SOME PHASES
OF THE
INTRACRANIAL CONTENTS

by

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PART 1.

ON THE POSSIBILITY OF EARLY DEMONSTRATION OF VARIATIONS IN THE DILATION OF THE VENTRICLES OF THE BRAIN.

Variations in the distention of the ventricles of the brain are directly dependent upon variations in either the total quantity or in the relative distribution of their contents, the cerebrospinal fluid.

The cerebrospinal fluid was undoubtedly known to the earliest anatomists. Galen (131-201 A.D.) held that this fluid contained the animal spirits. Vesalius (1514-64) considered that it was a lubricant. Vidus Vidius (Guidi D 1569) noted its presence, as also did Valsalva (1717). Varolius believed that the function of the choroid plexus was to pump water into the ventricles of the brain. Willis (1621-75) regarded the fluid as a distillation of the pineal gland, the "seat of the soul". Vieussens (1641-1716) also observed that the ventricular contents consisted of fluid. There was, however, considerable doubt as to whether the fluid existed during life, or was simply a post-mortem precipitation. Haller (1708-77) believed that the cerebral ventricles contained a vapor capable of condensation, which gravitated as water into the spinal regions. The cerebrospinal fluid finally was "discovered" by Cotugno in 1774.

It is interesting to note in passing that Magendie (1) re-"discovered" the fluid apparently independently in 1828, and it was while searching for its "inlet" into the cerebral ventricles that he discovered the foramen that bears his name.

It is also interesting to observe that Walter E.Dandy (2), of Baltimore, credits Magendie with the discovery of the fluid about 1842, although Cotugno is almost universally given credit for having demonstrated the presence of the fluid in the living subject some sixty years previously.

While endeavoring with Dr.C.S.Haugh and Professor W.H.H.Moorehouse to produce artificial internal hydrocephalus by plugging the aqueduct of Sylvius with a cotton plug, after the manner of Dandy, the writer was struck by the great difference

in size of the normal lateral ventricles as depicted by Dr.Dandy in his paper, and the size of these ventricles as found in the course of the work. Dr.Dandy's conception of a normal ventricle is reproduced here in Fig. 1, a & b. It will be observed that the brain has been taken out of its bony covering and then sectioned, presumably after hardening. The ventricles gape quite widely. The longitudinal sulcus also, it will be observed, is rather wide. When this is contrasted with Fig. 2 it will be observed that here, in a section at almost the same level, a little further back, as a matter of fact, where the ventricles would be likely to be still larger, the ventricular walls are almost in apposition. The space between the walls is more or less potential. This condition has been verified by the examination of a considerable series of animals. Bradley (3) states "Generally the cavity of the ventricle is not spacious; since its roof and floor are mostly in contact". This is very different from the condition depicted in Dandy's illustration.

It is obvious that before one can do any work on the production of artificial internal hydrocephalus, one must have a fairly accurate idea of the normal limits of variation in the size or turgescence of the ventricles. And in proportion as these variations in the normal are slight, the easier will it be to detect abnormal distensions following experimental procedures.

Dandy (4) (Ann.Surg.Aug.1919, page 135) apropos of a case of thrombosis of the Vena Magna Galeni, and the sinus rectus reported by Magendie in 1825, states that "The symptoms were only of a week's duration, an interval too short to give a demonstrable dilation of the ventricles. As the demonstration of excess quantities are untrustworthy, the diagnosis of early hydrocephalus may be questioned". When further it is observed that from 1 - 3 months are required to produce the cases of hydrocephalus presented by Dandy in his paper, one cannot avoid the impression that a long time is required to produce demonstrable dilation of these ventricles. It would seem, therefore, that if some method could be devised which would show

fairly accurately changes in the size or in the state of distention of the cerebral ventricles in a shorter time, this would be of considerable value in permitting of more rapid work in experiments of this nature.

It is the purpose of this paper to point out that a certain well known method of anatomical investigation lends itself admirable to this purpose, and further, that by the use of this method, definite dilations of the ventricles can be shown to occur, not only in less than a week's time, but may actually be shown to occur in animals killed half an hour after completion of experiment.

It is proposed to study the relative sizes of ventricles in animals that have been frozen at temperature of from 0° to -30° F and have them been subjected to transverse sectioning at various constant levels.

Methods of procedure

Various operative procedures were employed in attempting to vary the amounts of fluid in the ventricles. These will be detailed later. After these various operative procedures were completed, the animals in all cases were set out to freeze. Two methods of freezing were employed - 1. Natural. 2. Artificial.

The natural method was perhaps the more satisfactory, as without Manitoba winter conditions it permitted of more rapid freezing than the artificial method.

Temperatures 0° F to 30° F were obtained, and the animals hardened quite rapidly - within 24 hours. Freezing was materially hastened by soaking the animals fur with water, or better still, splitting the scalp and stripping the temporal muscles away from the cranium. The animals mouth was kept widely open with a gag. A breezy place was found a useful factor in hastening the process.

In the artificial method the animals were "dressed" in the manner above described, except that they were covered with a jute sack and placed in a commercial cold storage plant and then subjected to temperatures of about 0° to -5° F for several days. The animals when taken out were very well frozen indeed.

The animals were then fixed in a vice and prepared for the taking of transverse sections of the brain. Long shaggy haired animals were clipped, or the skin and hair chiselled away. The occipital protuberance was then used as a land mark, and vertical transverse sections taken every half inch, commencing 2 inches in front of the occipital protuberance and working backward. This in a medium sized animal. In large and small animals an effort was made to adjust these cuts so as to as nearly as possible hit off corresponding levels.

The sections were then, in some cases, flushed in a stream of cold water to wash away the debris, and photographed. This was the procedure of choice, as in that way excellent differentiation could be obtained. In some cases they were frozen again after flushing. It was not possible to arrange the taking of the photographs in a cold room, which would have been preferable, as there was a marked tendency for edges to become rounded due to thawing

Another method used was to flush the section in cold water, and then to put it directly into a 10% solution of formalin which has been cooled to the freezing point, and then keeping in a refrigerator for several days. In this way excellent preservation of relationships was obtained, though differentiation was not quite so good.

Early dilation of the ventricles had been observed in certain animals in which an attempt had been made to produce an internal hydrocephalus by plugging the aqueduct of sylvius after the manner of Dandy, of Baltimore.

