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EXPERIMENTAL HYDROCEPHALUS*

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THE production of all types of hydrocephalus by precise experimental methods finally lifts the idiopathic veil and reveals hydrocephalus as a disease with a clearly defined etiology and pathology. The first evidence that hydrocephalus could be experimentally produced was incorporated in an article with Blackfan in 1913.[1] It was demonstrated that when a tiny obstructing body was introduced into the aqueduct of Sylvius of a dog, all the cerebral ventricles proximal to the occlusion became dilated; distally, the size of the fourth ventricle was not changed.

The following year, Thomas [2] published additional experimental evidence that hydrocephalus was caused by obstruction. Following the injection of aleuronat granules into the lateral ventricles, the iter became plugged; organization of the granules resulted in total occlusion of the opening and hydrocephalus followed.

As early as the middle of the eighteenth century, Haller, Brunner and Littré looked upon an obstruction to the outflow of the ventricular contents through the pituitary body as the cause of hydrocephalus. Such a theory of obstruction can only be regarded as fanciful, since vapor and not fluid was at that time regarded as the normal content of the ventricles; the pituitary body was erroneously regarded as the main avenue of escape for the vapor in the ventricles.

Magendie (1825) first described an anatomical obstruction at the base of the brain in several cases of hydrocephalus, but he was not entirely convinced that the obstruction was the cause, because he regarded the pia as the source of all cerebrospinal fluid. Reasoning from this viewpoint, he

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† These studies have been conducted in the laboratories of Professor Halsted. His suggestions have been invaluable in the development of many new problems in a virgin experimental field. The success of many of the crucial experiments is in large part due to consultations with him.

[1] Dandy, W. E., and Blackfan, K. D.: Internal Hydrocephalus. An Experimental, Clinical and Pathological Study. J. Am. M. Assn., 1913, lxi, 2216. Also Am. J. Dis. Child., 1914, viii, 406; Am. J. Dis. Child., 1917, xiv, 424; Beitr. z. klin. Chir., 1914, xciii, 392.

[2] Thomas, W. T.: Experimental Hydrocephalus. J. Exper. Med., 1914, xix, 106.

expected an obstruction to cause dilation of the ventricles posterior rather than anterior to the obstruction. Throughout his publications he was much perplexed by his inability to correlate these pathological findings with his physiological conceptions. He never suspected the choroid plexus as the organ of secretion of the cerebrospinal fluid. The findings, therefore, were inconclusive. Despite his mistaken interpretations, the cases stand as probably the first in which a mechanical obstruction was described and considered to have a bearing on the disease.

Two additional discoveries of the greatest importance were made by Magendie, without which any consideration of the etiology of hydrocephalus would still be useless. He first established the fact that fluid and not air or vapor fills the ventricles and the subarachnoid space in the living; and he discovered the foramen of Magendie, an opening which establishes communication between the ventricular system and the subarachnoid space.

Hilton (1860) did a great deal more to confirm the view that obstruction was the cause of hydrocephalus. He accurately described and made drawings of obstructions in three cases of hydrocephalus; in one a stenosis was in the aqueduct of Sylvius, and in two cases the foramen of Magendie was closed by a scar. In each, hydrocephalus resulted proximal to the obstruction. Numerous examples of obstruction have since been added, but with little additional influence in overcoming a very strong prejudice against the acceptance of the obstructive theory of hydrocephalus.

Opposed to the obstruction theory was the impressive argument that in most cases of hydrocephalus there was no obstruction, and even no cause of any kind could be found. Those who held this negative opinion looked upon obstruction in the remaining cases as purely incidental and in no way etiological; all cases of hydrocephalus were considered idiopathic.

A third school conceived two entirely different types of hydrocephalus: (1) in which an obstruction produced the disease, and (2) in which no cause could be found. The second type they regarded as idiopathic.

The existence of the foramen of Magendie is even now disputed by eminent authorities. Magendie himself admitted, as is now well recognized, that his foramen is not present in dogs and other animals. Why then should it be significant for man? Many still consider this foramen an artefact, as other foramina which have been described have proved to be.

In 1855 Luschka made a discovery which clarifies much of the earlier confusion and makes a theory of obstruction tenable. He discovered two additional openings between the fourth ventricle and the subarachnoid space, making with the foramen of Magendie three in all. These openings, now known as the foramina of Luschka, are also present in all animals; their presence makes it clear why the foramen of Magendie may be absent without hydrocephalus.

But the knowledge of the anatomy of the cerebrospinal spaces and the circulation of the cerebrospinal fluid in these spaces has been very vague. If the fundamental facts are so uncertain, any discussion of the etiology

of the disease must be fruitless. The experiments here presented will clear any uncertainty about the grosser anatomy of the cerebrospinal spaces as well as the normal circulation of the cerebrospinal fluid and the results following the interference with the normal pathways for this circulation.

A very simple experiment will demonstrate the existence of a communication between the ventricles and the subarachnoid space. If phenolsulphonaphthalein or any other inert colored solution is injected into a lateral ventricle it will quickly appear in the spinal fluid removed by lumbar puncture. The location of the communication can be demonstrated by the exclusion of the third and both lateral ventricles, thus limiting the communication to the fourth ventricle. If the aqueduct of Sylvius is occluded experimentally or if, in a patient, it is occluded by any pathological process, the colored solution will not appear in the spinal fluid following an intraventricular injection. This limits the location of the communication to the fourth ventricle. This communication is by the foramina of Luschka and Magendie, can be demonstrated in any brain at necropsy. At any cerebellar operation the foramen of Magendie can easily be seen. So necessary are these openings that when all are absent, as indicated by the phenolsulphonaphthalein test, an internal hydrocephalus invariably must result. The presence of a communication can also be demonstrated by the introduction of air into the lateral ventricle. The air will pass externally and appear in the cisternæ and the sulci over the cerebral hemispheres. The air can be photographed in the X-ray,[3] and it can even be seen passing through the foramen of Magendie into the cisterna magna if one makes a fluoroscopic examination.[4] By these simple tests the possibility of producing an artefact is out of question. The remaining anatomical and physiological facts will be deduced from the succeeding experiments.

HYDROCEPHALUS PRODUCED BY PLACING AN OBSTRUCTION IN THE AQUEDUCT OF SYLVIUS

These experiments were conducted on dogs, under ether anæsthesia. The midportion of the squamous occipital bone, including the posterior margin of the foramen magnum, was removed with rongeurs and the dura opened in a stellate fashion. By gently elevating the cerebellum, the roof of the fourth ventricle was exposed, perforated, and a tiny piece of cotton cautiously pushed forward on the point of a fine graduated carrier. It was passed over the medulla and pons until it glided into the aqueduct of Sylvius, where it was deposited by withdrawal of the carrier. An improved technic of this procedure consists in inclosing the cotton in an oiled gelatin capsule, which soon dissolves in the cerebrospinal fluid (Fig. 1). The aqueduct of Sylvius is fairly easily recognized by the sense of touch imparted to the

[3] Dandy, W. E.: Ventriculography Following the Injection of Air into the Cerebral Ventricles. ANNALS OF SURGERY, July, 1918.

[4] Dandy, W. E.: Fluoroscopy of the Cerebral Ventricles. Bull. Johns Hopkins Hosp., February, 1919.

finger which is directing the entry of the obstruction. The constriction at the terminus of the funnel-like approach from the wide fourth ventricle denotes the entrance to the narrow aqueduct of Sylvius. The iter is, moreover, at a constant measured distance from the posterior border of the cerebellum. If the head is not held in a strictly median position, it is easily possible to make a false passage into the contiguous soft brain tissue, with permanent injury to the pyramidal tract and the nuclei of the cranial nerves.

By producing hydrocephalus with a tiny obstruction in the aqueduct of Sylvius, the etiological rôle of an occlusion is absolutely established. Being a single precise process and involving no neighboring structures, other possible explanations of the resultant hydrocephalus are precluded. When an obstruction is present in any part of the ventricular system, the ventricles always dilate anterior to the occlusion. Following occlusion of the aqueduct of Sylvius, therefore, the third ventricle and both lateral ventricles become distended. The size of the fourth ventricle remains unchanged.

Fig. 2 shows sections of dog's brain one month after the obstruction was introduced. Doubtless, for some time after the cotton was placed in the iter, there was only a partial occlusion, which became complete with organization of the foreign body. The animals become lethargic and there is intermittent vomiting. Ventricular dilatation is accompanied by a corresponding degree of cerebral destruction. The experiments were all performed on dogs after union of the sutures of the skull, so that enlargement of the head could not occur. In animals operated on at birth or soon thereafter, the characteristic hydrocephalic enlargement of the head will necessarily be an outstanding feature which cannot be duplicated when the animal is older.

From this series of experiments we have absolute evidence, (1) that *cerebrospinal fluid forms in the cerebral ventricles;* (2) that *absorption of fluid in the ventricles is at least less than the production;* (3) that *the aqueduct of Sylvius is a necessary outlet from the third and both lateral ventricles;* and (4) that *there are no collateral channels which assume the function of the iter when it is occluded.*[5]

UNILATERAL HYDROCEPHALUS PRODUCED BY OCCLUDING ONE FORAMEN OF MONRO

Since the third and both lateral ventricles distend following occlusion of the aqueduct of Sylvius, it is reasonable to expect that an obstruction at one foramen of Monro will produce dilatation of the corresponding lateral ventricle; that is, a unilateral hydrocephalus.

Spiller [6] has published a case of unilateral hydrocephalus with occlusion of one foramen of Monro. The occlusion of the foramen was due to a cica-

[5] For the data concerning the place and manner of formation and absorption of cerebrospinal fluid, the reader is referred to the article previously cited in the American Journal of the Diseases of Children.

