IRRIGATION OF THE SUBARACHNOID SPACE¹

BY L. B. ALFORD, M.D.

The classical experiments of Key and Retzius (1) demonstrated that the subdural and subarachnoid spaces of the spine are continuous with the respective spaces of the cranium, and a number of subsequent investigations have shown that substances readily pass in these spaces from spine to cranium and in the converse direction. It is now generally believed that in life the subdural space exists merely as a capillary space, the arachnoid everywhere lying in contact with the dura, and that the cerebrospinal fluid is contained in the subarachnoid space. This latter fact is probably a result rather of the position of the arachnoid in respect to the dura, however, than of the impermeability of the arachnoid to the spinal fluid, for it is common experience that when the normal relation of arachnoid and dura is altered, spinal fluid readily passes through the arachnoid (2). It is probably true that under pathological conditions, such as inflammatory processes, the arachnoid is less permeable, because in the acute meningitides the exudate is found almost exclusively in the subarachnoid space.

I have been able to find only once in the literature mention of an attempt at through and through irrigation of the meningeal spaces. Leonard Hill has this to say regarding some experiments of his: "On trephining the lamina of the vertebral column and screwing into it a tube, I have found normal saline can be driven into the vertebral canal. If a second trephine hole be made in the parietal region, none of the injection into the vertebral canal can be driven out from the hole. The mid-brain is floated up by the fluid into the isthmus of tentorium cerebelli and plugs this up, while the great brain likewise moves upwards and plugs up the trephine hole in the parietal region. If, on the other hand, the saline be injected into the parietal hole it can in most cases be driven through the cranio-vertebral canal and out of the hole in the vertebral column. The whole central nervous system can thus be freely irrigated. In some cases, and nearly always if the pressure of the injecting fluid be high and applied suddenly, this cannot be done. By the pressure of

¹ From the Laboratory of the Boston State Hospital. Received for publication July 25, 1918.

the fluid the cerebrum is driven into the isthmus of the tentorium cerebelli and blocks this up so that no fluid can be expelled" (3). The typical experiment given by Hill, however, was done on a dead animal and it may be that all of his other experiments were also.

Other experimental work having a bearing on these experiments may be referred to: Cushing and Week, studying in animals the manner of absorption of the cerebrospinal fluid from the cranial subarachnoid space, introduced solutions into the corresponding spinal space, constantly for several hours (4). In the course of some investigations of hydrocephalus Dandy and Blackfan injected phenolsulphonaphthalein into the lateral ventricles and a few minutes later were able to demonstrate it in fluid withdrawn by lumbar puncture (5). Keen passed salt solution from one lateral ventricle to the other in a conscious patient on whom he had previously operated (6). In a case of tuberculous meningitis Lannelongue attempted to irrigate the base of the brain with a weak bichloride of mercury solution from four trephine holes, but the patient died from hemorrhage (7). The intraventricular, subdural and intraspinal injections of salvarsanized and mercurialized sera in the treatment of neurosyphilis are now common practices. A weak perchloride of mercury solution has also been used to wash out the spinal subarachnoid space in cases of syphilitic meningitis.

Scope of Experiments.—At the beginning of this work it was the plan to develop a technic for passing solutions through the meningeal spaces from one extremity of the central nervous system to the other, and also to test the physiological effect of a few mild antiseptic solutions. It has been found advisable during the course of the experiments to attempt for the purpose of comparison irrigations of the meningeal spaces from below upwards, in the reverse direction and from the lateral ventricle of the brain through the spinal arachnoid space. The distribution of the solution in the meningeal spaces in these three types of irrigation has been investigated by means of solutions colored with methylene blue and by solutions of iron salts that are capable of being precipitated *in situ* by a fixing fluid containing hydrochloric acid.

In order to obtain so far as possible data for the application of the results of these experiments to the human subject, parallel experiments were done using the cadaver. As a result it is possible to reach some conclusions as to the distribution of the fluid in irrigations on the human subject and as to the technic of the operation.

