Occlusion of the Aqueduct of Sylvius in Relation to Internal Hydrocephalus

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OCCLUSION OF THE AQUEDUCT OF SYLVIUS IN RELATION TO INTERNAL HYDROCEPHALUS *

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The object of this report is to present with all possible accuracy the results of the clinical, postmortem and histologic investigations in eight cases of internal hydrocephalus of the obstructive type, bringing special emphasis to bear on the obliterating lesion of the aqueduct of Sylvius as a cause of ventricular distention.

Of this group, examined without selection, all show either complete occlusion of the aqueductus cerebri or obliteration of the fourth ventricle through severe pathologic changes occurring in the ependymal or subependymal tissues of these regions.

The first four cases have already been shown before the New York Pathological Society¹ and the records reappear at this time in greater detail, together with the findings in four other cases not reported heretofore.

Beside the congenital, obstructive form of the disease as it appears in this review, a subdivision of this type of hydrocephalus occurs apparently idiompathically, in previously healthy young adults and older children, in which occlusion of the aqueduct may readily be made out in histologic sections. In such cases it is probable that a predisposing constitutional weakness has existed from the earliest time and that the ependymal cells have been stimulated by some local factors to excessive formative activity, so that gliosis, with consequent closure of the iter, takes place.

Although interference with the normal passage of cerebrospinal fluid, whether due to mechanical obstruction or to some pathologic change in the ependyma or more deeply lying structures of the aqueduct, figures in the development of hydrocephalus, many cases have been recorded wherein no such factor can be made out. Similarly,

*From the Department of Pathology, Cornell University Medical College.
the generally accepted idea of an obstruction to free communication between the ventricles, and between the ventricles and the general subarachnoid space, implying closure of the foramina of Magendie and Luschka, and in some cases of unilateral hydrocephalus, closure of the foramen of Monro, cannot be verified in pathologic studies of these conditions.

This variety of hydrocephalus offers an opportunity for further study of the origin, the removal, and hindrance to the normal movement of the cerebrospinal fluid.

The recently published studies of the cerebrospinal fluid by Weed and by Wegefarth, with an introduction by Cushing consider this phase of the question in comprehensive manner, while the contributions of Frazier and of Frazier and Peet, based on clinical and laboratory observation, have done much to enlighten us with respect to those problems which have long resisted solution.

Dandy and Blackfan also in a report of their clinical and experimental work on hydrocephalus discuss the subject of the origin and disposition of the cerebrospinal fluid. Dixon and Halliburton go into the points in question and give the results of their investigations dealing with the effects of extracts of the choroid and other glands on secretion of the choroid plexuses.

The surgical aspect of the subject has been well reviewed by Haynes, who gives a detailed account of the physiology of intracranial pressure, discussing the modes of production and escape of fluid from the cavities of the brain.

Referring to the older literature on the subject, we find that L. W. Weber, in summing up the pathologic considerations in a number of cases, came to the conclusion, not greatly at variance with present-day ideas, that three mechanical factors figure prominently in the production of hydrocephalus:

First, an increased fluid production due to inflammatory changes in the choroid plexuses, the ependyma and brain substance as well as obstructive processes in the choroidal vessels.

Second, impediment to the outflow of cerebrospinal fluid, via the venous and lymphatic channels, besides the obstacle of a frequently existing chronic, diffuse leptomeningitis, causing an impermeability of the subarachnoid spaces.

Third, lessened resistance of the ventricular walls due to inflammatory, degenerative or sclerotic processes in the affected areas. Weber believes that these three cardinal factors are operative in both acquired and congenital hydrocephalus, but that in the case of congenital disease the second element is present to a greater degree, while in the acquired form increased fluid production plays the more important rôle.

In the matter of diminished resistance of the walls of the ventricles in congenital hydrocephalus, Weber contracts the natural pliability of the fetal brain with the general or localized diseased condition of the brain substance in cases coming on later in life when dilatation may be symmetrical or confined to one, or to a portion of one, ventricle.

In that form of hydrocephalus characterized by hypersecretion, Gowers has so frequently found meningitis associated with inflammatory changes in the ependyma and choroid plexuses that in his textbook he says, “the only known cause of hydrocephalus is meningitis.”

Spiller and Allen, in their report of two cases dealing with the causes of hydrocephalus, refer to Anton's support of Baginsky's opinion that acute hydrocephalus is identical with a nontuberculous inflammation involving not only the choroid plexuses, but also the walls and ependymal lining of the ventricles. Anton and Böninghaus appear to be in accord with the opinion held by Gowers and others that these inflammatory changes are always associated with a simple or purulent meningitis.

Quincke presents in detail the clinical studies of a number of cases in his effort to reach a definite understanding of the condition. Of the latter group of ten cases, two were examined post mortem, while in the others recovery, more or less complete, took place so that the clinical diagnoses could not be confirmed. In those cases which came to necropsy, no mention was made of the aqueduct of Sylvius. Beside the recognized causes of serous meningitis, Quincke points out the possibility of acute angioneurotic exudation from the choroid glands and ependyma, without fever or inflammation, a condition analogous to angioneurotic edema of the skin, and which he has designated angioneurotic hydrocephalus.

In summing up his conclusions regarding the pathologic changes in a number of cases of marked hydrocephalus in the adult, Parkes-Weber says that “apparent thickening or slight granulation of the

9, Gowers: Diseases of the Nervous System.
ependyma should not be accepted as evidence of a genuine inflammatory process.” Continuing, he recalls that “the whole ependyma has been subjected to chronic stretching and the pressure exerted by the effusion must of necessity damage the tissues immediately bordering it, and will probably cause a necrosis of individual cells, and, in chronic cases, a reactive change will follow and will be accompanied by a certain amount of cell infiltration, as it is wherever a local necrosis occurs.” Parkes-Weber believes that Quincke’s theory of the purely angioneurotic origin of some cases of hydrocephalus “lacks evidence to support it,” but he advances the idea of extravasation into the brain cavities, comparing such collections of fluid to the serous effusions into the pleural and peritoneal cavities resulting from a serous pleuritis or peritonitis.