[6] Spiller, W. G.: Two Cases of Partial Internal Hydrocephalus from Closure of the Interventricular Passages. Am. J. M. Sc., 1902, p. 44. Also J. Am. M. Assn., 1907, xlviii.

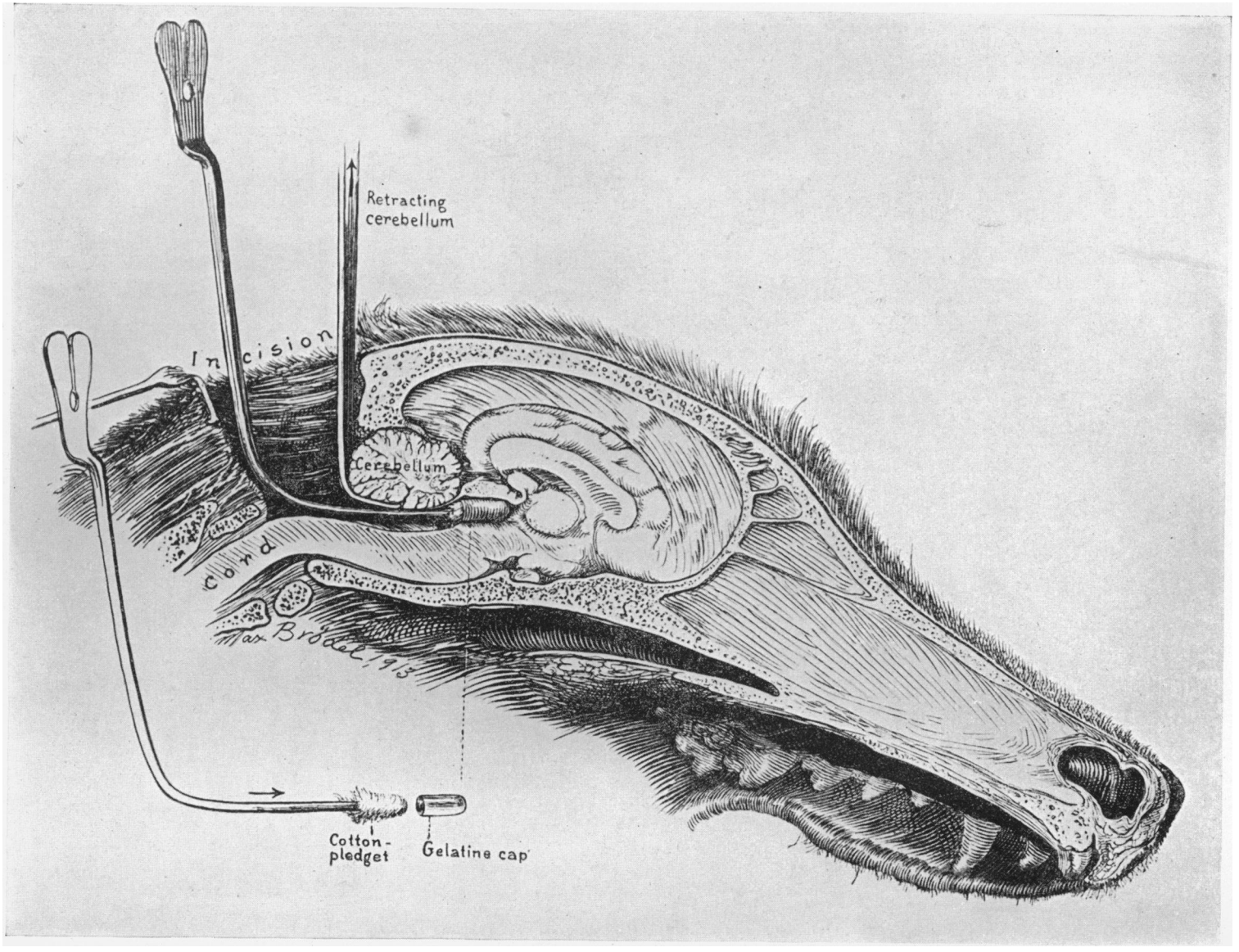


FIG. 1.—Mid-sagittal view of a dog's head to illustrate the method of procedure in occluding the aqueduct of Sylvius. By this method hydrocephalus results, involving the third and both lateral ventricles.

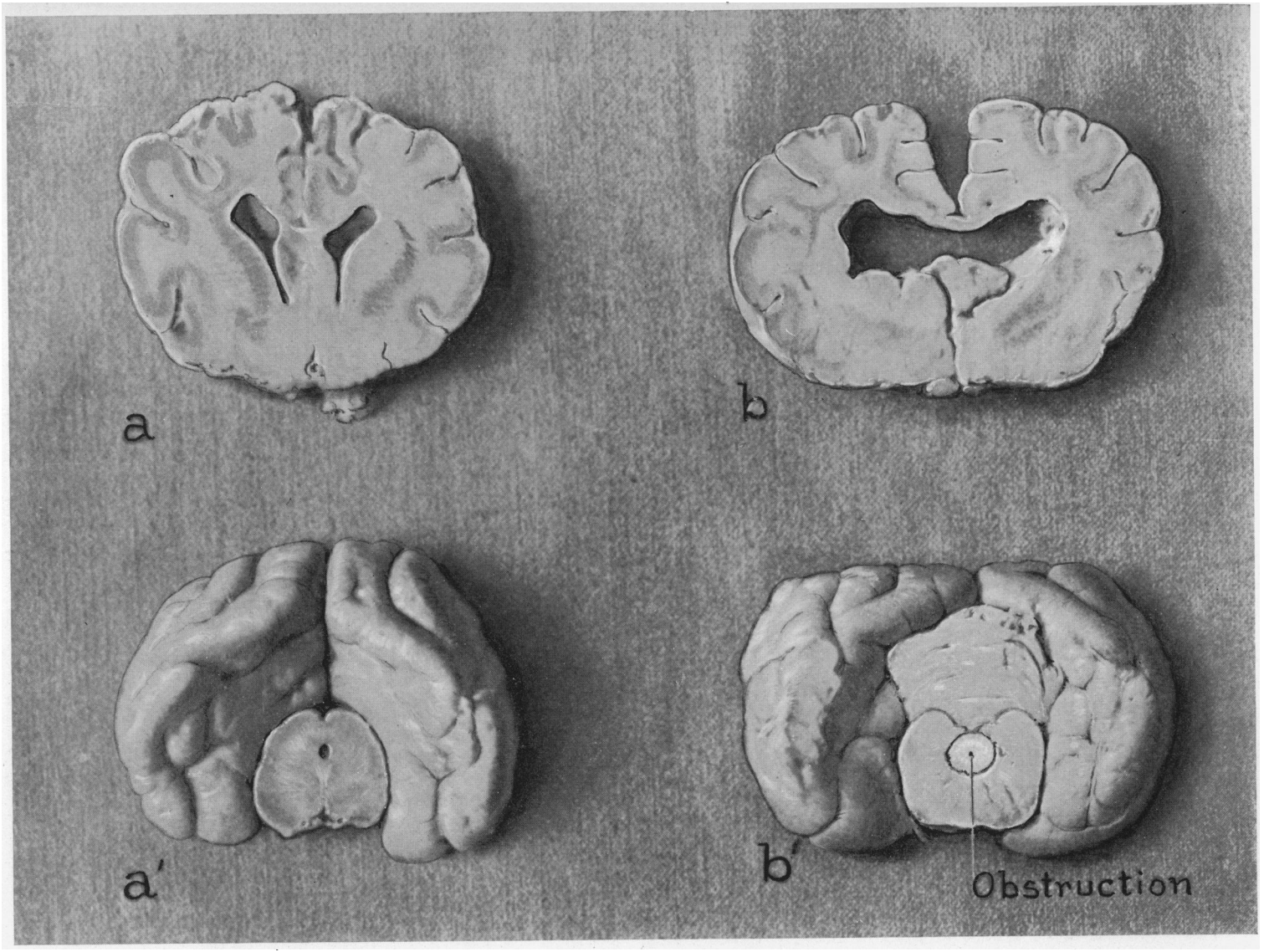


FIG. 2.—Hydrocephalus of one month's duration resulting from an occlusion placed in the aqueduct of Sylvius (*b* and *b'*), as demonstrated in Fig. 1. *a* and *a'* are sections of a normal dog's brain at levels corresponding to *b* and *b'*. Note the fusion of both lateral ventricles (in *b*) following atrophy of the septum lucidum. The obstruction is shown in the latter (*b'*).

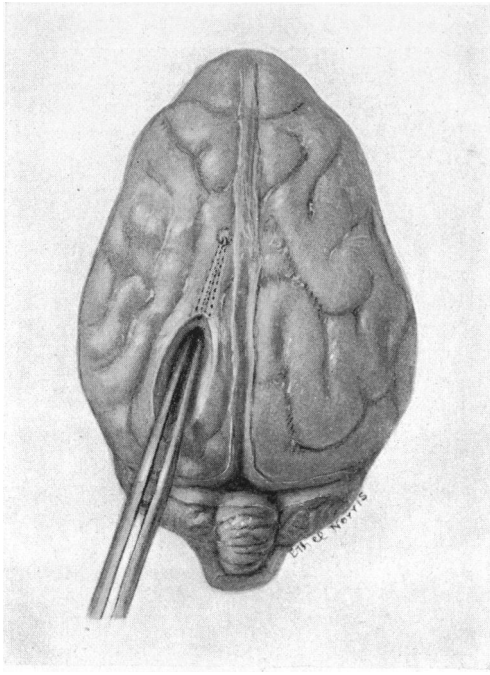


FIG. 3.—To demonstrate the method of introducing a piece of fascia into the foramen of Monro of a dog's brain. A transcortical incision into the ventricle at this point also permits complete choroid plexectomy of one lateral ventricle. Being well posterior, injury to the pyramidal tract is also avoided.

