

AN EXPERIMENTAL AND CLINICAL STUDY  
OF INTERNAL HYDROCEPHALUS\*

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Numerous methods have been suggested for the treatment of internal hydrocephalus, none of which have been productive of satisfactory results. So long as the etiology of this condition remains obscure, the treatment must necessarily be only symptomatic. In the hope of clarifying its etiology and thus affording a rational working basis for its relief, we have undertaken this investigation.

The present communication, which is presented as a preliminary report, includes observations on dogs after the production of experimental hydrocephalus, together with observations on patients suffering from the disease. We have also considered the manner and the place of formation and of absorption of the normal cerebrospinal fluid and the relation of these factors in the production of this pathologic condition.

## HYDROCEPHALUS EXPERIMENTALLY PRODUCED

From a survey of the literature we have been unable to find any record of hydrocephalus having been produced experimentally. In our experiments an obstruction has been placed in the aqueduct of Sylvius, and thus the only way of exit for the cerebrospinal fluid from the third and the lateral ventricles has been occluded. An internal hydrocephalus has invariably resulted. The following is the procedure:

A bilateral suboccipital decompression is made through an occipital midline incision. After exposure of the cerebellum it is retracted upward, and the foramen of Magendie carefully enlarged by incising the membrane joining the cerebellum and medulla. A piece of cotton in a small gelatin capsule, placed on the end of a graduated carrier, is inserted through this enlarged foramen of Magendie and gently passed along the floor of the fourth ventricle into the aqueduct of Sylvius, where it is deposited by withdrawal of the carrier. The symptoms which are observed following the operation are principally lethargy and vomiting (general pressure symptoms) dating from the time of operation. When carefully performed there are no irritative or destructive symptoms from the operation. This hydrocephalus therefore is due to a purely mechanical obstruction in the aqueduct, as there is no interference with the veins of Galen.

Since the venous obstruction is considered a possible cause of hydrocephalus, a series of experiments was conducted in which the vein of Galen and the straight sinus were ligated. In none of these cases did hydrocephalus result.

## ABSORPTION OF THE CEREBROSPINAL FLUID

There are many theories concerning the place and manner of the absorption of cerebrospinal fluid. In the study of absorption in the experimental and clinical work we have used almost exclusively phenolsulphonephthalein. This inert colored solution, first introduced into practical medicine as a renal test by Rowntree and Geraghty, has since been shown to be an accurate index of fluid absorption when the renal function is normal. It is very stable, is excreted in the urine with great

rapidity, is easily detected in minute traces and is readily adapted to accurate quantitative estimation.<sup>1</sup>

Since an internal hydrocephalus can be experimentally produced by occluding the aqueduct of Sylvius, it is evident that absorption of fluid from the ventricles is less rapid than its production. In the studies of the absorption from the ventricles of patients with an internal hydrocephalus due to obstruction in the aqueduct, after the introduction of phenolsulphonephthalein in the lateral ventricles, there is excreted in the urine from 0.25 to 1 per cent. during a period of two hours; but when it is injected into the subarachnoid space of the same patient there is an excretion of from 35 to 60 per cent. in the urine in the same period of time. This demonstrates that the absorption of cerebrospinal fluid takes place almost entirely in the subarachnoid space.

It is evident that the fluid must be absorbed either into the blood or lymph-vessels. When phenolsulphonephthalein or other inert colored solutions are injected into the subarachnoid space, they appear in the lymph of the thoracic and right lymphatic ducts only after an interval of from thirty to fifty minutes, and only a faint trace is present even after two hours, whereas, they appear in the blood in three minutes and in the urine in six minutes and, as mentioned above, from 35 to 60 per cent. is excreted in the urine at the end of two hours. These facts indicate that the cerebrospinal fluid passes directly into the blood and that the lymph-vessels are not concerned in its absorption. There are three principal views regarding the manner in which the cerebrospinal fluid passes into the blood: (1) by means of stomata arranged along the venous sinuses; (2) through the pacchionian granulations, and (3) by a general process of osmosis.

When a suspension of fine granules is injected into the subarachnoid space the granules do not pass into the blood except in very minute quantities and after a long interval of time. Consequently the assumption of special openings (stomata) from the subarachnoid space into the venous sinuses seems unlikely. This applies to granules injected into the subarachnoid space under normal conditions of pressure. If pressure is used, especially on young tissues, foreign materials can easily be forced into the veins. In adult animals this requires a very high pressure. It should be noted that stomata were formerly believed to exist in the peritoneum to explain the absorption from this cavity, but this has been shown not to be the case.

That the pacchionian granulations do not play any special rôle in absorption can, we think, also be shown. These granulations are absent in many species of animals, are always variable in number and size and develop principally in adult life. After fine granules are injected into the subarachnoid space, local collections are deposited along the sinuses—especially the superior longitudinal sinus—in the interstices of the fibrous meshwork which forms the walls of the sinuses. These deposits are in all essentials similar to those in the pacchionian granulations. There is always a layer of dura and arachnoid separating these masses of granules from the blood in the veins. This is a much greater mechanical barrier to absorption than is present in the exposed capillaries of the pia-arachnoid.

After the injection of phenolsulphonephthalein into the spinal subarachnoid space (the communication with

1. It should be emphasized, however, that ordinary solutions of phenolsulphonephthalein are made up in alkali, which is sufficient to militate against its use in the central nervous system. To overcome this defect we use a neutral solution specially prepared for us by Hynson, Westcott & Co.