He explains the occurrence of idiopathic hydrocephalus as due in all probability to localized meningeal or ependymal inflammation producing an increase of cerebrospinal fluid. As an illustration of such localized inflammation, Parkes-Weber directs attention to the frequency, in fatal cases, of involvement of the posterior part of the roof of the fourth ventricle, and points out that the increase of fluid is due, not only to closure by the inflammatory exudate of the foramina in this situation, but that this region is one of the sites of election for the localized inflammation which leads to hydrocephalus.

This view is substantiated by Joslin’s report of eight cases of hydrocephalus following meningitis which showed this selective preference for the roof of the fourth ventricle. In all of his cases the foramen of Magendie and the openings into the cisterna lateralis had been closed and the roof of the ventricle rendered impervious by the inflammatory exudate. No changes were observed in the choroid plexuses and microscopic examination showed no thickening about the blood vessels. In one case of the series, that of a boy 16 years old, the aqueduct was occluded by a cystic tumor about 13 mm. in diameter, and adherent at several points to the choroid plexus of the third ventricle.

That the fourth ventricle is peculiarly liable to become the seat of a lesion causing dilatation of the cerebral ventricles and widening of the aqueduct of Sylvius, is abundantly attested by other workers, and cases of this type presenting symptoms of cerebellar tumor have been reported by Bramwell, Spiller, Finkelberg and Rhein.

Rhein's case, which showed the presence of a cyst in each cerebellopontine angle, is of further interest on account of an associated syringomyelia extending from the second cervical to the eighth dorsal segment of the cord. In the article Rhein says that Hinsdale, in a collection from the literature of 150 cases of syringomyelia, found hydrocephalus in fifteen.

Guthrie\textsuperscript{18} says, in this connection, that primary hydrocephalus is frequently associated with syringomyelia, hydromyelia, and various forms of spina bifida, and these conditions he regards as being dependent on some abnormality of development of the meninges. Guthrie, in agreement with others, looks on meningitis as the principal etiologic factor in the majority of cases both of congenital and acquired hydrocephalus, and in his report of eight cases showing occlusion of the aqueduct, ascribes six to the results of meningitis, while one was due to the obliterating effect of a glioma of the pons, and, in the eighth, pressure of two symmetrical tubercular nodules effectually closed the iter.

The literature contains the accounts of a relatively small number of investigated cases of occlusion of the aqueduct, and the infrequency of careful and intimate examination in such instances is very much in evidence. Thus Bourneville and Noir cite a case of hydrocephalus in a child in which the aqueduct was completely closed, but a microscopic examination was not made. Touche, Oppenheim and D. Astros, without giving any specific instance, say that hydrocephalus affecting the third and lateral ventricles will follow plugging of the aqueduct of Sylvius, and von Becterew has observed obliteration of the aqueduct in some cases of cerebral syphilis with symptoms of dementia paralytica, but he does not go more into detail.

On the other hand, a considerable number of cases has been recorded in which hydrocephalus has been caused by obliteration of the fourth ventricle by papillary new growths springing from the floor, the roof and choroid plexus of the ventricle, notably the reports of Slaymaker and Elias,\textsuperscript{19} Jacobson\textsuperscript{20} and Douty.\textsuperscript{21}

Spiller\textsuperscript{15} reports a case of hydrocephalus internus presenting symptoms of cerebellar tumor due to closure of the aqueduct of Sylvius by proliferation of neuroglia, and in the same article he attributes a case of unilateral distention to partial blocking of the foramen of Monro from extension of an inflammatory process in the neighborhood. In another case of hydrocephalus which came under the observation of Spiller and Allen,\textsuperscript{10} there was found occlusion of the aqueduct probably

\textsuperscript{18} Guthrie: Practitioner, London, 1910, 53, 47.
\textsuperscript{20} Jacobson: Hilton's Lectures on Pain and Rest.
\textsuperscript{21} Douty: Brain, 1885, 8.
due to congenital malformation. The second of this group also seemed to be due to congenital malformation and was reported as a case of intense hydrocephalus without occlusion of the aqueduct.

The absence, in many instances, of demonstrable signs of a previous postbasic meningitis and the frequent development of a central gliosis, as demonstrated in this collection, lead to the belief that some form of obliterative process of the aqueduct, not necessarily associated with meningitis, could be discovered if diligently sought. As already suggested, the presence in the cerebrospinal fluid of some toxic product of metabolism or the influence of some disturbed function of internal secretion may be the exciting cause of a general or localized ependymitis leading, eventually, to closure of the aqueduct.

Thomas,²² in his experimental work, has shown that hydrocephalus can be produced by injection into the ventricles of an irritating substance, and, using for the purpose a suspension of aeuronat, he has demonstrated that, through the acute inflammatory reaction which follows, obstruction may occur at the foramen of Monro, the foramen of Magendie, or in the aqueduct of Sylvius.

Accepting the well established facts regarding the origin and disposal of the ventricular fluid, it follows that, with plugging of the aqueduct, the essential cerebral avenues of escape are not sufficient to drain the ventricles and distention consequently results. With a definite obstruction to the normal flow through the aqueduct toward the fourth ventricle, facilities for the removal of cerebrospinal fluid are diminished, since the influence of the great cisterns and spinal subarachnoid cannot be brought to bear, thus throwing the burden of absorption on the cerebral sinuses and lymphatics.

REPORT OF CASES

Case 1.—History.—L. T., who was admitted to the Beth Israel Hospital, March 29, 1911, and who died the day following an exploratory operation, was a boy 3½ years old, the second of three children. Of the other children the eldest was living and apparently perfectly normal at the age of 9 years; the youngest was born dead after an instrumental delivery.

The patient, who had never been seriously ill, was born, the mother stated, with a large head, but that up to nine months prior to his death the child seemed to be perfectly normal in every other respect, exhibiting at all times good mentality. Nine months before his admission to the hospital the patient had a fall, striking on the head; this fall did not cause any external injury, but unconsciousness for some minutes' duration ensued, and this was quickly followed by vomiting. Six weeks later a well-defined and typical attack of epilepsy developed, and thereafter the child complained much of headache and suffered repeated attacks of convulsions, with unconsciousness. The last convulsive seizure occurred four months before his admission to the hospital; at that time and five months after his head injury, the child's mother noticed that his gait had become slow and uncertain and it soon became impossible for him to stand or walk without assistance. Vomiting which had no relation to the

ingestion of food, increased in frequency and the boy became ill-tempered, excessively irritable and nervous. His mentality, however, remained clear.