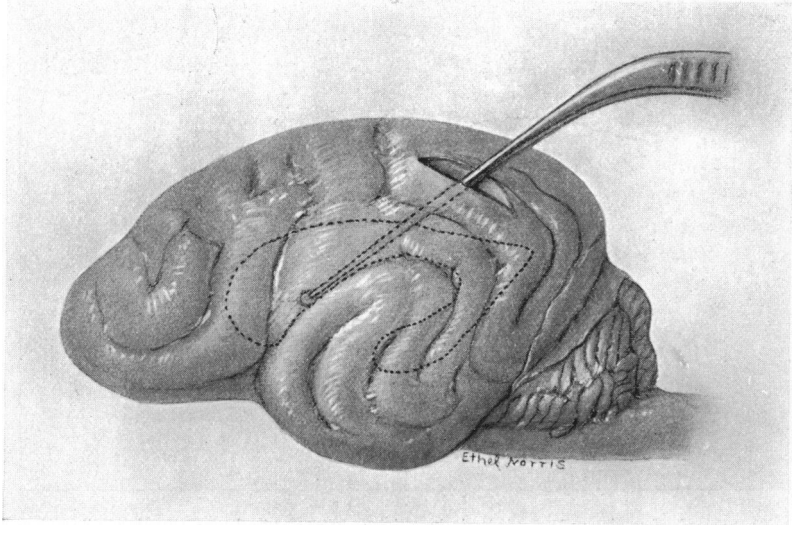


FIG. 4.—Lateral view of a dog's brain to show method of occluding the foramen of Monro. The outline of the lateral ventricle is shown by a dotted line.

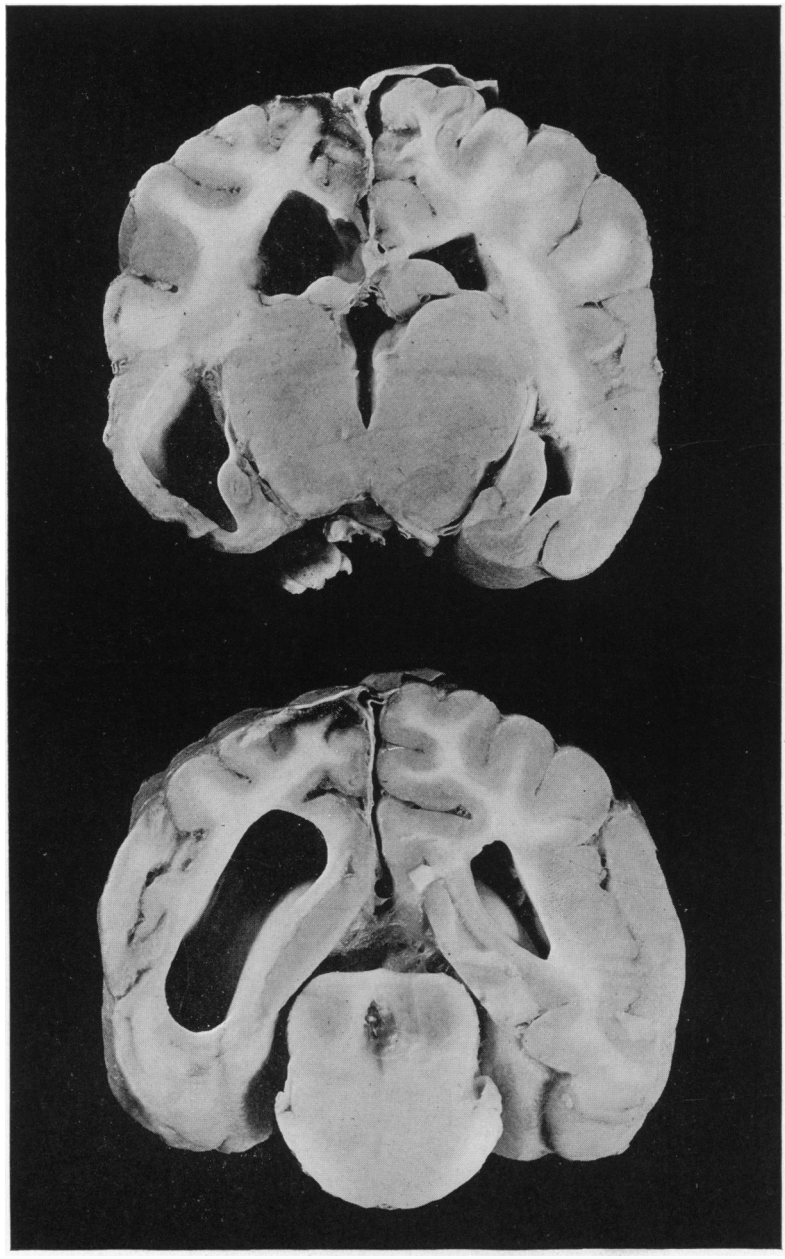


FIG. 5.—Photograph of sections of a dog's brain in which a unilateral hydrocephalus has followed occlusion of the left foramen of Monro. The right ventricle is normal.

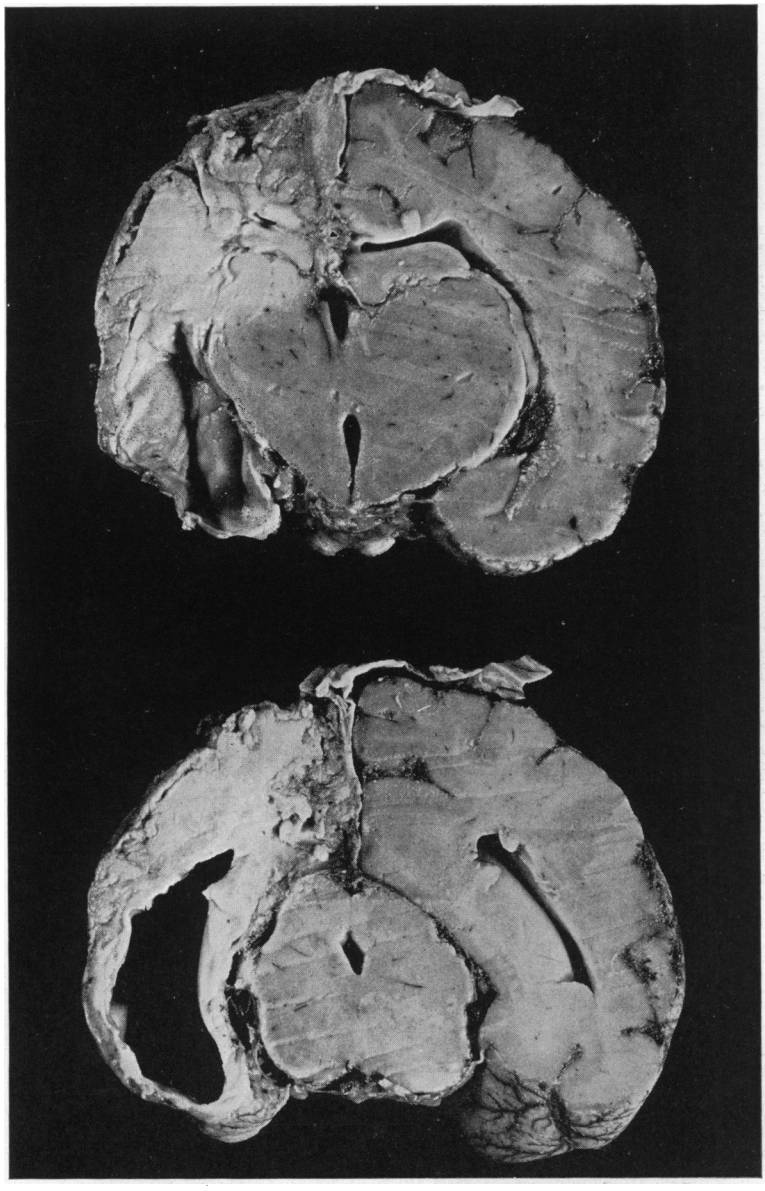


FIG. 6.—Views of another brain with unilateral hydrocephalus. Note the thinning of the cortex as contrasted to the normal (right). The scar in the cortex (upper photograph) is due to closure of the transcortical incision. A ventricular fistula never follows opening the ventricle.

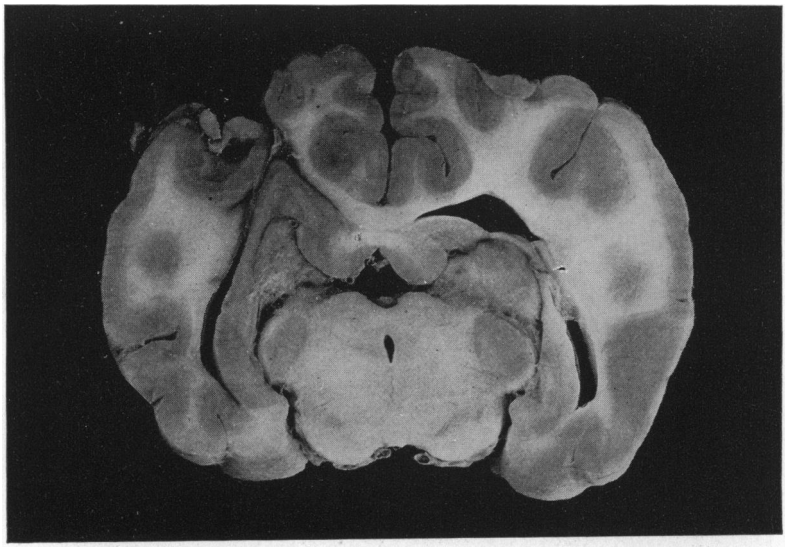


FIG. 7.—Section of a dog's brain three months after the left foramen of Monro was blocked, *but in which the entire choroid plexus of this ventricle was removed.* The left ventricle is a mere slit, the right ventricle is normal. The transcortical defect is shown in the left side. Contrast the left ventricle in Figs. 5, 6, and 7. In all, the foramen of Monro has been occluded but removal of the choroid plexus (Fig. 7) prevents hydrocephalus from forming. This is absolute evidence that the choroid plexus secretes cerebrospinal fluid and that eperndyma takes no part in its formation.