The general operative procedure consisted in doing sub-occipital decompression in dogs anaesthetised with ether. The hole was made with a trephine in the squamous portion of the occipital bone in the median line, and enlarged down into the foramen magnum. The dura was then opened by a long incision and the subarachnoid likewise. A considerable gush of cerebrospinal fluid was here always encountered. This was mopped up, and the fourth ventricle opened by snipping through its tectum. A small cotton plug mounted on the end of a suitable curved probe was then passed up through the fourth ventricle, while the vermis of the cerebellum was retracted. In some cases a gelatine capsule covered the cotton plug. Insertion is much facilitated by their use. After the introduction of the plug, all bleeding was stopped and the margins of the dura laid together. The muscles of the neck were then brought together loosely with sutures and the skin wound closed; the wound was then suitable bandaged and the animal allowed to recover.

The first figure here presented is that of an animal, whose aqueduct was simply plugged (Fig.3). This animal died a few minutes after the plug was inserted. It will be observed that the ventricles are not large and yet they are not quite collapsed. In this case as in all other cases in which the aqueduct was plugged there was considerable loss of cerebrospinal fluid on entering the subarachnoid. One would thus expect in these cases a certain emptying of the ventricles to have taken place, resulting in a collapse of the walls. Animals that have been decapitated before freezing showed ventricles almost entirely collapsed.

The second case is that of a normal dog. The ventricles here are slightly larger though the difference is certainly not very marked. The third ventricle is quite collapsed. (Fig.4).

The third case is that of a dog whose aqueduct was plugged with a cotton plug enclosed in a gelatine capsule. An attempt had been made to sterilize this capsule by immersing it in methylated spirits. There was practically no drainage of cerebrospinal fluid from the occipital wound after closure. The animal showed considerable symptoms of cerebral irritation and just before death it developed a yelping cry (Jacksonian) of which it was quite unconscious and would then go into convulsions. Death took place 28 hours after operation and shortly after it had been given a drink of water by stomach tube. The animal was small and short haired and froze rapidly on exposure. The illustration gives us a somewhat exaggerated idea of the intracranial conditions due to thawing of the ventricular contents during photographing. The ventricles were, however, quite appreciably dilated as compared with the established normal. (Fig.5)

The next figure presented shows still more marked dilation of the ventricles. (Fig.6) The aqueduct in this case was plugged in the usual manner, except that the cotton plug was not covered with a gelatine capsule when inserted. Some difficulty was experienced in passing the plug. It was pulled back and a second attempt to pass it made. During these manipulations the plug had become soaked with blood and the blood had clotted, thus rendering the plug itself more or less impermeable. The plug was then successfully passed into the aqueduct. The occipital wound was closed loosely. There was practically no oozing of cerebrospinal fluid in this case either. The animal did well for the first 24 hours after operation, except that it presented a gradually rising pulse rate. There developed later some signs of cerebral

irritation and nystagmus. The animal was easily aroused until shortly before death when it became somatose. It lived 42 hrs after the operation. It will be observed that here we have a slight, but distinct advance in the dilation of the lateral ventricles. This is not as apparent in the photographs as it was in the originals. The third ventricle is not quite as collapsed perhaps as in the normal, but that is about all one can say. There is here a slight reddish line between brain and bone, this ruddiness passes down into the sulci. There was here probably some meningitis present.

The last case of this series is that of an animal whose aqueduct was plugged in the usual way. (Fig.7) The plug was rather large and was passed just up to the mouth of the aqueduct and left there. This animal showed less irritative symptoms than any of the others. It seemed to do quite well, was able to move around, though not able to walk without staggering. There was practically no drainage of cerebrospinal fluid from the start. Fluids were limited during the first twenty-four hours. At the beginning of the second twenty-four hours the animal took a few laps of water. It seemed somewhat dul, but sat up whenever any one entered the room. It did not seem any more lethargic than one would expect in an animal that was not quite well. In the latter part of the second twenty-four hours it refused drink and food altogether. No vomiting was observed. The pulse was rapid throughout. The animal was seen at 11:30 P.M. and showed no apparent change in its condition. At 9 o'clock on the following morning it was found dead, cold and stiff. It was judged that this animal lived for about sixty hours after the operation.

The figure presented shows a well marked dilation of the lateral ventricles. This dilation extends into the third ventricle to a point where the aqueduct is occluded by an inflammatory mass just anterior to the large cotton plug. The left ventricle shows somewhat greater dilation than the right. There is not the usual sharp distinction between the white and grey matter of the cortex. But the sulci and gyri do not show any apparent change in shape or in the spaces between them.

It would seem, therefore, from the above cases that it is possible to show definite enlargement of the ventricles within sixty hours of operation in cases where the aqueduct of Sylvius is plugged after the procedure followed by Dandy, that is to say, with a plug in itself more or less permeable to liquids.

An attempt was then made to insert an impermeable plug, and then to fill the ventricles up with fluids so as to replace that lost when the subarachnoid space was opened into, and if possible to distend the ventricles still further.

It had been observed during the course of experimental work on dogs in Practical Physiology and in Practical Pharmacology, that when considerable amounts of normal saline were injected intravenously there was not only a marked diuresis set up, but a marked increase in salivation and even of the tears. From this it was thought that all the fluid secretions were probably increased by these injections and that cerebrospinal fluid would be increased as well as the others. This, coupled with a knowledge of Weed's (5) work, showing marked increase of cerebrospinal fluid pressure following intravenous injections of distilled water, led us to try to increase the fluid content of the ventricles by injecting distilled water intravenously.

Two animals were used. They were operated upon in the usual manner under ether anaesthesia, but instead of inserting a permeable cotton plug, fine catheters with thin rubber balloons attached to their ends were pushed up into the aqueduct of Sylvius. When in place the balloons were inflated and the tubes clamped off. There was no observable change in the animals condition following these procedures. Five hundred ccs. of distilled water were then injected into each animal (Wt.10 and 12 kilos, respectively). The results are shown in Fig. 8 and 9 post mortem it was found that the balloons had passed well into the third ventricles, but had tightly closed the aqueduct of Sylvius when inflated. There is also observed slight, but distinct distension of the lateral ventricles in both cases. This was quite apparent in the originals, and is not badly shown in the photographs.

It will be observed that in the above operation an occipital decompression was performed. The brain therefore was no longer contained within a rigid container as it is normally (Weed and Hughson).

Cerebral decompression was done on some animals, but the dura was not opened. Five hundred ccs. of distilled water were then slowly injected intravenously. Half an hour later the animal was killed by excess ether and frozen and sectioned in the usual way. Fig. 10 shows the size of ventricle produced. There is quite definite dilation of the space as compared with the normal.