*Physical Examination.*—The physical examination by Dr. Sachs showed that the patient was very well nourished, so much so, that the general and abundant distribution of fat suggested the possibility of some disturbance of the hypophysis.

The abdominal and thoracic organs showed no abnormalities. Neurologic examination demonstrated a spastic-ataxic gait, but there was no ataxia of the upper extremities and the Romberg sign was absent. The knee jerks were equal and not disturbed, but ankle clonus and the Babinski reflex were present on both sides. Apparently there were no sensory disturbances. Examination of the cranial nerves showed double choked disk, with the left more swollen than the right; the retinal vessels were tortuous but there were no hemorrhages. Slight nystagmus appeared when the eyes were directed toward the right, but otherwise the movements of the eyeballs were not affected.

![Fig. 1 (Case 1).—Section through the entire thickness of the cortex, showing the presence of small nodules on the ependymal surface of the lateral ventricle, a manifestation of a general ependymitis. The pia-arachnoid appear normal.](image)

The pupillary reactions were not recorded.

Vision and hearing appeared to be normal in response to the usual tests. There was no deviation of the tongue when protruded, and the act of swallowing was performed perfectly. The sense of smell was not tested and the other cranial nerves showed nothing pathologic.

In the right parietal region a small angioma was exposed when the scalp was prepared for operation. In its greatest circumference the head measured 62 cm., the fontanels were closed and the frontal eminences were unusually prominent. The veins of the forehead were much distended.

*Operation.*—Decompression was performed by Dr. Sachs April 15, and the following day the patient died.

*Gross and Microscopic Examination.*—The gross specimens of the case submitted for examination were cut through the crura and complete occlusion of the aqueduct clearly shown.
Microscopic section made through the pons confirmed the macroscopic appearance and demonstrated the existence of a central gliosis, with a marked proliferation of ependymal cells, which in places near the central lesion showed a glandular arrangement tending to the formation of cysts.

In the subependymal glia tissue fibrils were present to a considerable depth and the same process could be observed extending ventrically along the raphé, and in this portion cellular elements were also abundant.

Examination of a portion of the cerebral cortex presented evidence of a general ependymitis, and section through the cortex, including a portion of the ependymal lining on one lateral ventricle, showed the existence of small nodules in which cell elements predominated.

Fig. 2 (Case 1).—Showing central gliosis occluding the aqueduct of Sylvius, with proliferating ependymal cells arranging themselves in alveolar formation.

The meninges showed no inflammatory process and no abnormality of the hypophysis could be made out. From these changes it is to be inferred that closure of the aqueduct of Sylvius had existed from the earliest period of development of the child's brain, and the fall sustained may perhaps be considered as an exciting cause of an ensuing ependymitis with consequent increase of the cerebrospinal fluid.

Case 2.—History.—To Dr. John Howland, in whose service at Bellevue Hospital this case occurred, and to Dr. Charles Norris, pathologist, acknowledgment is made for the clinical history, the necropsy report and the pathologic
specimens in the case of G. N., a boy, 5½ months old, admitted to the hospital March 18, 1911, and who died March 27, 1911. It was said by the mother of this baby that she had noticed no abnormality of development until, during the second month of his life, her attention was directed to the increasing size of the baby's head. Shortly after this the child began to have peculiar spasms lasting about three minutes, during which the upper and lower extremities became very stiff. These convulsive attacks recurred three or four times a day. Later, when the patient was about 4 months old, a lumbar puncture was made. The removal of a little more than a pint of cerebrospinal fluid brought about a marked improvement, which continued for six weeks, when the child again grew gradually worse and died March 27, 1911.

Fig. 3 (Case 2).—Lesion of central gray matter showing closure of the aqueduct through a distinct proliferation of glia cells, giving to the new formation the appearance of a glioma.

The patient, who was the only child, was delivered at term with the aid of instruments, after an active labor of twenty hours' duration. The parents of this child were living and well and there was no family history pointing to any possible etiologic influence.

Physical Examination.—Physical Examination showed an abnormally developed, but fairly well-nourished infant with a high, protruding forehead, prominent parietal bosses, large open fontanels and the whole vertex soft and pulsating.
Measurements of the head were as follows: Cm.

Greatest circumference ........................................... 63
Occipito-mental circumference .................................. 61

Diameters:
Occipito-frontal .................................................. 22
Occipito-mental ................................................... 21
Biparietal .......................................................... 17
Bitemporal ......................................................... 13.5
Suboccipito-bregmatic .............................................. 18
Frontal-mental ..................................................... 18

Fig. 4 (Case 2).—Another section of central gray matter showing obstruction by the new formation.

Chest measurements, at full expansion at the level of the nipples, 39 cm.; at the costal margin, 41 cm. Abdomen, at the level of the umbilicus, 37 cm.; length of body, 68 cm.

The skin was rather mottled in appearance and showed a few erythematous areas. Examination of the thoracic and abdominal organs was negative.

On admission to the hospital the temperature was 99.6 F. and remained practically normal until the end; the day before death occurred the temperature fell to 94.8 and then rose again to normal. The limbs were somewhat spastic and the knee jerks were exaggerated.
Necropsy.—The necropsy confirmed the head measurements taken before death, and, in addition, records the dimensions of the anterior fontanel as 17 cm. in length; 15 cm. in its greatest width. The right parietal bone was considerably ossified and more prominent than the left. The tissues of the scalp were thin through distention, and, on removal of the cranial bones, the brain was revealed as a large sac filled with a clear fluid.