Technic.—For the experiments on animals, cats were used exclusively. Under ether anesthesia a laminectomy was done in the

lumbar region, the dura being exposed over several segments and a circular button of bone, about 1 cm. in diameter, was removed from the parietal region of the skull, particular care being taken in both cases not to injure the dura. Then, if the irrigation was to proceed from spine to brain, a slit was made in the cranial dura just large enough to admit a light-wall $\frac{1}{8}$ -inch black rubber tube which was inserted inferiorly from the slit. Through the spinal dura was passed a 20-gauge hypodermic needle to which was attached a small rubber tube connected with a burette. The solution was run in slowly from the burette, the rate of flow being controlled by a screw clamp on the rubber tube. The latter was some two feet long and lay coiled in a dish of water which was kept near a temperature of 54° C. Between the dish and the needle the rubber tube was inclosed in a larger tube in order to retard radiation. The head of pressure varied with the apparent need, being from 15 to 45 cm. Measures were taken to maintain the body heat of the animal.

In brain-to-cord irrigations the same procedure was followed except that the hypodermic needle was placed under the cranial dura and a slightly curved 15-gauge hypodermic needle containing fenestra was passed through a slit in the spinal dura to provide an outlet for the solution.

Ventricular injections were made by passing the hypodermic needle through the cranial dura into the brain to a depth estimated to be that of the ventricle. It has been found that even though the point of the needle does not lie exactly in the ventricle the path of least resistance for the fluid often does lead there.

This technic has been gradually worked out from a number of operations. In the earlier experiments with ascending irrigations the difficulty mentioned by Hill (3) was encountered, that is, the brain herniated through the trephine opening and stopped the flow. Attempts were made to obviate this difficulty by elevating the head of the animal, regulating the rate of flow of the solution, causing the solution to flow intermittently and placing cotton or glass wool under the dura, but all procedures were without constant success, until the rubber tube was tried. The solution often escapes around the tube, at least until the brain has pressed it firmly against the dura; and when the flow through the tube becomes interrupted, as it rarely does, it is an easy matter to shift its position until the flow is reestablished. The part of the tube lying beneath the dura contains a half dozen small (2 to 3 mm.) openings. The escape of the solution is freer if the tube is inserted downward than if it is placed anteriorly or posteriorly. The brain tissue should not

be injured when the tube is inserted. In the descending injections the fenestrated hypodermic needle must be placed under the spinal dura, else the escape of the solution will generally be interrupted.

In all experiments much care is necessary in maintaining the correct temperature of the irrigating fluid. A slight variation one way or the other at the medulla causes quick suspension of respiration. For this reason it is better not to have the solution flow too rapidly, 1 c.c. per minute being about the maximum rate consistent with safety. This precaution is less important in ascending irrigations because between the point of entrance and the medulla there is distance enough to permit of the adaptation of the temperature of the fluid to a limited extent. But in the ventricular irrigations it is most important; in fact the arrangement for maintaining the temperature of the solution, described above, is unsatisfactory in these irrigations and the animal frequently dies prematurely. A better apparatus has not seemed possible, however, with the means at hand.

Descending irrigations are liable to interruption by a plugging of the foramen magnum or incisura tentorii—it has not been possible to determine which, even from autopsies. Respiratory failure frequently follows such interruption and probably is a result of the increased intracranial pressure that follows. At such times it is generally, but not invariably, impossible to remove the obstruction by starting irrigation from below.

No mention of the arachnoid has been made in this description, and in the experiments it was not found necessary to take it into consideration. Evidently, the arachnoid offers no appreciable resistance to the passage of the solution, but whether this is a result of accidental injury or is due to natural permeability has not been ascertained.

Distribution of Solution.—Whatever the method of irrigation the distribution of the solution in the meningeal spaces is about the same. The entire surface of the nervous system is covered even when no more than 5 or 10 c.c. of solution is employed in the irrigation, although the superior surface of the cerebellum and of the hemisphere opposite to the cranial opening may be colored less deeply. No solution reaches the ventricles, but the velum interpositum is deeply colored. The sheaths of the optic nerves, the olfactory mucous membrane and the proximal end of the Gasserian ganglia are also stained, but no coloring of the spinal nerves is demonstrable beyond the foramina. In the ventricular irrigations the distribution over the surface of the nervous system is the same; both lateral ventricles are stained but that opposite to the side con-

taining the needle less deeply so. The third ventricle also contains the solution but the iter and fourth may or may not. Evidently, the solution is sometimes able to find its way out without passing through the fourth ventricle. It has not been ascertained by what path this occurs. Microscopical examination of sections taken from cases in which the iron solutions were used in the irrigations adds nothing noteworthy to observations already made (4).