Weed and McKibben (Loc.Cit.) found that on intravenous injection of a hypertonic salt solution there was a marked fall, even to negative values, of the pressure of the cerebrospinal fluid, but later (7) they stated that it had not been possible for them to demonstrate with certainty whether following intravenous injection of hypotonic solutions there was an increase in the quantity of cerebrospinal

fluid. Nor have they been able to show additional absorption following intravenous injections of hypertonic solutions. With the object of abstracting a portion or all the cerebrospinal fluid from the ventricles so securing the collapse of the ventricular walls, the better to demonstrate the variation in the size of their cavities a warmed thirty per cent solution of sodium chloride was slowly injected intravenously into two dogs.

It was hoped that the blood being thus rendered hypertonic would abstract the cerebrospinal fluid from the ventricles, thus accounting for the diminished pressures found by Weed and McKibbon. The skull and meninges of these animals had been left intact. The injection took twenty-five minutes. Half an hour later the animals were killed with excess ether and then frozen and sectioned in the same manner as the others. Fig.11 and 12 present the results obtained. The ventricles are not only not collapsed, but are distended with fluid to a degree more marked than that found by any other procedure, with the exception of the case of animal No.15 above (Fig.6), which had survived 60 hours after the plugging of its aqueduct of Sylvius.

Summary and Conclusions.

1. The normal ventricles in the dog are very small, the ventricular walls being mostly in apposition, except in the case of the lateral ventricles where they are usually separated by a few millimeters about the centre of the caudate nucleus.

2. Cross sections of the brains of animals frozen intact show this condition very well.

3. Variations in the state of distension of these ventricles are easily demonstrated by the sectioning of frozen intact animals.

4. Distension of the lateral ventricles can be shown twenty-four hours after the plugging of the aqueduct of Sylvius, even where only a semipermeable plug is used.

5. There may be a marked distension of lateral and Third ventricles sixty hours after the plugging of the aqueduct.

6. A slight distension of the ventricles follows the injection of distilled water intravenously provided a decompression has been performed somewhere on the skull.

7. A marked dilation of the ventricles is obtained in animals killed half an hour after injection of strongly hypertonic salt solutions into their veins.

References.

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4. Dandy - Ann. Surg. Aug.1919 p.135.

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PART II

On the relative distribution of the Cranial contents following injection into the veins of solutions of various concentrations.

Weed & McKibben (1), while attempting to determine whether, following intravenous injection of hypertonic solutions of sodium chloride, an increased amount of this salt could be detected in the cerebrospinal fluid, observed, that within a short time after the intravenous injection, cerebrospinal fluid could not be obtained when the subarachnoid space was entered. This observation led to the attachment of a manometer to the puncture needle for the purpose of making continuous readings of the cerebrospinal fluid pressure following such intravenous injections of hypertonic solutions of sodium chloride. They found not only that the average initial cerebrospinal fluid after an initial rise, pressure of 119 mm. of cerebrospinal fluid reduced, but that actually negative values were sometimes obtained. This fall of pressure was sustained over several hours. The injection of normal saline or of Ringer's solution had only a temporary effect, while the fluid was being actually injected. The injection of hypotonic solutions was followed by a slight temporary, and then a sustained rise in the pressure of the cerebrospinal fluid. These changes, both with hyper-and with hypotonic solutions reached their maximum within an hour after the injection.

The marked changes in the cerebrospinal fluid were soon found (2) to have a definite relation to the resultant volume of the brain itself. Thus, following intravenous injections of strongly hypertonic solutions which markedly lowered the cerebrospinal fluid pressure, definite shrinkage of the brain occurred, and, on the other hand, the brain bulk was appreciable increased by the intravenous injection of hypotonic solutions, which raised the pressure of the cerebrospinal fluid. They found such changes in the brain rapidly and uniformly brought about.

They found, after injecting distilled water intravenously, fixing, and after stripping off the bony material, that the dura was tense, the convolutions flattened and the sulci not as easy to distinguish as in the normal. On sectioning the dura was tense as before noted, and differentiation between grey and white matter diminished. The convolutions were found definitely flattened and the sulci were very narrow. The surfaces of the gyri no longer had gentle convexities, but acute angles. The superior longitudinal fissure was narrow.

After injecting 8 - 20 ccs. of 30 per cent sodium chloride solution into cats and sacrificing the animal 20 - 30 minutes later, they found on the other hand a marked decrease in the bulk of the brain. The dura was found loosely applied, and the brain seemed relatively small, occupying only a part of the intradural space.

The gyri appeared markedly rounded, and the sulci wide and deep. On sectioning they found grey and white matter more sharply contrasted. The dura was loosely applied, touching on the dorsal surface only the highest points of the gyri. The sulci are wide open. A gyrus has a rounded contour on sectioning. The superior longitudinal fissure gapes widely and the falx seems to hang loosely within this space.

It is submitted that after the methods of fixation used in these experiments these observations do not give a proper idea of the condition within the untouched brain case. In both cases the stripping of bone from the dura must have altered the fine delicate relationships between this membrane and the pia mater brain substance. This would be more especially certain to happen in those cases where shrunken brains occurred, as here the gyri, not being so firmly held together, would tend to fall apart and become rounded. The actual impressions of the relative bulk of the brains are undoubtedly accurate. The point here being made is that these appearances of looseness of the dura, the rounding of the gyri and the increase in the width of the sulci, are probably artefacts.

The undoubted importance of these discoveries by Weed & McKibben, and the probability of their becoming of great practical value not only from the scientific point of view, but from the clinical point of view as well, renders it most desirable to have light thrown upon these phenomena from all possible angles.

In work of this sort and with materials of the nature of the brain and its bony coverings, the blood and the cerebrospinal fluid, it is obvious that the methods employed are likely profoundly to affect the results obtained. The dura firmly attached to the bony calvarium cannot be stripped off without greater or less displacement and alteration of those fine relationships that constitute the normal within the cranial cavity.

No doubt much may be learned, even with the usual somewhat crude method of removing the brain, with or without its meninges, from its bony encasement, and then immersing it in a fixing fluid. The shrunken convolutions and wide sulci of the paretic or of the senile brain will undoubtedly be in a large measure preserved. The tendency of this method is to exaggerate the conditions found in these cases. It is also undoubted that cases of hydrocephalus, or of increased intracranial tension due to tumors, etc., will show flattening of the gyri, and perhaps even some narrowing of the intervening sulci. The increased size of the ventricles in these

cases will be preserved, even if the brain stem is cut across and the contained fluid finds an outlet. It must be remembered, however, that the conditions above mentioned have taken a long time to develop, and that in consequence internal tissue adjustments have had time to take place, so that collapse of the ventricles, or rounding out of flattened gyri, would not tend so much to occur. But when the relationship of these structures is profoundly changed within a few hours time, or even in an hour's time, as may occur in certain cases, it becomes obvious that if the factors which produce these altered relationships are removed, the resiliency of the brain substance and tissue around will assert itself and the organ tend to return to the normal. Weed and McKibben (2) tried to overcome these conditions by the ingenious method of injecting a strong fixing fluid, 10 per cent formalin, into the blood vessels of the part.