The cerebral cortex measuring 1 mm. in thickness was entirely without fissures or convolutions. The basilar ganglia appeared normal, the caudate nucleus on each side being especially well formed. The olfactory lobes and optic tracts were remarkably flattened and the hypophysis cerebri appeared softened. The cerebellum, the medulla and the nerves at the base of the brain showed no abnormalities and the vessels in these regions were normal, while evidences of meningitis were absent.

Microscopic Examination.—Sections made through the midbrain showed complete occlusion of the aqueduct of Sylvius and microscopically the obliteration was seen to have been brought about by proliferation of glia cells, which, with a great increase of glia fibrils, had practically erased the contour of the central gray matter, producing the appearance of a glioma. The disposition of the ependyma cells to arrange themselves in the form of cysts was pronounced.

Fig. 5 (Case 3).—Gross specimen showing greatly distended third and lateral ventricles, with thin cerebral cortex. The basal ganglia and entrance to the aqueduct are clearly pictured.

Above the point of obstruction the aqueduct became patent and appeared much wider than under normal conditions, and sacculated, while the immediately subjacent structures had been invaded by the same process.

The meninges appeared normal and the choroid plexuses presented no demonstrable changes.

Case 3.—History.—This patient, a girl, 2½ years old, was admitted to the children's ward at Bellevue Hospital, March 28, 1905, with the statement of the mother that the child was born with a very large head and that the condition had been gradually increasing. Of the family history little was learned beyond the fact that the parents were living and well, and that of several brothers and sisters all were perfectly normal.

Physical Examination.—It appeared that the child took its nourishment without any trouble, but had never been able to move her arms or legs. At the hospital it was found that, aside from complete paralysis of the extremities, the child, as far as could be determined, reacted to painful sensory stimuli by crying. The child was blind and did not seem to hear, but all the movements of the face were carried out in perfect coordination as observed when the patient
cried, or at times seemed to smile. This showed that coordinated movements of the facial muscles were possible through emotional stimulation.

In posture this patient lay with the head fully extended, pressure at the point of contact between the back and occiput causing an erosion of the skin. The eyes could not be closed on account of the tension of the skin which drew the eyelids upward. Any movements of the patient's head or extremities caused her great distress.

The temperature of the patient was normal until two weeks before death, when it reached an elevation of 103 F., and during the last week of her life it remained above 101, dropping at the last to 97.

The extremities were spastic, legs and feet extended; the arms were flexed at the elbows and fingers folded in on the palms. In the upper extremities marked tremor was present. The tendon reflexes were very active.

The pupils were moderately dilated, equal and insensitive to light. There were no ocular paralyses. There was some rigidity of the abdominal muscles, but otherwise examination of the thoracic and abdominal organs was negative.

Necropsy.—Necropsy was performed May 10 by Dr. Charles Norris, and to him acknowledgment is made for the pathologic material. In general, the post-mortem examination showed no special deviations from the normal, the findings being negative except for the presence in the posterior portions of the lower lobes of both lungs of hyostatic congestion and a cystic condition of the left suprarenal gland.
Head: Parietal, frontal and occipital bones were found to be about the thickness of heavy parchment. The measurements were as follows:

Posterior fontanel, small but open.
Anterior fontanel, along the coronal suture.............. 22 cm.
In direction of sagittal suture...................... 7 cm.
Lambdoid suture, closed.

Measurements of face:
Chin to nasion........................................ 10 cm.
Malar to malar........................................ 9 cm.

In its greatest circumference the head measured, over the parietal and occipital protuberances, 67 cm., and the greatest anteroposterior diameter from the nasion to the external occipital protuberance was 52 cm.

On opening the calvarium the dura was found to be adherent, thin and translucent. There was no distinct evidence of pacchionian granulations, and the superior longitudinal sinus was entirely empty.

After carefully removing the dura, the cortex appeared smooth and bloodless, with no suggestion of fissures or convolutions. The posterior third of both hemispheres consisted of a very thin, transparent membrane through which could be seen the large cavities of the distended lateral ventricles. The cortex of the anterior two thirds of both hemispheres was very thin, measuring 2 mm. in thickness, but gradually increasing toward the base of the brain where it passes over the lenticular nuclei. Here the cortex measured from 5 mm. to 1 cm. in thickness.

The lateral ventricles were opened dorsally, liberating about 5 liters (estimated) of a clear, light-colored fluid. The corpus callosum was missing.

The basilar ganglia were present, though somewhat diminished in size. Lying between the optic thalami, the third ventricle appeared as a depression, and leading from its anterior portion the distended infundibulum could be made out, surrounded only by a thin membrane with the normal nervous tissue missing.

From the posterior portion of the third ventricle there might be seen the entrance to the aqueduct of Sylvius which later sectioning showed to be completely occluded. The fourth ventricle was not distended.

The optic nerves were smaller than normal, but were not compressed as were the olfactory lobes and olfactory tracts; all of the other cranial nerves appeared to be somewhat small, but otherwise showed nothing pathologic. The crura and pons from the ventral surface appeared normal, while the medulla and spinal cord showed plainly the entire absence of the pyramidal tracts. The

Fig. 7 (Case 3).—Section of spinal cord in the dorsal region showing again that the motor tracts are missing. The gray matter is normal.
cerebellum and peduncles were normal. The accompanying photographs (Figs. 4, 5 and 6) clearly demonstrate the absence of the pyramidal tracts, and this explains at once the complete paralysis of the extremities. But how are we to account for the coordinated movements of the facial muscles, the motor neurons being absent?

Fig. 8 (Case 3).—The pons in the region of the nucleus of the third cranial nerve, showing obliterating effect of a central gliosis beginning about the aqueduct. In microscopic specimens the lesion has the appearance of having existed from a very early period of the child's life.

It is well known that, as we trace the phylogenetic development of the central nervous system from the lower to the higher forms of animal life, the function of motion is transferred from the basal ganglia to the cerebral cortex. If, for instance, the motor cortex of a dog or cat be destroyed, it will be found that
these animals, after the shock of the operation has subsided, are still capable of walking, although in a disturbed manner, showing that some center other than the motor center in the cerebral cortex still has an influence over movements of the extremities. This center is undoubtedly situated somewhere in the basal ganglia.