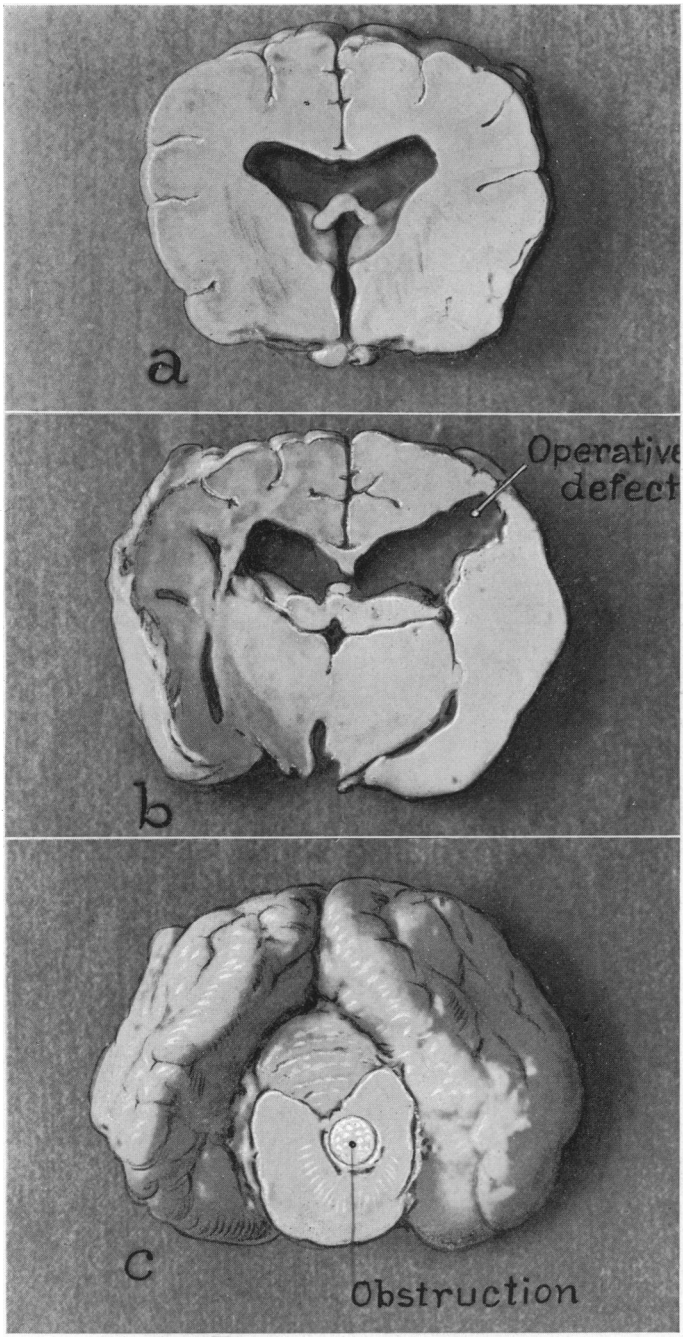


FIG. 8.—Sections of a dog's brain showing hydrocephalus of five weeks' duration resulting after occlusion of the aqueduct of Sylvius, *but in which the choroid plexus of both lateral ventricles was removed* at the same operation. The accumulated cerebrospinal fluid forms solely from the choroid plexus of the third ventricle. Since both foramina of Monro are patent the distention of the lateral ventricles is a necessary sequel to the obstruction in the aqueduct of Sylvius. The remains of the septum lucidum are still evident in *b*. The obstruction (*c*) is slightly beyond the midline but effectively closes the iter.

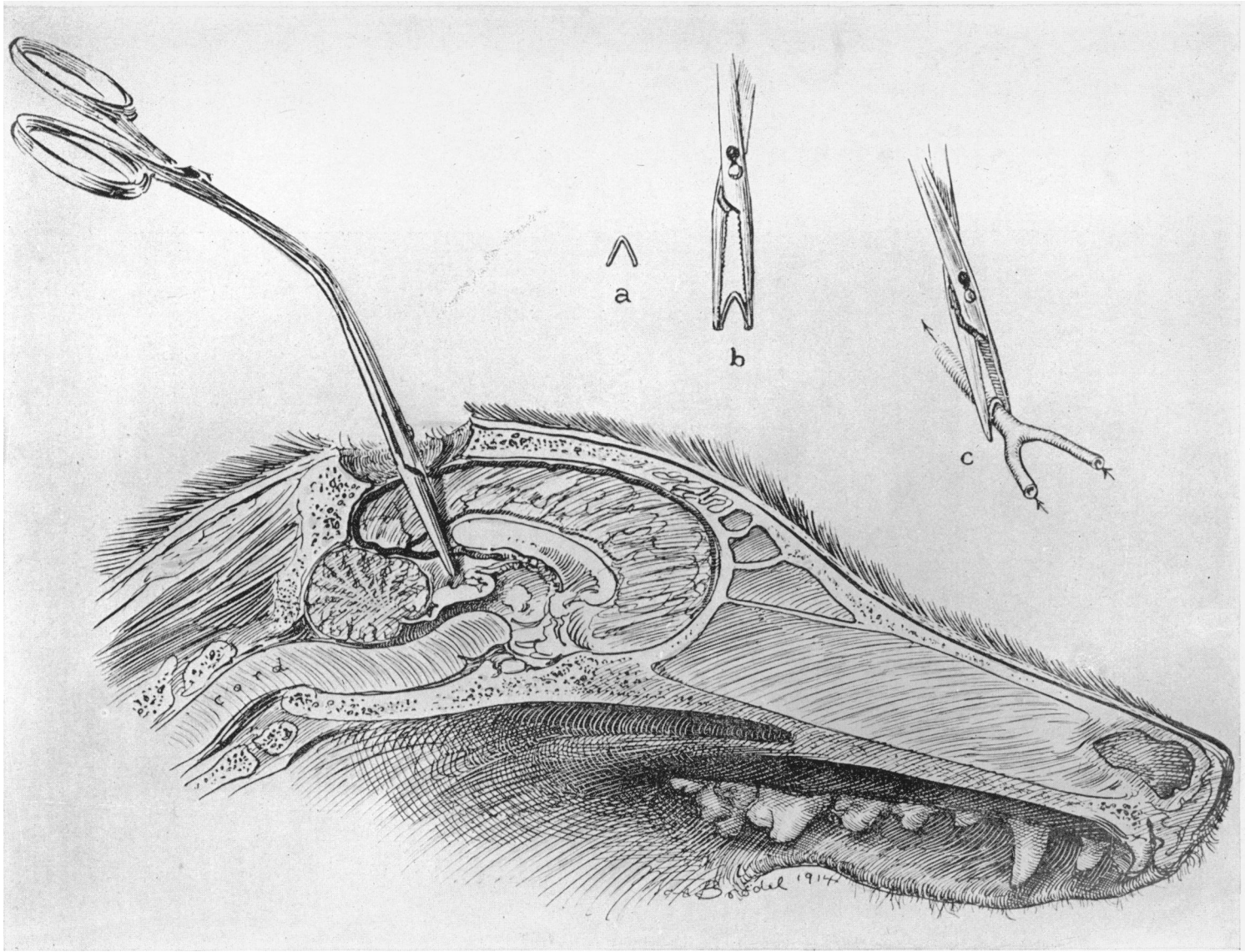


FIG. 9.—Illustration of the method of procedure in ligating the great vein of Galen in a dog. A silver clip is placed astraddle of the vein which is very deeply situated.

trix, probably, of tuberculous origin. I have had under observation a case in which a pedunculated giloma was suspended in the left lateral ventricle and periodically closed the left foramen of Monro. With each occlusion severe headaches, vomiting, partial hemiplegia ensued. Following each attack there was complete subsidence of the signs and symptoms. Doubtless the free intervals were synchronous with the period in which the foramen of Monro was open. Gradually the attacks became more frequent and more violent, and one week before death a final attack began and terminated in death. The affected ventricle was greatly enlarged; the foramen of Monro was completely filled by the tumor which had been forced into the foramen and there became impacted. Part of this obstructing tumor could be dislocated, leaving the foramen of Monro only partially occluded.

The foramen of Monro of a dog can be blocked by inserting either a small piece of fascia or peritoneum (Figs. 3 and 4). Eventually the transplanted tissue becomes incorporated in a cicatrix and total occlusion of the foramen results. The foramen of Monro is reached for this procedure by a transcortical incision which opens into the body of the lateral ventricle well posteriorly. The opening in the brain is maintained by an open nasal speculum. Through this window the foramen of Monro can be seen well forward, where the choroid plexus makes a sharp turn into the third ventricle. The margins of the foramen are scarified before introducing the piece of peritoneum or fascia. The cortical defect is sutured with fine silk. A unilateral hydrocephalus develops on this side (Figs. 5 and 6). There is, of course, no change in the opposite lateral ventricle. Curiously, the cortical opening heals without formation of a ventricular fistula or hernia, despite the total occlusion of the foramen of Monro and the resulting accumulation of cerebrospinal fluid. The healing is similar to the spontaneous closure of an opening made in the corpus callosum for the attempted relief of internal hydrocephalus. It is almost impossible to maintain an artificial opening in a cerebral ventricle.