They (2) describe their method as follows:- "After the lapse of time necessary for the maximum action of the solution intravenously introduced, the animals were killed with ether. In routine experiment 10 per cent formalin was injected immediately after death, through the aorta, at a pressure of not more than 300 mm. of water. When the cranial vessels were well filled, the central nervous system was removed (the skull and vertebral canal being partially opened), and the whole immersed in 10 per cent formalin." They (2) comment on this method as follows:- "In spite of all the care it was possible to exercise, it was soon very evident that by this method of fixation, the form and size relations of the central nervous system prevailing prior to the death of the animal were not being accurately preserved. Brains markedly shrunken during life, or at death of the animal, approached almost normal proportions after such fixations, and brains markedly herniated often subsided perceptibly during preservation."

In criticism of this method it may be pointed out in the first place, that the injection of 10% formalin, a fluid of certain osmotic possibilities, into the blood stream in cases like these where the reactions under investigation are due presumably to variations in relative osmotic values, may have a marked influence on the outcome, particularly in view of the well known fact, that alterations in the relative distribution of the intracranial contents may take place post mortem. Howel (3) says "After death, also, the liquid present in the subarachnoid space is soon absorbed."

In the second place it may be pointed out that though 10% formalin acts fairly rapidly as a fixing agent, it does not act with sufficient speed to hold tissues in place, when their support is removed within an hour or so. As soon as Weed & McKibben had filled

the cranial vessels with the formalin, they removed the central nervous system, and as they state, the skull and vertebral canal were partically opened. In these circumstances they would almost certainly lose more or less cerebrospinal fluid, whether the dura was opened or not, and so remove some of the fluid that was supporting the tissue of the brain, i.e., the walls of the ventricles and the sulci. Even were no fluid lost, the opening of the skull and vertebral canal would alter the "closed box" status of the system which would in the same manner result in lessening the support given to the semi-atheromatous brain tissue by the cerebrospinal fluid. If they contented themselves with injecting the 10% formalin and then leaving the animals intact for a sufficient period, a week or tow, renewing the injection of 10% formalin from time to time, they would almost certainly obtain much more dependable results, especially if they could decalcify the bone at the same time.

In connection with the tendency of shrunken brain to swell back to normal and of swollen brains to shrink, as indicated by bulging or depression when viewed through a decompression wound, it is desired to point out, as a third point for consideration, that these effects are easily produced as artefacts by simply raising or lowering the head of the animal in relation to the rest of the body. This has been observed by the writer in a number of instances.

It is the purpose of this paper to point out that the same old fashioned and well known method of anatomical study as was used in Part 1 is capable of giving considerable information on this subject, of the relative distribution of the cranial contents, and through this method to show some very interesting changes which take place in these relationships after the instillation of solutions of various concentrations directly into the blood stream.

This old fashioned method (4) consists then in freezing the experimental animal as soon after its death and as rapidly as possible, and then taking sections, in these cases verticle transverse sections, at various constant levels. The advantages of this method in dealing with structures, such as the brain, a soft, almost atheromatous material, encased in a tough membrane which itself is firmly adherent to the rigid bony box in which the whole is enclosed, are obvious. There will be here a minimum of displacement and of artefacts in the gross relationships, as everything is firmly fixed in position in a relatively very short space of time - a few hours,- the external parts in a few minutes. It is possible that there is some slight dislocation of cerebrospinal fluid due to the swelling of these moist structures in freezing, the tendency being to force some fluid out of the ventricles through the aqueduct of Sylvius into the subarachnoid space and then down the vertebral canal. This would

be the tendency, as the dogs head freezing from without inwards, and, the head being smaller than the body, the brain would probably be frozen through sometime before the vertebral canal, especially in those cases where the animals mouth is kept widely open with a gag during the process of freezing.

METHODS

Dogs were used exclusively. The intravenous injections of the various solutions were given from a burette, connected directly with the femoral vein. For hypertonic solution 30 per sodium chloride solution warmed to body temperature was used. For hypotonic solution, distilled water properly warmed was used. The animals were in all cases anaesthetized with ether in the ordinary way during the operation and injection. On completion of the injection all but trephined animals were permitted to recover. In all cases the animals were killed with an overdose of ether. The temporal muscles were then rapidly stripped away from the cranium and a gag put in the animal's mouth to keep it widely open. The animals were then put in a jute sack and taken to a commercial cold storage plant and frozen. Temperatures varying from zero to five degrees below zero were obtained. The animals were left there for several days. The people who work in these cold storage plants claim that a quarter of beef freezes through in twenty-four hours. The dogs were then removed, subjected to vertiele transverse sectioning with a fine toothed meat saw. When the saw is sharp and the animals well frozen, there is no visible tearing of tissue, but a smooth clean cut surface is exposed when a stream of cold (0°C) water is played on the surface to wash away the debris. In addition the different structures and tissues stand out remarkably contrasted one with another.

Whenever possible photographs were taken immediately after washing the debris from the cut surfaces. In this way the best differentiation and relative position of parts is obtained. As a second choice, the frozen sections were immersed in 10 per cent formalin which was cooled slightly below 0oC, and kept just above its freezing point with the sections immersed for a week. By this time, while there was some loss of color, the structures were so well fixed that the sections could be handled without injury, and so photographed. Study of the sections themselves, however, was possible immediately after their immersion in the fixing fluid, if the receptacles used were flat faced specimen jars. After prolonged fixation in formalin the grey matter tends to shrink more than the

white, and this leads to some distortion.

Some animals had as much as 10 ccs. per kilo of 30 per cent sodium chloride solution injected intravenously. Never less than 50 ccs. were used. When injections were timed to run in at about the rate of 1 - 2 ccs. per minute, there was but little visible reaction on the part of the animal. When more rapidly administered, dispnea would set in, the respiration would become gradually more shallow until it would cease altogether. The heart, in these cases, would stop very soon after. Resuscitations after respiratory failure was successfully performed in two cases - failed in one case.

From 300 - 500 ccs. of distilled water were injected into the other set of animals. This was often run in fairly rapidly without any apparent ill effect upon the animal. A considerable increase in salivation was observed, over and above that already caused by the ether.