Removal or destruction of the motor cortex of the human brain or brain of the higher monkeys, however, results in complete paralysis of the extremities.

Fig. 9 (Case 4).—Section taken at the beginning of the fourth ventricle, showing the first appearance of the obliterating process as a pedunculated mass composed of proliferating choroidal cells. Except near the choroid plexus, it shows no special disturbance.

a fact which shows that the motor function has been completely transferred from the basal ganglia to the cerebral cortex. It seems, however, that this transfer of the motor function has as yet not taken place completely in movements of the face, and particularly has it not taken in those muscular actions expressing the emotions; so we must conclude that the emotional movements of the face are still, to a certain extent, vested in the phylogenetic earlier motor centers of the basal ganglia. This conclusion is amply justified by the total absence, in Case 3, of a cerebral motor cortex.
Historically, the essential features of gliosis are present in the pathologic changes which closed the aqueduct in this case, and while the process does not appear to be as active and aggressive as in the preceding pictures, occlusion is complete. Above the lesion the aqueduct is much dilated and the ependymal lining is normal. Sections show clearly the absence of the pyramidal tracts at all levels of the cerebrospinal axis.

The meninges did not show the presence of any inflammatory exudate and there were no appreciable changes in the choroid plexuses.

Case 4.—History.—This child was admitted to the Presbyterian Hospital, Oct. 20, 1909, at the age of 6 months, and came immediately under the observation of Dr. John A. Hartwell, whose interest eventually made possible a histologic study of this case.

According to the records of the hospital, the child was born normally at full term, of perfectly healthy parents. Of the other children in the family, two brothers were living and well at the ages of 12 and 9 years, respectively; each of two sisters died within one hour after birth, the delivery in each case having been instrumental.

This baby nursed up to the time of her admission to the hospital. When 6 weeks old, however, she suffered from serious bowel trouble, a condition which was described by the family physician as marasmus. The illness continued about six weeks and the child had “weak spells”—“internal convulsions,” the mother called them—when she seemed dazed and almost unconscious for a whole day at a time. At the age of 3 months the child had a well-defined convulsion, lasting about five minutes; this was the only pronounced epileptiform attack which occurred, and was caused, the physician believed, by a condition of chronic constipation which required the daily use of a cathartic.

The mother stated that the child’s head had been large since birth and to her had never seemed like other children. She had never attempted to raise the head, and one eye had turned outward from birth. The baby’s eyesight during the last month had been very poor, and the mother believed that the baby could not see at all, but lately she had appeared to recognize her mother’s voice. During the previous six weeks the head had grown considerably in size.

Physical Examination (by Dr. Davis).—The patient was a moderately well-nourished child with an enlarged, square head.

Measurements:

<table>
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<tr>
<th>Measurement</th>
<th>Inches</th>
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<tbody>
<tr>
<td>Occipito-frontal</td>
<td>19½</td>
</tr>
<tr>
<td>Occipito-bregmatic</td>
<td>18⅛</td>
</tr>
<tr>
<td>Occipito-mental</td>
<td>19⅛</td>
</tr>
<tr>
<td>Fronto-mental</td>
<td>19⅛</td>
</tr>
<tr>
<td>Mastoid to mastoid</td>
<td>15½</td>
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The anterior fontanel was open and its anteroposterior diameter and the lateral diameter each measured 4 inches. The parietofrontal sutures had not yet united and there was no pulsation.

Eyes, ears, nose, mouth and face were of normal size. There were no glandular enlargements to be made out. Examination of the thoracic and abdominal organs was negative. The knee jerks were exaggerated and there was ankle clonus and the Babinsky reflex on both sides.

Operation and Course.—Oct. 22, 1909, an operation was undertaken by Dr. Hartwell for the purpose of draining the ventricles of the brain into the peritoneal cavity.
Procedure: Three incisions were made: first, in the right side of the abdomen and through the peritoneum, about two inches below the costal margin; second, over the middle of the right clavicle; third, 1 inch above and behind the right external auditory meatus. A probe was then passed upward subcutaneously from the abdominal incision to the clavicular incision. A grooved director was passed from this latter opening to the wound in the scalp, making a channel for the probe. A heavy silk thread was then drawn through these tracks, making a subcutaneous channel from the skull to the abdomen. A double twisted wire was then made to replace the silk. The dura was incised through a quarter-inch trephine opening in the skull and the end of the loop of

![Fig. 10 (Case 4).—Section greatly enlarged, showing at the level of the eighth cranial nerve invasion of the pons and cerebellum by the proliferating new growth, causing complete occlusion of the ventricle.](image)

wire was driven by means of a probe into the brain in the direction of the opposite external meatus. The lower end of the wire, formed into a loop, was passed into the peritoneal cavity and the three wounds closed.

A considerable amount of cerebrospinal fluid was lost at the time of the operation, but the patient's condition was satisfactory, and on October 30 she left the hospital improved.

The temperature following the operation ran along at 102°F. or over, 104 being the highest temperature recorded. On the sixth day the temperature began to fall and then remained below 100. The pulse varied from 140 to 200 per
minute and slowed finally to 110 to 100; respirations from 40 to 30. On the fifth day following the operation the sutures were removed and the wounds were found to be clear. In spite of the rapid pulse it always maintained fair quality. The patient had numerous muscular twitches bilaterally for several days, but these gradually lessened and finally disappeared. The fontanels became very much depressed, showing that drainage from the ventricles was actively taking place.

The child remained with the parents until Jan. 4, 1911, when she was admitted to Bellevue Hospital suffering with mastoiditis complicating her hydrocephalus, which had not greatly improved during the interval. The baby's general condition was good and the neurologic examination gave about the same results as at first observed. The fontanels were closed. There was slight internal strabismus, and while the pupils reacted sluggishly to light, it was evident, that the child was blind.

Fig. 11.—(Case 5).—Cross section in the region of the nucleus of the third cranial nerve showing presence of small tumor mass, histologically a glioma, proceeding from the floor of the sylvian aqueduct and partly occluding the lumen.