OCCLUSION OF THE FORAMEN OF MONRO AFTER REMOVAL OF THE CHOROID PLEXUS

The entire choroid plexus of one lateral ventricle can be removed through the same transcortical incision that is made in order to plug the foramen of Monro. If choroid plexectomy is to be done, the incision in the cortex should be even more posteriorly—into the posterior horn of the ventricle—so that the descending horn and the body of the lateral ventricle can be directly illuminated at the same time. The choroid plexus can then be seen through its entire extent. The choroid plexus is picked up with delicate forceps at the foramen of Monro and stripped from its attachment to the velum interpositum as far as the glomus. The tip of the choroid plexus in the descending horn is then picked up and stripped in a similar manner until the glomus is reached. In this way the entire choroid plexus can be removed in one piece.

Numerous tiny blood-vessels enter the choroid plexus through its narrow edge of attachment to the ventricular wall. The vessels, however, are quite small, and the slight bleeding can be easily controlled by pledgets of cotton moistened in warm saline solution.

If the entire choroid plexus is removed and the foramen of Monro is blocked at the same time, the ventricle becomes obliterated (Fig. 7). A marked contrast is produced by blocking the foramen of Monro on the opposite side without removal of the choroid plexus. Both foramina of Monro being occluded, a collapsed ventricle results on the side from which the choroid plexus has been removed, but the ventricle becomes greatly enlarged on the side in which the choroid plexus is intact. From these experiments *we have the only absolute proof that cerebrospinal fluid is formed from the choroid plexus. Simultaneously it is proven that the ependyma lining the ventricles is not concerned in the production of cerebrospinal fluid.*

EXTIRPATION OF THE CHOROID PLEXUS FROM BOTH LATERAL VENTRICLES FOLLOWED BY OCCLUSION OF THE AQUEDUCT OF SYLVIUS

In a few dogs the choroid plexus was extirpated from both lateral ventricles and at the same operation or shortly thereafter the aqueduct of Sylvius was occluded. In these animals hydrocephalus developed and involved both lateral ventricles and the third ventricle (Fig. 8). There was, however, a pronounced retardation in the development of the hydrocephalus when compared with that which follows the introduction of a similar occlusion, but without a bilateral choroid plexectomy. Hydrocephalus develops because the amount of cerebrospinal fluid which is produced from the choroid plexus of the third ventricle and which cannot escape through the closed aqueduct of Sylvius, is still greater than the amount of the absorption which is possible from the three ventricles. The open foramina of Monro permit the fluid which is formed in the third ventricle to pass freely into and distend both lateral ventricles. We have tried removal of the choroid plexus of the third ventricle, but this has proved unsuccessful. The veins of Galen must be removed together with the roof of the third ventricle to obtain all the choroid plexus from the third ventricle. The animals always succumb to the effects of intraventricular hemorrhage if this operation is attempted. It would doubtless be possible (though we have not done it) to obliterate both lateral ventricles by occluding both foramina of Monro and later to obstruct the aqueduct of Sylvius, thereby producing enlargement of the third ventricle alone.

HYDROCEPHALUS FOLLOWING LIGATION OF THE VENA MAGNA GALENI

Hydrocephalus has often been attributed to an occlusion of the vena magna Galeni or sinus rectus, or both, but in most instances the evidence has been inconclusive. Hydrocephalus forming in this way would be analogous to ascites following stenosis of the inferior vena cava. In either instance the accumulation of fluid indicates an inadequate collateral circulation.

The vena magna Galeni drains the venous blood from the entire interior of the cerebrum, and these vessels, being largely terminal, have but little communication with the extracerebral veins. After the formation of the vena magna Galeni, however, numerous channels establish a free anastomosis between the intra- and extracerebral venous circulation. The basilar, superior cerebellar, temporal, internal occipital, posterior corpus collosal, and other veins bring the two systems into free communication.

Whether hydrocephalus results from venous stasis depends entirely upon the amount of collateral circulation which can develop. If both jugular veins are compressed in a dog, the amount of cerebrospinal fluid is immediately and rapidly increased. This increased production of fluid, however, disappears within a few minutes as the collateral venous circulation becomes established.

As early as 1768 Wyeth looked upon venous obstruction as an important factor in the production of hydrocephalus. Magendie (1825) records a case of thrombosis of the vena magna Galeni and sinus rectus. The symptoms were only of a week's duration, an interval too short to give a demonstrable dilation of the ventricles. As the determination of excess quantities of fluid postmortem is very unsatisfactory and untrustworthy, the diagnosis of early hydrocephalus may be questioned. In the vast majority of cases in which venous stasis is regarded as the cause of hydrocephalus, a tumor has been in the corpora quadrigemina, mesencephalon, corpus pinale, or elsewhere in the vicinity of the vena magna Galeni. Owing to the size of brain tumors, one is not justified in assuming that the hydrocephalus is due to a specific occlusion of the blood-vessels, especially since in the midbrain the aqueduct of Sylvius soon becomes obstructed by tumors; and this we know always results in hydrocephalus.

Undisputed increase of cerebrospinal fluid from a vascular occlusion can be assured only when a pure vascular obstruction exists, as in thrombosis. The authentic cases in which thrombosis of the vein of Galeni or straight sinus has caused hydrocephalus are few, but apparently definite. Newman [7] (1882) reports a case, and Browning [8] (1887) another. Undoubtedly, others have been described but have escaped notice. A few cases of a sharply localized thrombosis of the vena magna Galeni with hydrocephalus are sufficient to establish the causative relationship.

Experimentally, we have been able to establish this point with accuracy. In a series of ten dogs we have ligated the great vein of Galen and the straight sinus in varying places. In a single instance hydrocephalus resulted, and in this case the obstruction was placed at the point of origin of the large vein of Galen (Fig. 10). In the remaining 9 cases the size of the ventricles

[7] Newman, D.: Two Cases of Ventricular Hydrocephalus; One Due to Pressure on the Sinuses by a Tumor in the Cerebellum, the Other to Thrombosis of Galen's Vein. Glasgow M. J., 1882, iii, 161.

[8] Browning, William: A Case of Internal Hydrocephalus Due to Disease (Thrombotic) in the Wall of the Straight Sinus. J. Nerv. and Ment. Diseases, 1887, xli, 260.

was not altered. In other words, hydrocephalus results when an occlusion of the great vein of Galen is located at its origin, but not when the obstruction is placed more distally or along the straight sinus. Above the origin of the great vein of Galen there is apparently sufficient venous collateral circulation to overcome the effects of the obstruction. In dogs, the vein of Galen can be fairly readily exposed at operation by retracting the occipital lobe and carefully dissecting the vein from its bed over the mesencephalon. For a very low occlusion, the splenium of the corpus callosum must be divided. The beginning of the vein of Galen can then be seen just above the pineal body. Ligation of the vessels by a ligature is difficult because of the depth of the wound. The same result is accomplished by compressing a small silver clip over the vessel at the desired point (Fig. 9).

The animal in which hydrocephalus resulted presented no symptoms which distinguished it from the others. The diagnosis of hydrocephalus was made solely from the post-mortem examination. The hydrocephalus developed very much more slowly than that following an occlusion of the aqueduct of Sylvius. In hydrocephalus resulting from venous stasis, all the cerebral ventricles and the aqueduct of Sylvius are enlarged. In gross appearance hydrocephalus so produced is exactly similar to that in the hitherto so-called "idiopathic" or communicating hydrocephalus. The aqueduct of Sylvius, the foramina of Monro, Magendie and Luschka, all become enlarged, because the accumulation of fluid is due to over-production, and there is no obstruction to localize the dilatation. This type of hydrocephalus is different from other chronic types. It is due to over-production of cerebrospinal fluid, whereas other forms are due to a diminished absorption. Possibly this type of hydrocephalus may subsequently be differentiated clinically, but we have had no case under observation. It must be quite rare, for from the pathological examinations of over thirty cases of hydrocephalus we have not encountered a single occlusion of the great vein of Galen or of the straight sinus.

CHANNELS FOR THE CIRCULATION OF CEREBROSPINAL FLUID IN THE SUBARACHNOID SPACE

Before considering the cause and the experimental production of the communicating type of hydrocephalus, it will add clearness to briefly consider the normal channels through which the cerebrospinal fluid is distributed. As heretofore mentioned, all the cerebrospinal fluid in the ventricular system must pass into the subarachnoid space through the three basal foramina of Luschka and Magendie. Of these foramina, not infrequently one or even two may be obliterated, and the third alone will maintain adequate communication. The arrangement of the channels of the subarachnoid space is in a general way that of the trunk and branches of a tree. The basal cisternæ—forming a water-bed under the brain stem and artificially subdivided into the cisterna cerebellomedularis (cisterna magna), cisterna pontis, cisterna interpeduncularis, cisterna chiasmatis—are homologous to the trunk

of the tree. From these cisternæ, fluid is distributed along the major branches of the subarachnoid space which accompany the blood-vessels and traverse the sulci between the cerebral convolutions. The exact number and the relations of the smaller channels have not yet been worked out. The closure of large areas of the subarachnoid space over either cerebral hemisphere, apparently produces no general effects on the absorption of cerebrospinal fluid because the main channels are intact and there is a sufficient absorbing area remaining to easily compensate for this loss. If, however, the cisternæ are obliterated, the trunk is occluded and fluid cannot reach the branches of the subarachnoid space which spread over both cerebral hemispheres. There are no collateral channels which can reëstablish this circulation of cerebrospinal fluid, consequently cerebrospinal fluid cannot reach the cerebral subarachnoid spaces where most of the absorption takes place. An obstruction in the cisternæ is comparable to transection of the trunk of a tree. Whereas death of the tree results from division of the trunk, only local effects result from the destruction of many branches. Occlusion of the cisternæ results in hydrocephalus; many of its branches may be obliterated without hydrocephalus.