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the cerebral subarachnoid space being closed), there is found to be a quantitative absorption proportionately as great as from the entire subarachnoid space. This shows that the absorption from the spinal subarachnoid space is similar to that from the cerebral. It is obvious, therefore, that cerebrospinal fluid is absorbed by a diffuse process from the entire subarachnoid space and is not restricted to any special locality, as, for instance, the region of the venous sinuses or the paccionian granulations. From the foregoing observations, absorption from the subarachnoid space appears to be very similar to that from the pleural and peritoneal cavities, though it is somewhat less rapid.

#### FORMATION OF THE CEREBROSPINAL FLUID

It has long been known that there is an active formation of cerebrospinal fluid as evidenced by the rapidity with which the fluid reforms after it has been withdrawn either by lumbar or ventricular puncture. The endowment of the chorioid plexus with an elaborate blood-supply indicates that it is a structure with a special function. Since the work of Faivre (1854) and Luschka (1855) showing the secretory character of the cells, the chorioid plexuses have been regarded as glands, from which at least part of the cerebrospinal fluid is formed. The discovery of secretory granules by *intra-vitam* staining by Francini, and also by Bibergeil and Levaditi, leaves but little doubt as to the secretory nature of this function.

We have shown that practically no absorption takes place in the ventricles, at least under the pressure from an abnormal accumulation of fluid. Since this is true and since hydrocephalus results from an experimental block in the aqueduct of Sylvius, it is evident that the fluid forms in the ventricles. These facts demonstrate an irreciprocal permeability of the fluid-forming structures, and emphasizes the secretory rather than the mechanical formation of the cerebrospinal fluid.

#### OBSERVATIONS ON PATIENTS WITH HYDROCEPHALUS

In these cases we have applied the phenolsulphonephthalein test in order to determine the amount of absorption from the ventricles, the amount of absorption from the subarachnoid spaces and whether or not there was free communication between the ventricles and the subarachnoid spaces. Subsequently the results of these tests have been compared with the pathologic findings. Phenolsulphonephthalein, as has been said before, is perfectly harmless, and when used for injection into the ventricles or subarachnoid spaces produces no reaction.

From observations made on patients without hydrocephalus it has been possible to establish a normal standard for the excretion of phthalein after its injection into one or the other of these cavities. In all cases the kidney function has been shown to be normal. When injected into the ventricles phenolsulphonephthalein normally appears in the urine in from ten to twelve minutes, and after two hours from 12 to 20 per cent. is excreted. After its injection into the subarachnoid space, it appears in the urine in from six to eight minutes, and from 35 to 60 per cent. is excreted in two hours.

When phenolsulphonephthalein is injected into the ventricles, it appears in the lumbar spinal fluid within two or three minutes. In hydrocephalus this becomes a most important test, for it enables one to determine accurately the patency or obstruction of the channels of exit from the ventricles to the subarachnoid space. Furthermore, fluid passes upward into the ventricles after the injection of phenolsulphonephthalein into the lumbar subarachnoid space.

By comparing the results of these tests with those obtained in hydrocephalus, we are enabled to establish two types of this disease. In the first type, after the injection of phenolsulphonephthalein into the ventricles, the time of its appearance in the urine is greatly delayed (from twenty to forty-five minutes) and the quantity excreted in two hours is practically negligible (from 0.25 to 1 per cent.). The excretion of phenolsulphonephthalein in this group after its injection into the subarachnoid space, however, is practically normal (time of appearance from six to eight minutes, quantity excreted in two hours from 35 to 60 per cent.). Furthermore, after the injection of phenolsulphonephthalein into the ventricles, it has not, in the cases observed, appeared in the spinal fluid. In this group, we have found at necropsy an obstruction to the passage of cerebrospinal fluid from the ventricles to the subarachnoid space. In two cases there was a congenital closure of the aqueduct of Sylvius, a third showed old adhesions obliterating the basal foramina of Magendie and Luschka, and in the fourth these foramina were closed by a thick tuberculous exudate which completely covered the base of the brain.

In the second type the excretion of phenolsulphonephthalein after its injection into the subarachnoid space is greatly diminished (from 8 to 15 per cent.), and the appearance time delayed (from twenty to thirty minutes). The amount excreted after its injection into the ventricles likewise is greatly diminished, undoubtedly due to the low subarachnoid absorption. In contradistinction to the first type the communication between the ventricles and the subarachnoid space is open. This is shown by the prompt (from two to three minutes) appearance in the spinal fluid of phenolsulphonephthalein after its injection into the ventricles. We have had the opportunity of examining two patients of this type, but as yet have made no pathologic observations. In both there has been an antecedent history of meningitis, one of which was due to the meningococcus.

These two types of hydrocephalus may be readily differentiated by determining the patency or occlusion of the channels of exit from the ventricles. In Type 1 these channels are obstructed and hydrocephalus results because there is no absorption from the ventricles. In Type 2 the channels are patent and hydrocephalus is due to the diminished absorption from the subarachnoid space.

It is a pleasure to express our gratitude to Professors Halsted, Howland and Cushing for suggestions during the course of the work, and for the opportunity of carrying out these investigations.

#### SOME RECENT CONCLUSIONS ON ABDOMINAL ROENTGEN-RAY WORK

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At present the Roentgen-ray bismuth method of diagnosing conditions of the alimentary canal is generally utilized. Since the work of Holzknecht was advanced, roentgenologists, and following them, surgeons and internists, have been accepting various reports as diagnostic. During the present winter I have checked up my Roentgen-ray findings with those of the laboratory