The mastoid condition was relieved by operation, and at the same time Dr. Hartwell removed the silver wire which, in the first instance, had been introduced for purposes of drainage of cerebrospinal fluid. It was found that the subcutaneous channel was completely lined by epithelium and permanent drainage into the peritoneal cavity established. Improvement was manifest for a time after these aspirations, but death occurred in her own home a few weeks later.

Microscopic Examination.—This shows complete obliteration of the fourth ventricle and the aqueduct of Sylvius.

In Figure 7 may be seen the process beginning in the raphé of the floor of the ventricle, appearing as a pedunculated tumor mass composed of choroidal cells, with invasion of both the cerebellum and medulla. Passing cephalically, these choroidal cells increased in quantity, and in Figure 8, at the level of the nucleus of the eighth cranial nerve, the ventricle appears to be completely filled.
Here as at other levels proliferating choroidal cells invade the nerve tissue of the cerebellum, medulla andpons in typical neoplastic fashion.

The aqueduct of Sylvius throughout its course is entirely closed, not by choroidal cells, but by proliferation of the surrounding glia cells.

At those points where the cerebellum and medulla have been invaded, choroidal cells, having taken on the characteristics of ependymal cells, have arranged themselves in the form of small cysts.

The choroidal cells are unquestionably spongiosiblastic, derived from the same mother cell, which gives origin to the glia and ependymal cell.

CASE 5.—History.—The only clinical history obtainable in this case is taken from the records of the City Hospital and from the nurses' bedside notes, and relates principally to the surgical treatment which this child of 15 months received from the time of his admission to the ward, Feb. 11, 1911, to the date of his death, Oct. 26, 1911.

The specimens of this and the following case were furnished by Dr. John H. Larkin, pathologist to the Department of Charities, New York City.

The case is that of a boy, 1 year and 3 months old, who showed on physical examination a large head, globular in form, with greatly enlarged fontanels, through which fluctuation could be plainly felt. The face was small and pinched in appearance, eyes prominent and bulging, and the superficial veins of the head distended.

Dr. Dawbarn, in whose service at the City Hospital the case occurred, attempted to drain the lateral ventricles into Stenson's duct, and with this end in view an operation was performed by him, Sept. 25, 1911.

Operation and Course.—The records state that a large semicurved needle was introduced into the anterior fontanel well away from the middle line and made
to merge from the anterior part of the parotid gland. A No. 18 silk tape was then carried through, cut off at each end even with the surface, and the ends buried by closing both incisions.

The greatest circumference of the head before operation was 67.5 cm. After operation, which was attended by a considerable loss of cerebrospinal fluid, measurement of the head showed a circumference of 65 cm., and by September 30 this was further reduced to 63.7 cm.

During the month of August it appears that the baby had four severe convulsions of from five to seven minutes' duration, and again on September 24, the day before the operation, a very severe convulsion occurred; and on September 25, shortly after the operation, there is a history of repeated slight

Fig. 13 (Case 6).—Syphilitic gumma proceeding from the pia-arachnoid, invading and partially occluding the fourth ventricle. Characteristic changes in the lymph and blood vessels are much in evidence.

attacks. Vomiting and unusual restlessness then set in and continued for two days, when the child again became quiet and retained most of his nourishment. It was noticed on September 27 that the patient's body and extremities had become very stiff and vomiting occurred more frequently. During the whole of his stay at the hospital the baby was, at times, extremely restless and frequently cried throughout entire day and could not be pacified.

Gradually increasing weakness and frequent periods of restlessness marked the progress of the succeeding days, and on October 9 a second operation similar
to the first was performed on the opposite side of the head. During the three days following this operation the child seemed better and was making satisfactory progress, when a marked weakness supervened, and, although the patient took nourishment fairly well, this weakness increased and gradually it became more and more difficult to administer nourishment. Death finally took place Oct. 26, 1911.

Examination of Brain.—The gross specimen in this case was of unusual appearance, the bases of the anterior crura being almost unrecognizable as such. The right crus, very much enlarged, appeared as a tumor mass about 1.5 cm. long and 2 cm. in its transverse diameter; the left crus was smaller, measuring about 1 cm. in thickness.

Fig. 14 (Case 6).—The region of the nucleus of the third cranial nerve, showing complete occlusion of the aqueduct and activity of the ependymal and perivascular changes in the subependymal tissue.

These masses disappear at a point where the crura pass into the pons; cephalically, they extend to a point considerably above the red nuclei. Between these two masses the neutral fissure reaches between the red nuclei to the level of the aqueduct.

The aqueduct in the region of the nucleus of the third cranial nerve appears to be entirely closed, but microscopically a minute sacculated opening remains, and this is partly filled with a small tumor formation growing in from the roof of the aqueduct; similarly, at a point where the aqueduct normally tends to widen out centrally, another small growth makes its appearance, invading the
lumen of the aqueduct from above. At this same level a very small new formation may be seen taking origin from the subependymal structures of the floor of the aqueduct.

**Microscopic Examination.**—Histologically, these invading masses are gliomata. The choroid plexuses do not appear to be the seat of inflammatory changes, but many choroidal vessels are engorged, indicating a lesion of obstructive type interfering with the normal functioning of these glands.

The general ependyma shows no abnormality, but in the more deeply lying tissues there is very evident abnormal cell activity, with extensive perivascular round cell infiltration. Here several contributory factors in the production of hydrocephalus may be seen in combination. Not only is the aqueduct encroached on by protrusion into its lumen of various small gliomata, but the processes of secretion and absorption have been disturbed through involvement of the choroidal vessels and ventricular walls.

![Fig. 15 (Case 7).—Showing congenital malformation of the sylvian aqueduct, which has had the effect of closing the passage.](image)

**CASE 6.—History.**—As in the preceding case, the hospital records are incomplete, the available history dealing chiefly with incidents of the child's birth. The baby was born at full term of a young multipara, who, as far as could be learned, was a perfectly normal individual. Her other children were born normally, and they made entirely satisfactory progress through infancy and childhood. In this instance, however, labor was prolonged and difficult, the second stage lasting thirty-six hours, and it was only after craniotomy had been performed that delivery could be accomplished. The mother made a good recovery and returned the next year to the maternity wards of the City Hospital, where she gave birth to a perfectly normal child.