A number of animals, six in all, were selected as control animals. These were killed with ether and set out to freeze in various positions. Two were frozen lying on their sides. Two were strung up by the snout, and two were suspended by their hind legs and frozen in these positions. Fig. 5 is a typical example. This animal was frozen lying on its side. Of the others, frozen head up and head down, all that can be said is, that there is only very slight alteration in the relative distribution of cerebrospinal fluid, blood or brain tissue. If anything, the animals frozen in the head down position show a slight dilation in the size of their ventricles. Fig. 13 shows a section of the brain of an animal frozen in the head down position. Fig. 14 was frozen head up. The lateral ventricles in Fig. 13 are obviously larger than those of No. 14. The same sort of thing, but to a somewhat slighter extent, was observed in the other set of animals. This is the opposite to what one would expect from a consideration of the relative specific gravities of the blood and cerebrospinal fluid. Possibly, had the animals been suspended in these various positions while under the anaesthetic and kept so for a time prior to killing, different results would have been obtained. Of the relative distension of blood vessels no differences could be detected between the two sets of animals.

All these animals were taken to represent variations within the normal, especially in so far as relationships of bone, dura and brain tense over the external surface of the cerebral ventricles was concerned.

Hypotonic solution: Two animals were injected with hypotonic solution per femoral vein. Cross sections of their brains shows a slight paling of the grey substance. Fig. 15. The lateral ventricles are smaller than normal. The grey matter fits snugly up against the calvarium and the line of demarkation between bone and brain is perhaps not as clear as in the normal, suggesting that the brain, dura and bone are in somewhat closer contact. The sulci are a little more difficult to trace than in the normal. No flattening of gyri could be observed. The differences, however, are very slight. The dura dips down somewhat between the gyri as in the normal. It is kept in this position by the bone of the skull. These observations may be taken, however, as confirming those of Weed and McKibben relative to the swelling of brain bulk under these conditions. Most of the increase in the size of the brain is at the expense of the lateral ventricles.

Trephined animals. Two animals were anaesthetized, and a subtemporal decompression performed on one side. The animal was then injected with 500 ccs. of distilled water. They were then killed, frozen and sectioned in the usual manner. One of these animals showed an enormously distended ventricle on the trephined side. On further investigation, however, it turned out that this animal had evidently at one time in life suffered from one sided internal hydrocephalus. Spontaneous cure had evidently taken place through destruction of brain tissue between the dilated ventricle and the bony calvarium well forward. In this region fine strands traversed the space, and this space opened out upon dura and bone directly. No abnormality of behavior or gait had been observed in this animal prior to death.

The other animal, Fig. 10, shows a slight bulging of the brain and dura (intact) through the trephine opening. There was no recession away from the trephine opening when the animal's head was raised slightly above the rest of the body. The differentiation between grey and white matter is perhaps a little nearer normal. There is a distinct, though slight increase in the size of the ventricles.

The subarachnoid spaces over the cerebral hemishperes are not appreciably altered from their normal condition. The sulci are easily traced. In a number of other animals on whom suboccipital decompression had been performed, the subarachnoid space opened, and an impermeable plug inserted into the aqueduct of Sylvius, before distilled water was injected, these observations were confirmed. The increased size of the ventricles would point to an increased secretion of cerebrospinal fluid after injection of distilled water where there was room for expansion.

This is in line with increase salivation, tear formation and urine secretion observed under these conditions in experimental animals generally.

Hypertonic solutions - Next, a series of six animals were injected with strongly hypertonic solutions as above described. The brain and spinal column had all bone and meningeal coverings untouched, so that the closed box condition of the system was not affected.

The brains of these animals in transverse section presented striking appearances. The grey matter was all of a brownish color, setting off the while matter very strikingly. There is no visible space between brain and dura, nor are the sulci dilated into spaces. At most one can say that the line of demarkation between brain and bone is a little more distinct than in the case of animals that had distilled water injected intravenously. The difference from the normal is perhaps definite, but it is slight. The same applies to the sulci. While they are only a little more definite than in the case of the normal animal, they are distinctly more definite than in animals injected with distilled water. But definite spaces as described by Weed and McKibben between brain and dura do not exist.

The outstanding feature of these sections of animals injected with hypertonic salt solution, is the dilated appearance of the lateral ventricles of the brain. The third ventricle shares this dilation to only a slight extent. The dilation of the lateral ventricles, however, was striking in four out of six animals used, marked in one, and definite, but slight, in the sixth. The animal showing the most striking dilation was an oldish dog - teeth beginning to show the wear and tear of age, but not badly gone by any means. (Fig. 12). In Fig. 11 is presented a case with the average dilation of the ventricles obtained as a result of the intravenous injection of hypertonic salt solution. The ventricular contents in all these cases was a clear transparent ice.

Trephined animals - A series of four animals had a one sided subtemporal decompression performed under ether anaesthesia prior to receiving the injection of hypertonic salt solution. They were killed in the same manner as the others and after the same length of time and frozen. On cross section these animals show an appearance more approaching the normal. The differentiation between grey and white matter is a little more distinct than normally occurs. The sulci are of about normal distinctness, and the line demarking brain from dura and bone is of about normal distinctness. The animals were frozen with head at the same level as the rest of the body. The dura and brain are not detracted away from the decompression

opening. There was no concavity of the dura as viewed through the trephine opening just prior to the animals being sacrificied unless the head was raised slightly above the level of the body. If this was done a concavity was easily observed. The ventricles in these animals are not dilated beyond normal limits, certainly not comparable to the dilation of the ventricles observed in animals whose crania and meninges were left intact.

These observations would confirm those of Weed and McKibben (2) that strongly hypertonic solutions injected intravenously cause a marked shrinkage in brain bulk. But these obsdrvations indicate very definitely that the shrinking in the brain bulk is compensated for by an increase of the cerebrospinal fluid, not on the exterior of the brain, but within the cerebral, especially the lateral ventricles. This increased cerebrospinal fluid within the ventricles is probably due to increased secretion caused by the lowered intracranial as compared with the capillary pressure. The compensatory function of the cerebral ventricles holds good only so long as the central nervous system is contained within a rigid closed cavity. And thus incidentally these observations constitute another proof of the essential soundness of the Munro-Kellie doctrine in that they show that the major role in compensating for alteration in the size of the brain is played, not by the blood, but by the cerebrospinal fluid.

It would therefore seem to be a permissible generalization, that, within certain limits, variations in the bulk of the brain in dogs are compensated for by variations in the size of the cavities of the lateral ventricles, and by corresponding variations at least in part in the total quantity of cerebrospinal fluid.

Conclusions

1. The usual methods of studying relationships within the cranial cavities are almost certain to result in distortion and error of interpretation, because of mechanical difficulties.