The circulation of cerebrospinal fluid can be strikingly demonstrated by substituting India-ink for cerebrospinal fluid in an anæsthetized dog. The ink follows the normal channels of the subarachnoid space; by sacrificing the animals at varying intervals of time after the injection, the various stages of distribution can be observed. Almost immediately all the cisternæ are filled with ink; the cerebellar subarachnoid space also rapidly fills, owing to its intimate relationship with the cisterna magna. Gradually filaments of ink fill the sulci over all surfaces of both cerebral hemispheres; the sulci radiate from the cisterna and appear to anastomose over the cerebral hemispheres. In a series of animals it required from 45 to 75 minutes to reach the most remote spaces along the longitudinal sinus. Very artificial results follow injections of fluids under pressure. Incidentally, if it takes such a long period of time to reach the longitudinal sinus, the hypothesis that absorption occurs through special structures along the longitudinal sinus is immediately vitiated, because normally the rate of absorption from the subarachnoid space is 20 to 25 per cent. an hour (by the phenolsulphonaphthalein test). Therefore, 20 to 25 per cent. absorption has already occurred before the longitudinal sinus has been reached by the dye. Such an hypothesis is also precluded by the fact that a considerable part of this absorption takes place from the spinal subarachnoid space.

THE CAUSE OF HYDROCEPHALUS WITH COMMUNICATION

The type of hydrocephalus in which no pathology has been found and which has been regarded as idopathic hydrocephalus is characterized by dilatation of all the cerebral ventricles and by a free communication between the ventricular system and the subarachnoid space. By the phenolsulphonaphthalein test this type of hydrocephalus has been shown to be caused by

a diminished absorption from the subarachnoid space. It will be remembered that fluid normally forms in the cerebral ventricles but does not absorb there; that absorption takes place only in the subarachnoid space. Therefore, the aqueduct of Sylvius and the foramina of Luschka and Magendie must be patent to maintain the balance between the production and the absorption of cerebrospinal fluid. In communicating hydrocephalus there is a greatly reduced absorption, despite a perfectly free communication. By the phenolsulphonephthalein tests the absorption from the subarachnoid space has been shown to be only 10 per cent. in two hours, or about one-fifth of the normal rate of absorption from this space. The absorption of this dye from the ventricles in communicating hydrocephalus is also about one-fifth of the normal. The ventricular absorption, however, is but a reflection of the absorption from the subarachnoid space, since the absorption of ventricular fluid occurs only after it reaches the subarachnoid space.

In a recent paper [9] this type of hydrocephalus was shown to be due to adhesions which obliterated the cisternæ. The adhesions were not present over the entire brain, but mainly at the base and around the incisura tentorii; that is, where the major effects of meningitis are usually distributed. Obliteration of the cisternæ or a circle of adhesions around the mesencephalon prevents cerebrospinal fluid from passing to sulci over the cerebral hemispheres. Absorption of cerebrospinal fluid is a general process, which takes place from the entire subarachnoid space. With the major part of the subarachnoid space mechanically eliminated by an obstruction in the trunk of the subarachnoid tree, the area in which absorption of cerebrospinal fluid can occur is limited to about one-fifth of the normal amount. Consequently, hydrocephalus results from a greatly diminished absorption. In reality, therefore, communicating hydrocephalus is caused by an obstruction, and differs from the so-called obstructive hydrocephalus only in the location of the obstruction. To disclose adhesions and obliteration of the subarachnoid space, the brain must be carefully removed and studied during its removal. A subsequent examination of the brain reveals but little, because the adhesions have all been liberated by removal of the brain, and the gross appearance of thickened pia-arachnoid is not striking after fixation. A striking demonstration of the location of the obstruction will no doubt result by injecting colored solutions into the spinal canal under minimal pressures. The colored injection mass, of course, will stop at the obstruction. This color contrast will be seen in one of the cases of experimental hydrocephalus which will appear in the following pages. A demonstration equally striking can be shown in the living by intraspinous air injections. These observations will appear in a subsequent paper.

These pathological findings are in perfect harmony with the appearance of the brain at operation. At operation, in both the obstructive and the communicating types of hydrocephalus, the sulci over the hemispheres are seen to be shallow and contain but little fluid. If the subarachnoid spaces

[9] Soc. cit., Am. J. Dis. Child., 1917, xiv, 424.

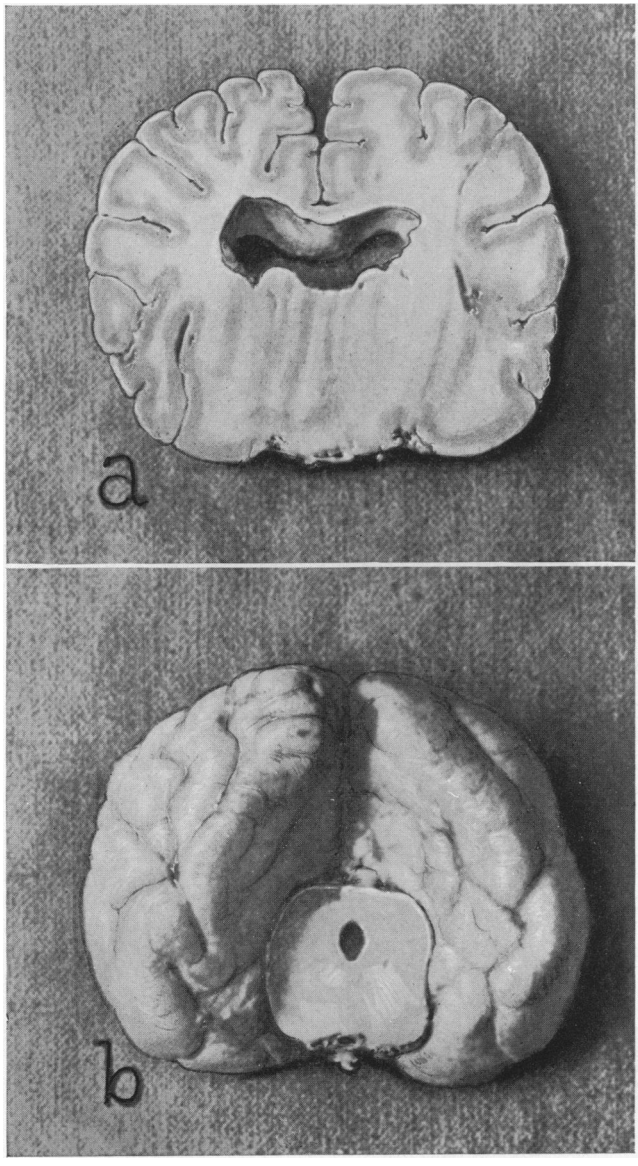


FIG. 10.—Hydrocephalus of three and one-half months' duration, resulting from a ligature on the vena magna Galeni near its origin. The aqueduct of Sylvius is also enlarged. This form of hydrocephalus results from an overproduction of fluid; all other forms from a diminished absorption of fluid.

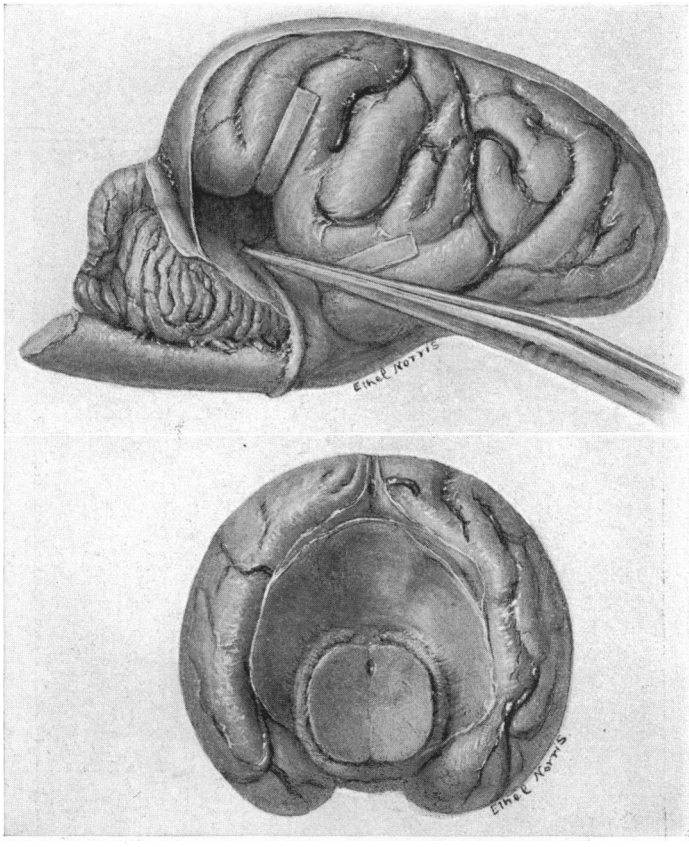


FIG. 11.—Drawings by Miss Norris to show method of placing a perimesencephalic band in position, and also to show its approximate location. The lower figure shows the band in place. Adhesions form between the brain and the gauze and occlude the cerebrospinal spaces, including the cisterna. "Communicating" hydrocephalus results from this procedure.