While nothing was discovered in the history on the part of the mother to suggest a possible cause of the hydrocephalus, the fetal brain was examined
by the Noguchi method and *Spirochaeta pallida* were found in the cerebral tissue. This placed the origin of this case definitely on a syphilitic basis, and is the only one of the series to react in this manner.

Further microscopic evidence of the syphilitic nature of this lesion is to be found in high-power study of the sections.

**Examination of Brain.**—The gross specimens showed fairly well-developed pons and medulla, while the basal ganglia were of fair size and consistency. The cerebral cortex, however, was thinned out to a mere sac-like formation, containing very little brain substance and possessing no convolutions or fissures.

**Microscopic Examination.**—Microscopically, the picture is that of meningoencephalitis with characteristic blood-vessel changes in which the perivascular lymph spaces are crowded with infiltrated round cells and lymphocytes. The aqueduct in the sections is completely closed and considerable cell activity is to be made out in the ependyma and periependymal tissues.

Many small spaces lined by cuboidal cells give the appearance of cysts, suggesting the tendency of certain modified ependymal cells under stimulation to arrange themselves in this manner, but undoubtedly these stand in relation to obliterated vessels remaining as evidence of earlier lymph stasis with consequent changes in adjacent areas.

In the region of the nucleus of the eighth cranial nerve a small gumma encroaches on the fourth ventricle, impeding the flow of cerebrospinal fluid. This pedunculated mass, originating in the pia-arachnoid, stands in close association with the choroid plexus of the fourth ventricle, and while the plexus and the choroidal cells themselves show no changes, the inflammatory exudate extends laterally, following for a considerable distance the pia covering of the gland. The exudate itself, marked by the presence of many lymphocytes and polymuclear leukocytes and showing areas of necrosis, is the seat of an active as well as a chronic inflammation.

**CASE 7.**—**History.**—To Dr. Elise L'Esperance, pathologist to the New York Women's Infirmary and assistant in pathology at the Cornell University Medical College, we are indebted for the specimens and history of this case.

The history shows that the parents of this child were young and healthy, and that the birth occurred as a miscarriage in the seventh month of pregnancy. The child lived about one hour.

**Necropsy.**—At the necropsy, performed by Dr. James Ewing, the head presented a high grade of hydrocephalus, with all the ventricles dilated. Measurements, however, were not taken.

The convolutions were flattened and the cerebral cortex measured from one-eighth to one-fourth of an inch in thickness. The lungs were completely collapsed and the heart on the right side was hypertrophied.

Both kidneys were cystic, the left atrophic, measuring 1.5 cm. by 1 cm.; the right hypertrophied, measuring 7 by 4 by 3.5 cm. There were cysts in the dilated renal tubules. The suprarenals were not affected; thyroid normal. The spleen and gastro-intestinal tract showed no abnormalities.

**Microscopic Examination.**—To the naked eye the aqueduct appears to be closed, but microscopically a passage remains in the shape of a minute slit, about which an active proliferative process may be made out, while at either end of the opening there is a well-advanced gliosis. Inflammatory and vascular changes have occurred in the choroid plexuses, with lymphocytic infiltration of the vessels of the medulla, pons and cerebral cortex.

**CASE 8.**—**History.**—An infant, 7 months old at the time of her death, was born, so the mother declared, with a head of normal size, but labor was difficult and delivery was finally effected after the ordinary forceps operation.

On admission to the hospital, Oct. 9, 1913, the chief complaints, as entered in the clinical history, were abnormally large head, great weakness and listlessness.
During her earliest infancy the baby suffered from obstinate constipation, but otherwise was perfectly normal, and the increase in the size of the head was so gradual that the abnormality was not definitely recognized until, in the fifth month of life, a friend directed the mother's attention to the now apparent disproportionate size of the child's head.

The mother then placed the infant in the Babies' Hospital, where she remained under observation for a short time. It had been the mother's custom to return to the hospital daily for the purpose of nursing the baby, and on the occasion of her last visit she found the child in a weak and exhausted condition following a lumbar puncture, and against advice removed the patient to her own home. Later, on the same day, however, the mother applied for admission to Bellevue Hospital, where eventually the child came under the observation of Dr. John Hartwell, who later performed an operation for the relief of the hydrocephalus.

In the family history it is perhaps significant that the Wassermann reaction in the blood of the mother was found to be positive, but this examination was made only after operation had been done.

The mother was in ordinary good health at this time and the father died a short time before of spinal meningitis. No definite venereal history was obtained. As a predisposing cause of the hydrocephalus the traumatic influence

Fig. 16 (Case 7).—Showing, under high magnification, active gliosis taking place about embryologically defective structure.
of an instrumental delivery may possibly be considered. The patient was the only child and the mother gave no history of abortion or miscarriage.

Physical Examination.—The appearance of the patient at the time of admission to the hospital was that of a hydrocephalic, female infant, well nourished, but very weak and listless. There was an abundant growth of hair.

The head in its greatest circumference measured 52 cm. The fontanels were open; the anterior, bulging and fluctuating, measured 16.5 cm. in its transverse diameter; the posterior was 3 cm. across.

Fig. 17 (Case 8).—Section of medulla in the midolivary region of the fourth ventricle, showing complete obliteration by a central gliosis.

The eyes showed external strabismus, the defect being more marked in the right than in the left eye. The conjunctivae were blue and congested. Examination of the eyegrounds showed the absence of choked disk. The vessels were slightly congested but there were no hemorrhages or papilledema.

The nose, ears and tongue were normal. There was no rigidity of the muscles of the neck; the hands were flexed and thumbs adducted. There was no abnormality of the lower extremities except webbing between the second and third toes of the left foot. The knee jers were somewhat exaggerated.

The heart, which showed poor muscle tone, was otherwise negative. The action was slow, regular, and there were no murmurs. The lungs were clear.