2. The frozen section method permits of a high degree of accuracy in judging variations in intracranial relationships.

3. Injection of hypotonic solution intravenously results in increasing the apparent brain bulk as perceived in transverse sections of the frozen animal. This increase of bulk is at the expense of the size of the cavities of the lateral ventricles.

4. There is a tendency to increased secretion of cerebrospinal fluid following injections of distilled water into an animals veins. This becomes apparent only where a decompression has been performed. In undecompressed cased the increased brain bulk does not permit room for increased secretion of fluid. It is possible this apparent increase is due to the decompression alone.

5. Intravenous injection of hypertonic sale solution leads to definite diminution in the bulk of the brain.

6. This diminution is compensated for by increase in the cerebrospinal fluid.

7. This increased amount of cerebrospinal fluid is found not on the exterior of the brain, but within the ventricles, particularly the lateral ventricles of the brain. In other words, diminution in the bulk of the brain is compensated for by an increase in the size of the cavities of lateral ventricles.

8. In decompression cases, injection of hypertonic salt solution does not lead to distension of the lateral ventricles, or to increase in the cerebrospinal fluid elsewhere in the cranial cavity.

References

Part II

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APPENDIX

Weed and McKibben (1), as pointed out in the foregoing papers have shown that variations in the cerebrospinal fluid pressures follow the injection of fluids of various concentrations into the blood stream of cats. Later the same authors (2) showed that these variations in pressure were found to correspond with definite variations in the bulk of the brain itself. The increased cerebrospinal fluid pressure following intravenous injection of hypotonic salt solution was found to correspond with a frank swelling in the actual bulk of the brain. And they found that the decreased pressure of the cerebrospinal fluid following injection of hypertonic solutions was found to correspond with a frank diminution in the actual bulk of the brain. And they state further (2) "Within certain limits, these observations substantiate this assumption, namely, that the amount of fall in pressure of the cerebrospinal fluid is an index of the extent to which the volume of the brain has been reduced."

Following the publication of this work in 1919, there appeared a number of contributions to the subject, in which the general physiological findings were confirmed and somewhat extended. Baden (3), in a short note, reported an amelioration of the symptoms of intracranial pressure in two meningitis patients, following the intravenous administration of hypertonic glucose solution. Cushing and Foley (4) demonstrated the significant fact that similar reductions of the pressure of the cerebrospinal fluid could be obtained after the ingestion of strongly hypertonic solutions. Foley and Putnam (5) confirmed the findings of Weed and McKibben mentioned above, that the changes in the cerebrospinal fluid pressure were accompanied by changes in the size of the brain. They are of the opinion, however, that "The manometer readings obtained after salt ingestions are not solely due to changes in the brain volume and the capacity of the cerebrospinal fluid spaces, but primarily represent new ratios between secretion and absorption of cerebrospinal fluid." They also extended the previous work of Cushing and Foley (4), showing that variation in the cerebrospinal fluid pressures followed the administration of solutions of various concentrations whether the solutions were given by stomach duodenum, or per rectum. Keough and Stevenson (6) studied intracranial tension in a epileptic with a subtemporal decompression. These authors reported a marked fall in administration of hypertonic solutions, and an increase in the pressure after oral administration of 4000-8000 ccs. of water.

These observations are also supported by the undoubted fact pointed out by Cushing, as quoted by Foley & Putnam (5) "That people who suffer from headaches, suggesting "tension headaches" may get relief by a thorough intentinal evacuation, particularly when this is accomplished by saline. This has led to the view that constipation itself is provocative of such discomforts". The old time remedy for concussion of the brain was bleeding and the exhibition of cathartics, particularly calomel followed by infusion of senna and magnesium sulphate. (Cooper 7). The opposite condition to this, however, was shown by two dogs operated upon by Dr. O. S. Waugh and the writer in an attempt to produce internal hydrocephalus by plugging the aqueduct of Sylvius. In these cases rather large cotton plugs had been used. The animals showed scarcely any drainage of cerebrospinal fluid from the wound. Both showed signs of cerebral irritation and of intraventricular pressure. One of these animals was given an injection of 500 ccs. of water per rectum. The animals symptoms became markedly aggravated, and the animal became comatose in a few minutes and died within a hour. The other animal had been given water, of which it lapped up about 400 ccs. Its symptoms became markedly worse in some 20 minutes time, and it was thought the animal would expire. It gradually recovered, however, and has been alive for over two months at the time of writing. At autopsy the ventricles of the first animal were found definitely distended with fluid.

These observations suggest variations in intracranial pressures are more or less common occurrences in the life of animals, the brain volume and the cerebrospinal fluid pressure being capable of undergoing marked variations as a result of diet, or of accidents of ingestion.

It would not seem to be fairly well established by the work of Dandy and Blackfan (8), and also by that of Dickson and Halliburton (9), and later by Dandy (10) again that the cerebrospinal fluid is secreted by the choroid plexus within the lateral and the third ventricles. It is well known (Howel 11) that this fluid can be very promptly formed from the blood, and when in excess be absorbed quickly into the same stream. In fractures of the base of the skull, for instance, the fluid has been observed to drain off steadily at the rate of 200 ccs. per day. That is to say, in cases where the intracranial pressure is lowered as it is in these cases, it would seem that an attempt is made to bring this pressure back to normal by the pouring out of this excess of fluid. On the other hand when one injects physiological saline into the subarachnoid space under some pressure it is absorbed with surprising rapidity.

It is to be noted that the only escape of the fluid from the ventricles has been shown by Dandy (10) to be through the aqueduct of Sylvius, a relatively small and narrow passage as compared with the ventricles and so situated as not to favor drainage when it is considered that it is surrounded by tissues and fluids of greater specific gravity than the fluid to be drained through it. The work reported in the first part of this paper tends strongly to confirm this part of Dandy's work, namely, that plugging of the aqueduct of Sylvius is followed by dilation of the ventricles.

The normal course of the fluid, as set out by Dandy (10) is from the lateral and third ventricles through the aqueduct of Sylvius into the fourth ventricle from which it passes through the foramina of Magendi and Luska into the subarachnoid space, where it tends to collect in the basal cisternae. From these it spreads up along the channels of the subarachnoid space, and the sulci to be spread over the cerebral hemispheres.

Dandy (10), in his work on hydrocephalus, has shown that at least four fifths of the absorption of the cerebrospinal fluid takes place in this area. There is practically no absorption from the ventricles. By the use of phenolphthalein as a physiological dye and by the injection of india ink into the lateral ventricles and tracing its course, together with the production of the communicating type of hydrocephalus by the formation of a band of adhesions about the mesencephalon, he has been able to establish fairly conclusively that it is over the area of the cerebral hemispheres that by far the greatest amount of absorption of cerebrospinal fluid takes place.