Results of Irrigation with Antiseptic Solutions.—This table gives the results of the tests with various solutions. Comment is scarcely necessary. A non-lethal concentration is underscored. The formalin used had been neutralized with calcium carbonate.

Exp.	Irrigation	Solution	Amount	Time of Exp.
43	Ascending	(a) Form, 0.5 per cent.	33 c.c.	23 minutes.
		(b) " 1 " "	8 "	5.5 "
45	Ascending	Form, 1 per cent.	3.5 "	6 "
56	Ventricle	" 0.5 " "	1.8 "	6 "
XIII	Ventricle	" 0.25 " "	18.1 "	40 "
12	Ascending	Boric, 3 " "	36 "	31 "
XI	Ascending	" 3 " "	37.5 "	60 "
27	Ascending	Potassium permanganate, 1/10,000	21 "	56 "
47	Descending	" " 1/2,500	15.8 "	43 "
48	Ventricle	" " 1/2,500	2.5 "	2 "
53	Ventricle	" " 1/1,000	0	0
29	Ascending	Lysol, 1/300	20 "	78 "
7	Ascending	Argyrol, 10 per cent.	3 "	3 "
9	Ascending	" 1 " "	40 "	29 "
55	Descending	Potassium iodide, 5 per cent.	1.5 "	13.5 "
54	Ventricle	" " 5 " "	1 "	1 "
10	Ascending	H ₂ O ₂ , 10 per cent.	1 "	2 "
4	Ascending	HgCl ₂ , 1/10,000	1 "	1 "

Results on the Cadaver.—The procedures carried out on cats were repeated on the cadaver. These comprised ascending and descending irrigations and irrigations from ventricle to spine. In addition it was possible and easy, since the lateral ventricle is easily located on the human subject, to pass fluid from the spinal subarachnoid space out through a needle inserted in the ventricle. The operative procedure in these experiments is much simpler than in the case of animals. The trephine opening is easily made with burr drills and a long needle inserted between two lumbar vertebræ serves for the spinal outlet or inlet.

In the earlier experiments on the cadaver, as in those on cats, the brain persistently floated against and obstructed the trephine opening in ascending irrigations, despite all such attempts to prevent it as changing the position of the trunk and head, but the use of a fenestrated rubber tube inserted through a slit in the dura was sufficient to remove this difficulty. A 1/4-inch black rubber tube

seemed to be the best kind. The flow is freest when the tube lies over the parietal or temporal lobes but when it lies forward over the frontal lobe or backward over the occipital, the fluid will find its way to those parts of the brain. No obstruction to the flow occurred in the descending injections. From 35 to 80 c.c. of fluid escapes from the burette before it can be detected at the outlet, and from five to ten minutes are consumed in its passage.

Cadaver. Ascending irrigation. The stippling indicates the areas colored by the solution. The cross shows the location of the trephine opening.

In the cadaver a much smaller proportion of the brain comes in contact with the irrigating fluid than is the case with animals. Unless the inner end of the tube lies anteriorly or posteriorly, the fluid will flow up or down through the anterior portion of the Sylvian fissure. Plate I illustrates about the parts colored whether the flow be ascending or descending. The basal region is always deeply

colored. In the ventricular irrigations, whether ascending or descending, the fluid passes through the openings under the cerebellum and of the brain, only the basal region is stained. All ventricles are stained but the lateral ventricle on the side opposite to the ventricular puncture less deeply so.

In these experiments the arachnoid apparently never offered an important obstacle to the flow. When the solution was introduced into the cranial subdural space it usually passed downward partly under the dura and partly under the arachnoid, but in places like the occipital region where the brain lies in close approximation to the skull, the fluid passed almost immediately through the arachnoid to escape by the way of the sulci. That part of the fluid that continued downward in the subdural space usually passed through the arachnoid at the foramen magnum.

Discussion.—These experiments have demonstrated that it is possible to irrigate the subarachnoid space from one extremity to the other in either direction, from the lateral ventricle to the lumbar region of the spine, and in the cadaver from spine to ventricle; and also that it is possible to employ in these irrigations weak solutions of neutral formalin, boric acid, potassium permanganate, lysol and argyrol, without causing the death of the animal.