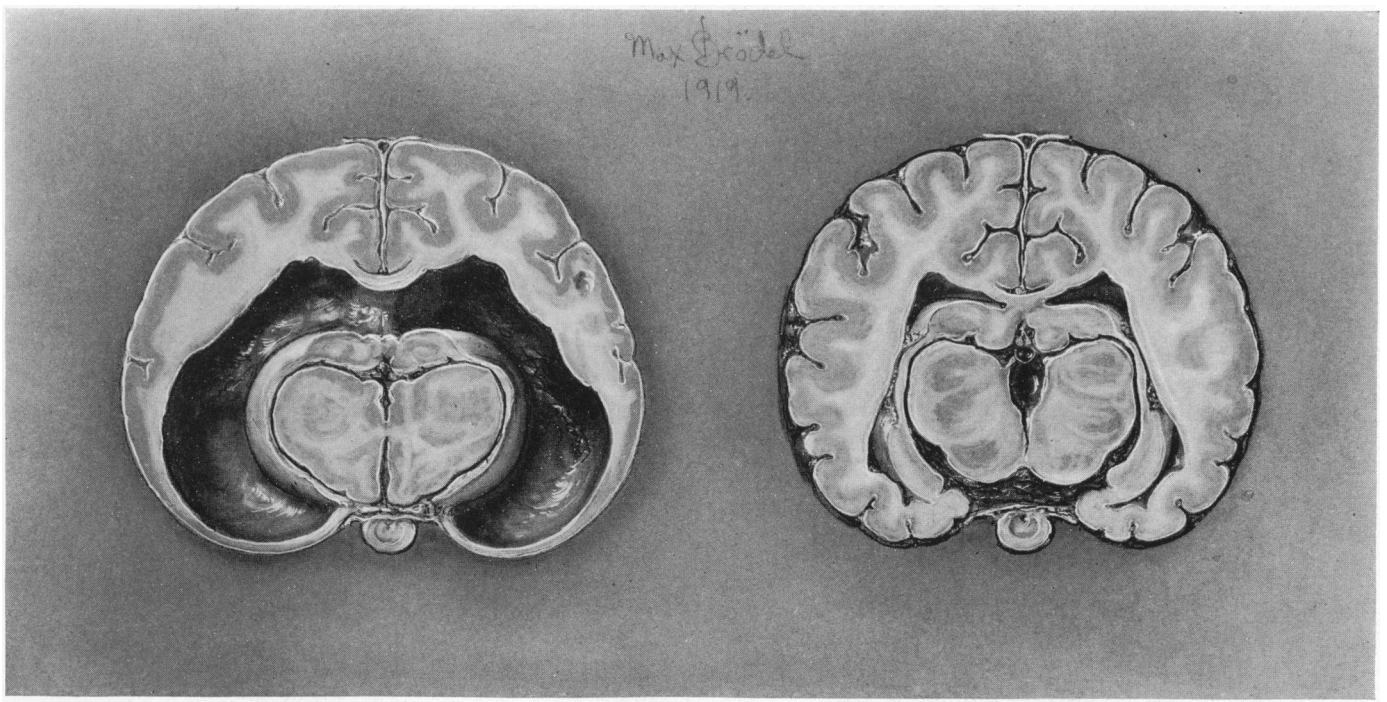
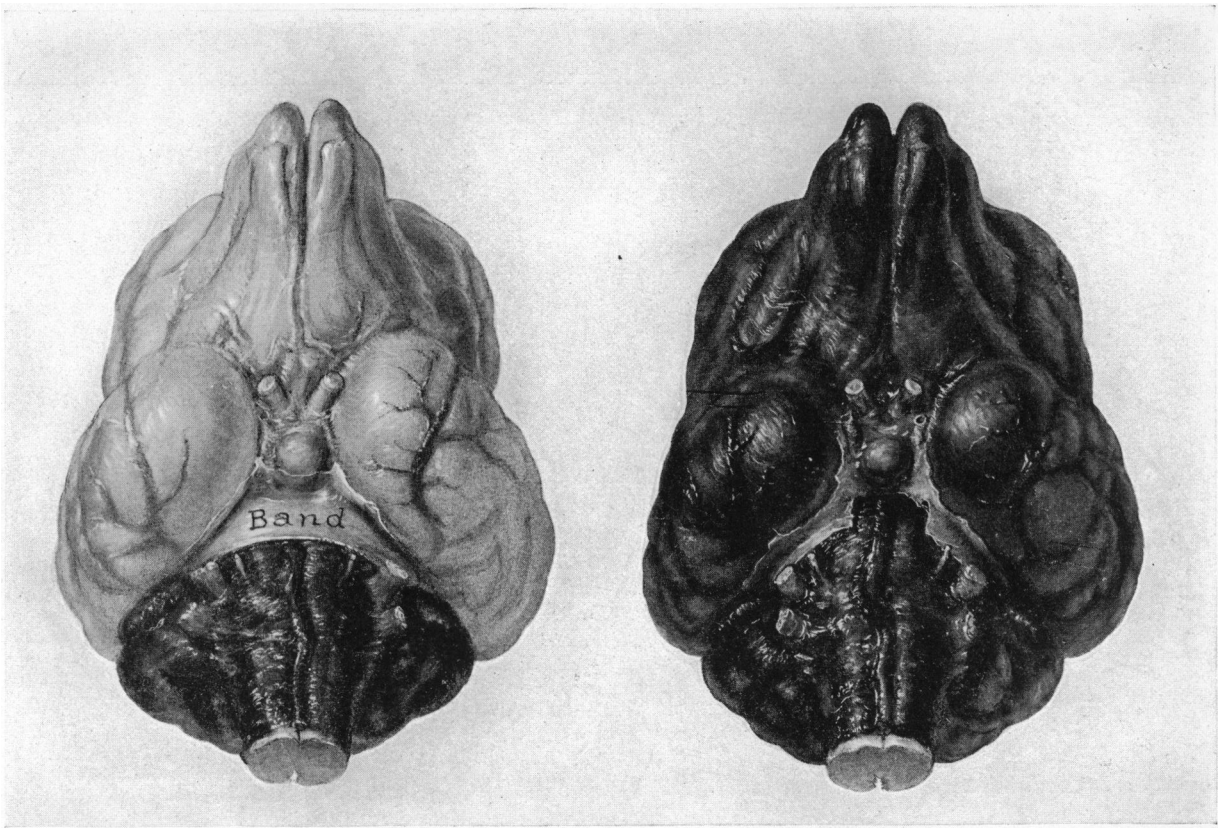


FIG. 12.—Section of a dog's brain in which hydrocephalus has followed the application of the band around the midbrain, as described in Fig. 11. The figure on the right is a section of a normal dog's brain at the same level. The hydrocephalus is of three months' duration. These sections are taken from the brains shown in Figs. 13 and 14. Compare the ventricular dilatation with that in Fig. 10, in which the vein of Galen was ligated. Drawing by Mr. Brödel.



A *B*

FIG. 13.—Drawings by Mr. Brödel, showing the result of injections of India ink into the spinal canal two hours before the animals were sacrificed. On the right the entire brain is colored black, as occurs normally. On the left the ink stops at the perimesencephalic band and can get no farther. In other words the black area represents the amount of subarachnoid space reached by the cerebrospinal fluid—*A*, in the animal in which a band is around the midbrain, and *B*, the normal. Hydrocephalus of the "communicating" type results because most of the absorbing area of subarachnoid space has been eliminated by this extraventricular obstruction.

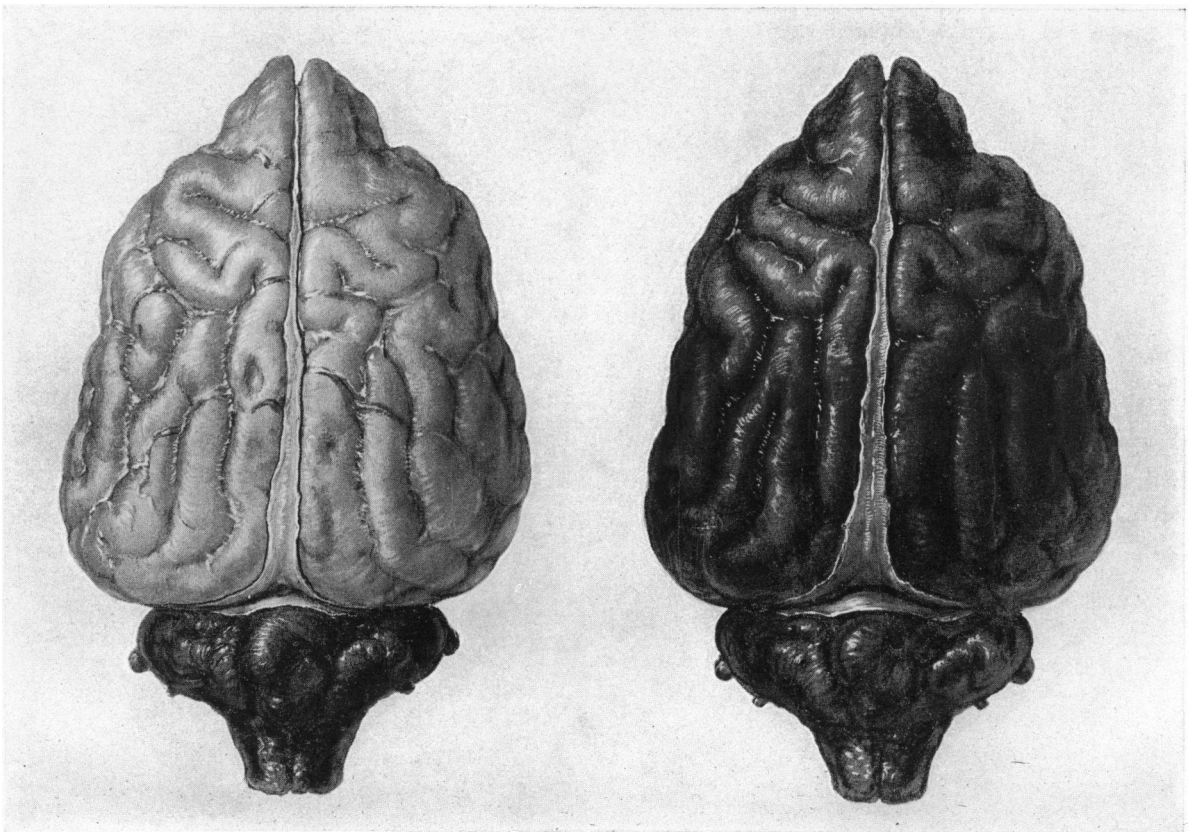


FIG. 14.—Drawings by Mr. Brödel of dorsal view of same brains as Figs. 12 and 13. It will be seen that the black ink stops at the tentorium cerebelli, it covers the cerebellum completely but none of the subarachnoid space over either cerebral hemisphere is reached. Section of these brains is shown in Fig. 12. Mr. Brödel has shown the light and dark surfaces of the brain in transverse sections also (Fig. 12). The ink filled the ventricles in the hydrocephalic brain but did not reach them in the normal brain (Fig. 12).

