no more than 4 to 5 mm beyond the balloon (Fig. 2 left). Since many of the balloons inflated unsymmetrically, the catheter was introduced so that the expanding mass was directed toward the roof rather than the floor of the fourth ventricle, to avoid unacceptable trauma to the floor of the fourth ventricle and brain stem. Once the balloon was in place, it was inflated with saline so as to produce a mass of 1 to 1.5 cc. The catheter was then tied off with double ligatures of heavy silk. This maneuver completely sealed the cavity of the fourth ventricle and blocked the exit of the caudal aqueduct (Fig. 2 right).

It was found that when the balloon was inflated with air rather than saline, it frequently collapsed after several days. This probably results from diffusion of air through the slightly permeable walls of the balloon and emphasizes the importance of
clearing the saline syringe of any air bubbles. Similarly, inflation of the balloon with various contrast substances, such as Hypaque, was not successful, for the opaque material proved injurious to the rubber of the balloon and resulted in spontaneous rupture in some cases.

When the animals were used for continuing experiments, great care was taken to secure the catheter once it was tied off. This was done by suturing the catheter to dura after the latter had been closed as completely as possible. Another heavier anchoring suture to muscle or skin was also used, and the wound was carefully closed in layers of medium silk. The catheter was then brought out through the lower pole of the incision or through a separate stab wound, and the catheter was completely incorporated into a bulky figure-of-eight tape dressing. By this means it was possible to return the animals to their cages with little or no danger of injury to the catheter.

Although it was probably unnecessary, animals on long-term experiments were treated with prophylactic antibiotics.

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**Fig. 1. Left:** Surgical exposure of the posterior fossa. For purposes of illustration the defects in bone and dura have been made slightly larger than usual. **Right:** The foramen of Magendie is dilated by introducing a bluntnosed staphlorraphy into the cavity of the fourth ventricle, which makes it possible to introduce a No. 8 Foley catheter into the ventricle without further manipulation.

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**Fig. 2. Left:** Intact and amputated No. 8 Foley catheters inflated to a volume of 1.5 cc with saline. **Right:** No. 8 Foley catheter in place within the 4th ventricle. The balloon has been inflated to a volume of 1.0 cc with saline.
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Results

In all 230 monkeys that survived surgery, gross ventricular dilatation was apparent within 1 hour, being well-advanced within 3 hours (Fig. 3). Once the technique had been perfected, the operative mortality was small, and in the last 170 animals of this series all but three survived the immediate effects of anesthesia and surgery. The clinical and pathological findings will be reported in Parts 2 and 3 that follow.5,12

In a number of animals in which serial ventriculograms were performed, it was a simple matter to anesthetize the animal, untie the catheter, and inject the desired volume of air through the direct channel of the catheter. Other determinations, such as serial CSF specimens, were also available for study in this manner without resorting to ventricular puncture or other compromise of the experimental model.

Figure 4 illustrates the fourth ventricular lesion and testifies to the completeness of the block accomplished in all animals. It might be mentioned that phenosulphothalein (PSP) studies in these animals failed to show passage of dye from the ventricular system into the cisterns or subarachnoid space over intervals as long as 3 weeks after intraventricular injection.

Discussion

The technique of Dandy and Blackfan,6 probably the most successful of previous efforts to produce experimental obstructive hydrocephalus, consisted of passing a cotton pledget on the end of a graduated carrier into the fourth ventricle and depositing the cotton plug in the aqueduct of Sylvius. Although this produced reasonably consistent ventricular dilatation within 3 to 8 weeks in dogs, it was not successful in producing hydrocephalus in either the cat or the monkey.

Other investigators have repeated this original work with varying degrees of success. In 1914, Frazier and Peet7 and Wegeforth13 had good success with their techniques for obstructing the aqueduct of Sylvius. Güleke, in 1930, however, failed to achieve consistent results following the introduction of iodine-soaked fascia into the aqueduct.6 In less than one fourth of his experimental animals did he observe hydrocephalic changes in spite of what he believed to be a complete aqueductal block. This experience was not unique and other authors had difficulty producing ventricular dilatation.2,9

To improve results, various modifications such as cotton soaked in Canadian balsam,1 cellophane soaked in zepherin,11 and cotton impregnated with lamp black10 were suggested. In none of these or other published papers, however, could a report be found of hydrocephalus having been successfully produced in the monkey. The current paper, therefore, is believed to represent the first such report.

The current technique was found to provide a number of experimental advantages. First, the technique was reliable. In the 230
monkeys that survived the immediate effects of anesthesia and surgery, all animals developed hydrocephalus. Second, the hydrocephalus that did develop was well advanced within a few hours. This was of particular value for the animals were available for study soon after surgery rather than weeks or months later. The finding of these early advanced changes was unexpected and will be discussed in detail in Parts 2 and 3 (see pp. 390–413 following). Needless to say, the findings suggest that when the obstruction of the ventricular system is essentially complete, hydrocephalus develops as an acute rather than as a chronic pathological process. Third, the results produced by the current technique were surprisingly consistent. The findings at specific intervals following surgery were so predictable, in fact, that it has been possible to identify a regular sequence of pathological changes in early hydrocephalus.\(^5,12\) Finally, the technique was found to be experimentally practical. Compared to older techniques, the current technique was faster and simpler. Once it had been perfected, the operative mortality was acceptably low.

The development of a successful model of obstructive hydrocephalus in the primate appears to have several other advantages. For obvious phylogenetic reasons, the primate is superior to the dog, cat, or rabbit for studying problems relating to human hydrocephalus. Perhaps more important, however, is the fact that there are few variations in the ventricular anatomy of the monkey. This is not true of other species such as the dog, where anatomical variations are extremely common. In the monkey, the ventricular cavities are invariably slit-like in size, and the incidence of occult hydrocephalus is negligible. In the experience of one investigator who has studied 5000 rhesus monkey brains of an age and weight comparable to those in this report, no cases of occult hydrocephalus were found and ventricular size was noted to be consistently small.\(^4\) In the dog, however, there is evidence\(^3,4\) that in some breeds the incidence of occult ventricular enlargement or hydrocephalus approaches 60% to 80%. Little attention has been given to this point, but it is an important qualification in assessing both current and past literature. Unfortunately, many of the classical studies and many of our current concepts come from poorly controlled experiments in the dog. It is suggested that, without available information about preoperative ventricular size, data on the dog are open to criticism. On the other hand, ventricular size in the monkey has no such variability, and this, perhaps more than any other argument, favors this animal as an experimental model.

**Summary**

A technique for producing acute obstructive hydrocephalus in the monkey has been reported. It has been found to be a simple and reliable means for producing pronounced ventricular enlargement in a matter of hours. Since an experimental model for producing hydrocephalus in the primate has been unavailable until now, the technique is expected to have general applicability.
References


4. CLARK, R. G. Personal communication.