It has been shown in Part II of the present paper that variations in the bulk of the brain in dogs is, within certain limits, compensated for by variations in the size of the cavities of the lateralventricles, and by corresponding variations, at least in part, in cerebrospinal fluid. This holds good also only so long as the basal conditions for the Munro-Kellie doctrine hold good. This basal condition is well set forth by Abercrombie (12), quoted by Weed & Hughson (12) "The cranium is a complete sphere of bone, which is exactly filled by its contents, the brain, and by which the brain is closely shut up from atmospheric pressure and from all influences from without, except which is communicated through the blood vessels which enter it." This view is substantially confirmed by the work reported by Weed and Hughson in this paper (12).

It would also seem somewhat odd, from a consideration of the relative specific gravity of the cerebrospinal fluid and that of the brain substance and the blood that the cerebral ventricles are not always completely collapsed, and that the large cisternae of the subarachnoid space should occur, at the base of the brain, instead of at the topmost point ofthe cranial cavity whither one should expect the fluid to gravitate.

Now all these observations seem to have a certain close relationship when viewed from a certain point of view. Let us summarize these observations briefly for the sake of clearness.

1. The brain varies in bulk from time to time, even as a result of the ingestion of certain substances.

2. The cerebrospinal fluid is secreted into the lateral and third ventricles by the choroid plexus and at a certain pressure.

3. These ventricles have a considerable potential cavity.

4. The only outlet from these cavities is the comparatively small aqueduct of Sylvius.

5. The cerebrospinal fluid is absorbed over the surface of the cerebral hemispheres, in man the highest portion of the central nervous system.

6. Variations in the bulk of the brain are compensated for by variations of the cerebral ventricles.

7. The brain substance is specifically much heavier than the cerebrospinal fluid which bathes it and which forms an envelope around it of varying thickness.

An hypothesis as to an important function of the cerebral ventricles and the cerebrospinal fluid has suggested itself to the writer which may be of value in not only explaining the relationship of the various observations and phenomena above listed, but which may suggest, it is hoped, certain lines of enquiry which may prove not unfruitful if carried out.

A moments consideration of the gross anatomy of the brain and spinal chord is necessary.

The spinal chord, suspended in the spinal canal, a flexible tube of long rings and the ligaments uniting them has the more delicate tissue of which it is composed, the grey matter situated in the centre of the chord. Presumably the grey matter isthe more important of the two kinds of nervous tissue. Also, from its

character this grey tissue is the less able of the two to withstand alternations of stretching and compression, as it would inevitably be subjected to were it placed on the exterior of the flexible chord. It is therefore found in that place where it is safest from injury, and where it is least subject to stretching or compression on movements of the spine, namely in the centre of the chord.

Within the cranium, on the other hand, a very different state of affairs exists. Here is a rigid inflexible box, with a somewhat roughened or wavy interior surface. This hard inflexible rough box is almost completely filled by a delicate, almost porridge-like structure, the brain. It would seem that the area of great protection here lies against the rigid calvarium, provided there is some mechanism to guard against movement of the tissue over the wavy internal surface. It is a fact that in the brain the more delicate, and more important (Howel 13) of the two elements of the brain tissue, the cortex is here found not lining the ventricles, but up against this bony tissue. It is submitted again that the cortex of the brain is in a safe position only if it is protected from movement. Any considerable movement of the delicate cortex over the projections of the bone would certainly tend to cause injury.

Study of transverse sections of the brain of frozen animals shows that in all cases the cortex is closely applied to the bone covering of the skull, the projections of bone fitting between gyri. Where the volume of the brain has shrunken the cortex does not recede from its covering, but the ventricles dilate with cerebrospinal fluid, and so take up the difference in volume.

It is therefore conceived as the special function of the ventricles, the lateral ones in particular, to afford, as it were, the spring cushion which takes up the variations in the bulk of the brain, which may occur from a long list of conceivable accidents, especially those of ingestion, and so to contribute to the safety of the animal by keeping the delicate cortex of the brain at all times in close apposition to the bony calvarium.

Important factors implying corresponding functions on the part of the cerebrospinal fluid and contributing to this same end are:-

1. The secretion of the cerebrospinal fluid at a pressure. If its outlet is blocked a hydrocephalus results.

2. Owing to this secretion taking place in distensible ventricles, which have a single small outlet,

rather inconveniently situated from the point of view of drainage, there is a certain tendency to distension of these cavities. This tends mechanically to push the brain substance outward against the bony coverings.

3. The absorption of the cerebrospinal fluid mainly over the cerebral surfaces. This of itself tends to keep the pressures between the cortex and dura covered bone less than the pressure within the cortex itself and the interior of the brain and its ventricles, thus tending to force it against the bony calvarium. That is to say, the absorption of the fluid tends to produce a relative negative pressure in the subarachnoid space over this area, and this would tend to support the brain tissue up against the bone. This may be a material factor in overcoming the difference in specific gravity between the cerebrospinal fluid and the brain substance. This would alse tend to keep the basal cisternae clear.

4. Finally it is submitted that the general shape of the ventricles, particularly the lateral, and their contour upon distension is admirably adapted to this function of keeping the various peripheral parts of the brain uniformly pressed against its bony covering.

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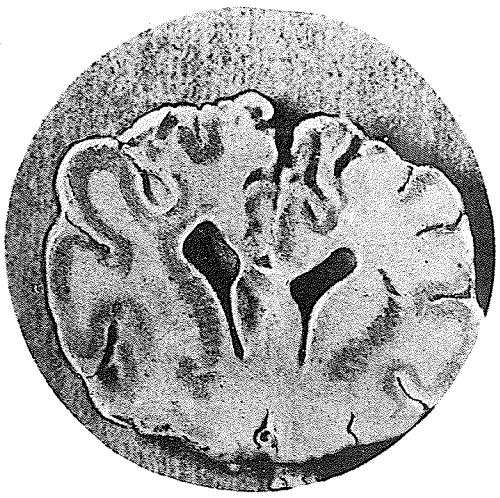
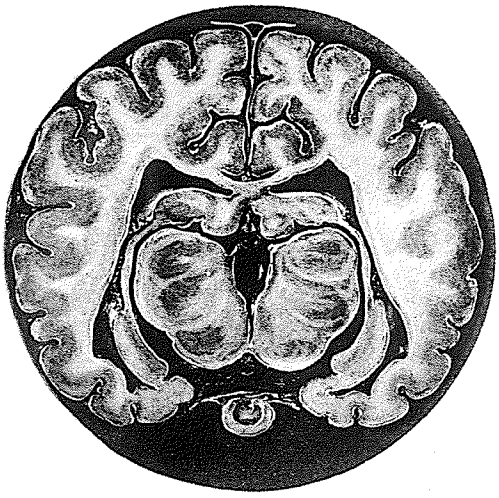


Fig. 1.A.