were not obstructed at the regions mentioned, fluid would accumulate in the sulci and cause their dilatation up to the point of obstruction, just as bile accumulates up to the obstruction in the common bile duct. There is but little fluid in the cerebral sulci because the barrier of adhesions has prevented the cerebrospinal fluid from reaching the cerebral hemispheres. As mentioned previously, the physiological tests (by phenolsuphonephthalein) show about one-fifth of the normal absorption from the subarachnoid space, apparently indicating a reduction in the subarachnoid space to one-fifth of its normal area.

THE EXPERIMENTAL PRODUCTION OF COMMUNICATING HYDROCEPHALUS

The absolute test that the pathological findings described for communicating hydrocephalus are correct lies in the ability to reproduce this disease in animals. The effects of meningitis are so diffuse that differences of opinion in the interpretation of the findings are permissible. A single, sharply defined experimental lesion eliminates speculation. The experimental methods which I have used were suggested by the results of the physiological phenolsulphonephthalein tests, and were developed before any pathological material had been obtained.

The object of the experiments is to eliminate the subarachnoid space above the incisura tentorii, and thereby to exclude the entire cerebral subarachnoid space from participation in the absorption of the cerebrospinal fluid. A glance at the intracranial topography will show that the only communication between the posterior and middle cranial fossæ is through the incisura tentorii, through which the mesencephalon passes. Except for this opening, the tentorium cerebelli acts as an impermeable diaphragm, which divides the cranial chamber into two cavities. We propose to produce adhesions around the entire circumference of the midbrain where it traverses the incisura tentorii (Fig. 11). This will obliterate by a circular band the subarachnoid space along the midbrain. The principal part of the subarachnoid space which will be obstructed by this procedure will be the cisterna. This cisterna is the part of the main trunk through which all the cerebrospinal fluid must pass. In other words, if the experiment is successful, cerebrospinal fluid cannot pass beyond the posterior cranial fossa into the middle, and thence subsequently also the anterior, cranial fossæ. *All cerebrospinal fluid enters the cisterna magna from the fourth ventricle,* but the experimental obstruction prevents it from passing into the cisterna interpeduncularis and cisterna chiasmatis. The cerebrospinal fluid therefore cannot reach the subarachnoid space which forms a mantel over both cerebral hemispheres. By eliminating the entire cerebral subarachnoid space the amount of absorption of cerebrospinal fluid should be tremendously reduced and hydrocephalus should follow.

This sharply defined area of adhesions can be produced by encircling the midbrain with a tiny strip of gauze which has been saturated with an irritant.

In the course of time a circle of adhesions forms between the margins of the incisura tentorii and the midbrain.

The technic of this procedure is as follows:

A subtemporal bony defect is made on each side and extending posteriorly to the tentorium (osseum in the dog) and inferiorly to the base of the skull. The temporal and occipital lobes are elevated on one side with a spatula until the carotid artery and third nerve are brought clearly into view. With a little additional elevation these structures are put on a stretch and the inferior surface of the midbrain can be seen. The third nerve is the most important landmark. The end of the gauze strand is passed under the mesencephalon to a point on the opposite side of the brain and emerging contralaterally just behind the third nerve. The operator then shifts to the opposite side of the table and elevates the other side of the brain until the third nerve is exposed on this side. The end of gauze will then be seen protruding and can easily be grasped with forceps. By gentle traction half of the strip of gauze is pulled under the midbrain, so that an equal length of gauze is on either side. The brain is then allowed to settle. The next step consists in retracting the occipital lobes forward, first on one side and then on the other, until the margins of the incisura tentorii can be distinctly seen. The gauze strip is then carefully inserted between the midbrain and the margins of this dural opening. The gauze is then in close apposition to the entire circumference of the midbrain and also of the dural edge. (Fig. 11.)

It has been found by experience that it is necessary to saturate the gauze with iodine in order to produce adhesions. Gauze not so treated becomes incorporated as a smooth foreign body, without adhesions, and has no effect upon the continuity of the subarachnoid space, and consequently there is no effect upon the distribution of cerebrospinal fluid. It is entirely probable that the irritant alone will produce the same result. In areas over the surface of the occipital lobe, which was unavoidably touched with the iodine, firm adhesions bound the tentorium to the brain. There has been no mortality incident to this operation.

Following the application of the perimesencephalic band, hydrocephalus develops almost as rapidly as following occlusion of the aqueduct of Sylvius (Fig. 12). That the subarachnoid space around the midbrain is obliterated by adhesions can be graphically demonstrated, by substituting India-ink for cerebrospinal fluid in the cisterna magna two hours before the animal is sacrificed. The ink granules are distributed through every part of the subarachnoid space which is open to the cerebrospinal fluid. By fixing the brain with intravascular formalin the ink granules are deposited, making a striking and permanent record. Normally, ink so introduced into the subarachnoid space will cover the whole brain in this period of time and a small amount may even pass through the foramina of Luschka into the fourth ventricle. When hydrocephalus results from a perimesencephalic barrier of adhesions, the ink cannot pass beyond this obstruction (Figs. 13 and 14). On the other hand, in the specimen of hydrocephalus which has resulted from the perimesencephalic band, all the dilated ventricles are full of ink because the foramina of Luschka (the foramen of Magendie is absent in the dog) are enlarged, permitting an easy backward passage of cerebrospinal fluid into all the cerebral ventricles. Although valves are not present, normally the approximation of the cerebellum to the medulla prevents more than a

trace of the colored fluid, which is in the spinal canal, reaching the ventricles. In experimental communicating hydrocephalus the presence of such a large amount of ink in the ventricles, together with a sharp color-line at the obstruction, is positive proof that there was ample opportunity for ink to reach the cerebral subarachnoid space if it were possible. This barrier of adhesions was therefore the sole cause of the hydrocephalus. The accumulation of fluid can be explained by assuming a reduction in the amount of the area for the absorption of cerebrospinal fluid. The dilatation of the aqueduct of Sylvius and presence of ink in the lateral ventricles also demonstrate that the circle of adhesions around the midbrain did not in any way constrict the aqueduct of Sylvius and thereby cause the hydrocephalus. The band of adhesions need not hermetically seal the subarachnoid space to produce hydrocephalus, for in one case a slight channel permitted a little fluid (ink) to trickle through for a short distance. It is entirely possible that if adhesions are not too dense such tiny channels may eventually dilate and modify the rate of development of the hydrocephalus or even overcome the effects of obstruction, and reaching the cisternæ beyond, reëstablish the continuity between the cerebellar and cerebral subarachnoid spaces. Spontaneous cures of hydrocephalus not infrequently occur, and such a development could readily afford an explanation.

SUMMARY AND CONCLUSIONS

1. Hydrocephalus has been produced by placing an obstruction in the aqueduct of Sylvius. Dilatation of the third and both lateral ventricles results.

2. One foramen of Monro has been occluded; this is followed by a unilateral hydrocephalus.

3. If the choroid plexus of one lateral ventricle is completely removed at the time the foramen of Monro is occluded, not only does no dilatation occur, but the entire lateral ventricle collapses.

4. This is the only absolute proof that the cerebrospinal fluid is formed from the choroid plexus. At the same time it proves that the ependyma does not secrete cerebrospinal fluid.

5. If the choroid plexus of both lateral ventricles is removed, and an obstruction is placed in the aqueduct of Sylvius, hydrocephalus still results in the third and both lateral ventricles, but at a reduced rate. The fluid forms from the choroid plexus of the third ventricle but cannot escape into the subarachnoid space.

6. Cerebrospinal fluid forms in all the cerebral ventricles. It is absorbed almost entirely in the subarachnoid space. The sole communication between the ventricular system and the subarachnoid space is through the foramina of Luschka and the median foramen of Magendie.

7. The phenolsuphonephthalein test will prove conclusively whether the foramina of Luschka and Magendie are open or closed. Closure of these foramina invariably causes hydrocephalus.

8. Hydrocephalus follows ligation of the vena magna Galeni if the ligature is placed at the origin of this vein. Ligatures beyond or in the sinus rectus have no effect because there is sufficient venous collateral circulation.

9. The communicating type of hydrocephalus has been produced in dogs by a perimesencephalic band of gauze, saturated in an irritant which induces adhesions. This obstruction prevents cerebrospinal fluid from reaching the cerebral subarachnoid space where most of the cerebrospinal fluid is absorbed. The resultant diminished absorption of fluid results from hydrocephalus.

10. Hydrocephalus follows ligation of the great vein of Galen because of an overproduction of cerebrospinal fluid. In other types of hydrocephalus, both obstructive and communicating, the accumulation of fluid is due to a diminished absorption of cerebrospinal fluid.