October 10 a lumbar puncture was made and 10 c.c. of a blood-tinged fluid withdrawn. The records do not show that a Wassermann test was made.
Operation.—October 22, Dr. John A. Hartwell performed an operation designed to drain the ventricles into the jugular vein. The proceeding was as follows:

A section of a vein 4 inches in length was taken from the mother's arm, and this was sutured, one end to the cardiac end of the external jugular vein of the patient, the other end carried by means of a cannula and sutured to the dura mater, the cannula itself being made to enter the lateral ventricle and the external jugular vein, which effectually drained the cerebral cavities.

A considerable amount of cerebrospinal fluid was lost during the operation, so that the fontanels, which previously had been hard and bulging, were, after the procedure, soft and flaccid, while the diameter of the head was reduced to 51 cm.

The fluid in the ventricles was confined under pressure, but the subarachnoid space appeared to be empty. The partial collapse of the skull was due in a measure to loss of cerebrospinal fluid during the operation, but this condition continued afterward, thus demonstrating the fact that drainage had been established and maintained.

The child's condition, however, was not more satisfactory than before the operation, and the weakness and depression, which had marked the case from the beginning, continued until death ensued the following day. The temperature of the patient continued practically normal during the whole period of observation.

Necropsy.—A full necropsy was refused by relatives, but the report as made by Dr. G. H. Wallace is as follows:

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Cm.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Greatest circumference of the head</td>
<td>51</td>
</tr>
<tr>
<td>From glabella to external occipital protuberance</td>
<td>33</td>
</tr>
<tr>
<td>Distance between mastoid processes</td>
<td>34</td>
</tr>
<tr>
<td>Anterior fontanel (depressed)</td>
<td>9 by 14</td>
</tr>
<tr>
<td>Posterior fontanel</td>
<td>1.5 by 1</td>
</tr>
</tbody>
</table>

A linear incision 4 inches in length extended downward parallel to the external carotid artery from a point 2 cm. above and 1 cm. posterior to the tip of the right mastoid, which was sutured and clean.

On opening the incision the right external jugular vein was found to be sutured to a transplanted vein which was attached to a cannula at its upper extremity, the cannula itself extending through the brain substance into the right lateral ventricle. The tissues of the scalp were otherwise normal. On opening the skull the dura was found to be adherent to the bone, the cerebral cortex was flattened and fissures and sulci were practically obliterated. In places the cortex was so thin as to be almost transparent.

The cranial nerves were softened and edematous.

The bridge of the nose was depressed and alae nasi flattened. The hair of the head was fine and abundant and extended over the forehead on each side to the supra-orbital ridge.

Macroscopically, the pathologic specimen revealed obliteration of the fourth ventricle by a tumor formation, and complete occlusion of the lower portion of the aqueduct of Sylvius, which showed marked dilatation in front of the posterior corpora quadrigemina. The dilated aqueduct opened into a greatly distended third ventricle, and the wall of the lateral ventricles was stretched to extreme thinness.

Structurally the lesion causing occlusion in this instance is practically identical with that of Dr. Hartwell's previous case, and the same invasion of surrounding tissues by choroidal cells is to be observed microscopically, but the cerebellum does not participate to the same extent as in Case 4.

The fourth ventricle and lower part of the aqueduct were involved in the obliterating process, and while the upper part of the aqueduct was open, active gliosis, with cell proliferation and fibril formation, was a marked feature.

The choroid plexuses did not show any demonstrable changes.
Reviewing the facts as they appear from our own observations and from a survey of the literature, it seems not unreasonable to attribute many, if not the majority, of cases of the congenital form of this disease to closure of the aqueduct of Sylvius through proliferation of the glia and ependymal tissues, or to invasion of the fourth ventricle by tumors having their origin in the floor, the choroid plexus or the membranous roof of the ventricle.

Those cases, also, developing acutely in previously healthy adults and older children, and which have shown microscopically the same pathologic changes, may have been brought about in the same manner, namely, through the stimulation by some chemical poisoning of a tissue which is embryologically defective. These cases, no doubt, differ etiologically from that large group following meningitis, the acute infectious diseases and those due to bacterial invasion of the brain substance and ependyma from extension of suppurative processes of the middle ear or cells of the mastoid, frontal and ethmoid bones.

A consideration of the life processes of the cell offers an explanation of the occurrence of many cases of congenital and acquired closure of the sylvian aqueduct.

Metabolism is nowhere more delicately expressed than in the highly complex chemical reactions of the cells of the central nervous system; and while knowledge of these reactions is still far from complete, it is, nevertheless, conceivable that any slight noxious influence may be sufficient seriously to disturb the latent forces of the glia cells, resulting in the dominating influence of one or another of the processes residing in these cells. These life processes may be divided into the nutritive, the formative and the functional activities. In the first, which involves an appropriation of nutritive substances from the blood, potential energy is stored up and is subsequently translated into formative or functional activity, as represented by cell division, on the one hand, or by functionation of the specialized cell, on the other. In cells which have become highly specialized, as the nerve cell, gland cell and muscle cell, the potential energy of the cell body is converted into the predominating activity, and the formative process is held in abeyance, and, so long as the normal relation between synthesis and catalysis is maintained, functional activity of the cell remains in a state of constancy. On the other hand, in those cells not highly specialized, as the ependymal, glia and the connective tissue cells, formative activity is easily awakened, and so it happens that in many cases of hydrocephalus, stimulation of these cells by some irritating substance results in an active proliferative process which involves not only the ependyma but the subependymal tissues of the aqueduct of Sylvius, as seen in the obliterative glioses which figure conspicuously in the accompanying photographs.
The exact nature, source and means of access of such damaging stimuli are not always readily determined, and, barring the possible influence of syphilis and bacterial invasion of the meninges, ependyma and choroid plexuses, there remain to be studied more closely the causal effects of circulating toxic byproducts of fetal or maternal metabolism, and variation in function of the endocrine glands.

Syphilis has not operated as a known etiologic factor in this sequence, with the exception of Case 6, in which *Spirochaeta pallida* have been found in the cerebral tissue. The Levaditi method has failed to show the presence of spirochetes in two other cases (2 and 7) which it was thought might be explained on the ground of a luetic infection. The clinical records do not include reports of the Wassermann reaction in the blood or spinal fluids of the parents of these children.