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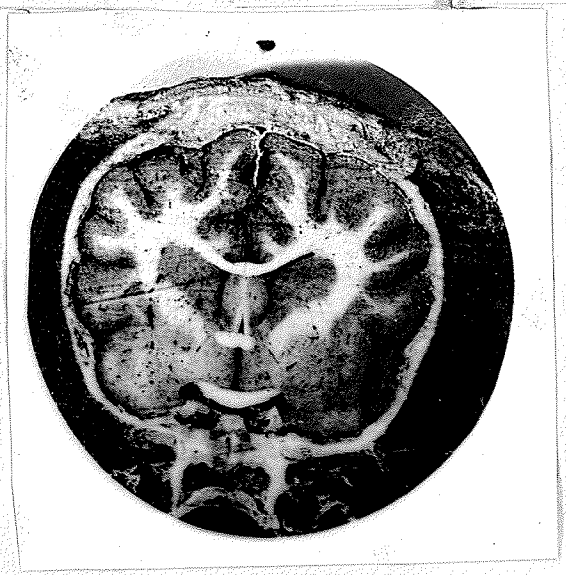

Fig. 2.

Fig. 3.

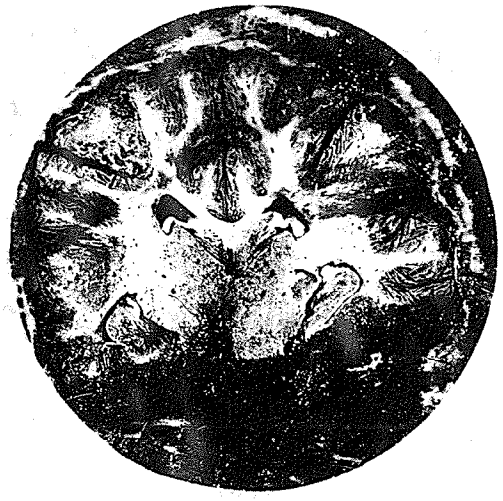

Fig. 4.

Fig. 5.

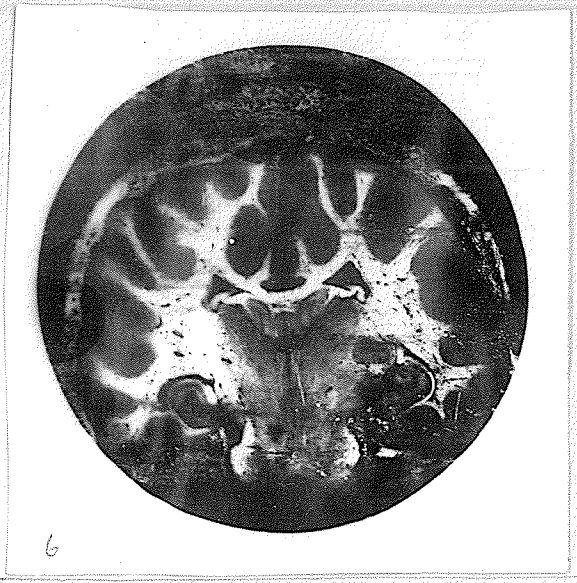

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 9.

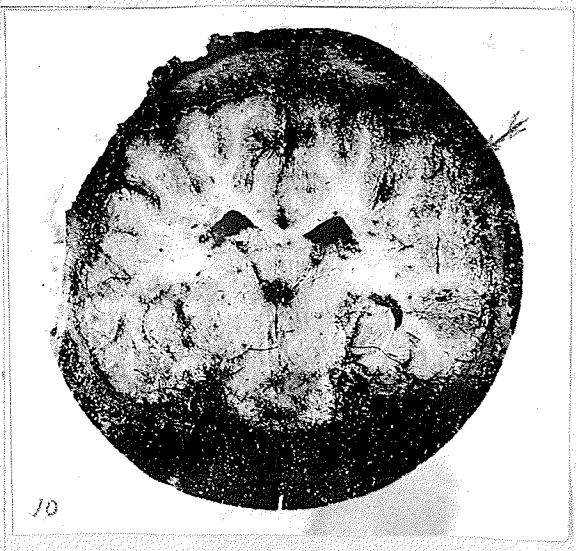

Fig. 10

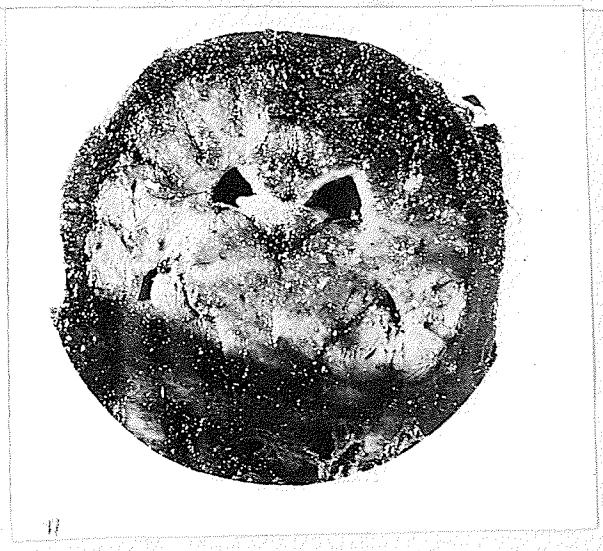

Fig. 11.

Fig 12.

Fig. 13.

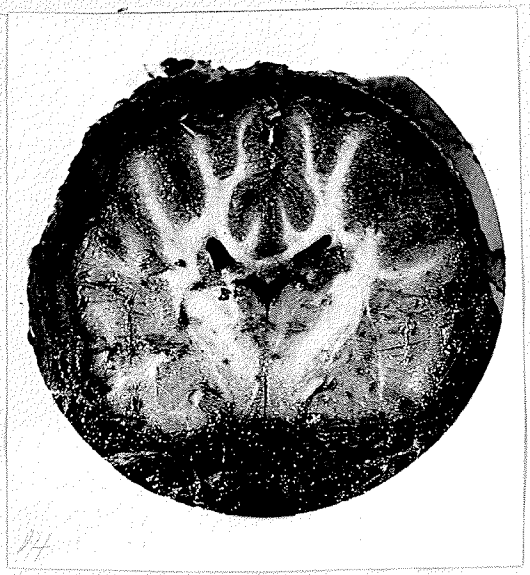

Fig. 14.