In this procedure it would seem we have a method of testing the toxicity and action of drugs in the meningeal spaces which is superior to procedures now in use because it is possible to bring the drug into contact with the entire surface of the nervous system and to maintain it there in a known concentration for considerable periods of time, and under pressure conditions not greatly different from those of the spinal fluid. With drugs in the meningeal spaces there is, of course, a double physiological action, (1) that resulting from their presence in the spaces and (2) that due to the drug absorbed into the blood stream. To estimate the former factor, it would be necessary to determine the effect after injection into the blood stream and compare it with the double action in the meningeal spaces.

It would also seem that this procedure offers a very satisfactory approach to a study of the physiology of the cerebrospinal fluid. Solutions of varying concentrations of salts, sugars or other substances can be practically substituted for the spinal fluid for long periods and the physiological and anatomical effects observed.

Whether the procedure can be applied in human therapeutics is a very doubtful question. Judging from the experiments on the cadaver, the mechanical part is entirely possible, but doubt remains

as to the ability of the human nervous mechanism to tolerate the solutions under the same conditions as animals. It must be remembered that in animals the operation is a difficult one and untoward symptoms frequently develop without warning. The experiments of Keen (6), Cushing (8) and others afford somewhat encouraging examples, but they by no means parallel this procedure. If at all applicable it would be in desperate conditions, such as septic, pneumococcus or tuberculous meningitis, for which little can be done otherwise and in which almost any risk is justifiable.

In certain cases of epidemic meningitis, too, it should be desirable to bring Flexner's serum in contact with the medulla. As shown by the experiments on the cadaver and also by the work of Dandy and Blackfan, this can be accomplished by following a subdural or intraventricular injection by lumbar puncture.

Conclusions.—By employing a suitable technic it has been possible both with animals and the human cadaver to pass solutions from one extremity of the subarachnoid space to the other.

In the case of animals, solutions were passed from the spinal subarachnoid space out through a cranial trephine opening, in the opposite direction and from a lateral ventricle through the spinal subarachnoid space. In the case of the cadaver, in addition, solutions were passed from the lumbar region of the spine out through a needle inserted into a lateral ventricle.

In animals the solutions came in contact with practically all of the surface of the central nervous system, whatever the procedure. With the cadaver, however, the base and only a limited part of the convexity, that in the neighborhood of the trephine opening, are touched. In ventricular irrigations on the cadaver, whether ascending or descending, only the basal and medullary regions come in contact with the solution.

The following antiseptic solutions were successfully used in the irrigations on animals: formalin (neutral) 0.5–0.25 per cent., boric acid 3 per cent., potassium permanganate 1–2,500, lysol 1–300, argyrol 1 per cent. Potassium iodide 3 per cent., hydrogen peroxide 10 per cent. and perchloride of mercury 1–10,000 were toxic.

It is the belief that this procedure offers a useful method of investigating the action of drugs in the meningeal spaces and perhaps of studying the physiology of the cerebrospinal fluid.

It is possible, also that it may be utilized in patients suffering from certain types of meningitis to clear away the exudate and to bring immune sera or antiseptic solutions into contact with the vital centers of the brain.

(I wish to acknowledge my indebtedness to Dr. E. E. Southard, of the Boston Psychopathic Hospital, for encouragement and many useful suggestions.)

BIBLIOGRAPHY

1. Key & Retzius. *Anatomie des Nervensystems und des Bindegewebe*. Stockholm, 1896.
2. Hill, L. *Experimental Pathology of the Cerebral Circulation*. Albutt's System, 1910, Vol. VIII, p. 3.
3. Id. *The Physiology and Pathology of the Cerebral Circulation*. London, 1896, p. 21.
4. Cushing and Weed. *Studies on the Cerebrospinal Fluid*. Jour. Med. Research, 1915-16, XXVI, 1.
5. Dandy and Blackfan. *Internal Hydrocephalus, an Experimental, Clinical and Pathological Study*. Am. Jour. Dis. Children, 1914, VIII, 406; 2d contribution, *Ib.*, 1917, XIV, 424.
6. Keen—see Keen & Ellis. *Removal of Brain Tumor*. Jour. Am. Med. Assn., 1918, LXX, 1905.
7. Lannelongue: quoted by Barlow. *Tuberculous Meningitis*. Albutt's System, 1910, Vol. VIII, p. 201.
8. Cushing and Sladen. *Obstructive Hydrocephalus following Cerebrospinal Meningitis, with Intraventricular Injection of Antimeningitic Serum (Flexner's)*. Jour. Exp. Med., 1908, X, 545.