OBSTRUCTIVE HYDROCEPHALUS FOLLOWING CEREBROSPINAL MENINGITIS, WITH INTRAVENTRICULAR INJECTION OF ANTIMENINGITIS SERUM (FLEXNER).[1]

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Plate XXXI.

Despite the ultimate fatality and the failure to secure a post-mortem examination in the case of this unfortunate patient, the interest, from a therapeutic standpoint, of finding, long after the primary infection, the meningococcus still viable in the cerebral ventricles in association with an obstructure hydrocephalus, whereas the spinal fluid retained no trace of organisms, makes it seem desirable to place upon record even this single experience with the intraventricular injection of serum.

History.—A baby six months old was brought by its mother to the children's dispensary of the Johns Hopkins Hospital on the 21st of March, 1908, with the statement that the child had been wasting for four month and its head enlarging.

There was nothing in the parent's story as then related to Dr. J. H. M. Knox, the physician in charge, to indicate that the condition was other than a simple so-called essential hydrocephalus, but owing to the unusual degree of tension of the head and the infant's apparently critical condition Dr. Knox was insistent that some immediate steps be taken to even temporarily relieve the pressure, and the child was brought by him to the surgical operating room where, as will be related, lumbar and ventricular punctures were performed.

On *physical examination* the patient (Fig. 1) proved to be a frail, weak, semi-comatose baby possessing a greatly and somewhat asymmetrically enlarged head with widely separated sutures and fontanelles. The cranial enlargement was the more apparent when contrasted with the emaciated trunk and limbs. The skin over the small body hung in folds; the ribs were prominent; the abdomen was scaphoid. There was a macular rash over the chest and abdomen. Rectal temperature 99.6°; pulse 110; weight 3,900 grms.

There was a convergent strabismus; the pupils were dilated but reacted to light. Conjunctivæ were clear. Ears were negative. No herpes. No erupted teeth; nursing reflex active.

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The head was large, measuring 47 cms. in its greatest circumference. The fontanelles were widely opened and tense; in the center of the anterior fontanelle lay an island of bone measuring about 5 cms. in diameter (Fig. 2). All of the palpable sutures were separated. The tense scalp was covered with greatly dilated and tortuous vessels. There was a network of dilated venules in the eyelids. The general appearance of the head was that of infantile idiopathic hydrocephalus.

The head was markedly retracted; neck very stiff and resistent to passive movement; no arching of spine. There was a coarse tremor and marked spasticity of all four extremities. The arms were held flexed at elbows in "driving position"; the legs were occasionally (more usually the left) held flexed at the knee and ankle, but a slight stimulus would cause them to straighten out with accompanying dorsal flexion of the great toes.

The deep reflexes were all exaggerated; Babinsky's toe phenomenon was bilaterally positive. Kernig's sign was not definite; the limbs could be easily straightened by using a little force.

Thoracic and abdominal viscera were practically negative.

Lumbar and Ventricular Puncture No. 1.—Only a small amount of clear fluid was obtained from the lumbar meninges—not enough to diminish appreciably the intracranial tension; consequently a left ventricular puncture was performed at the outer angle of the open fontanelle, 120 c.c. of clear fluid being removed. Cultures were taken from each specimen, and smears were immediately examined, the lumbar fluid showing no organisms, whereas the ventricular fluid contained an abundance of Gram-negative, intracellular diplococci. The cultures from the lumbar fluid remained sterile, whereas those from the ventricular fluid gave a diffuse heavy growth, which proved to be a pure culture of the *Diplococcus intracellularis meningitidis* (Weichselbaum).

Not until the smears were examined did we for a moment suspect that there had been a previous meningeal infection—far from anticipating the actual presence of living organisms. In consequence of this disclosure the child was admitted to Prof. Barker's service, where, in the light of our acquired information, the following somewhat more detailed history (indicative of an acute illness, probably meningitis) was extracted from the parents.

Family History.—Unimportant.

Past History.—This, the fourth child, was born at full time after an easy labor. The head was not large at birth. For the first three months the child was breast-fed; since then, under a physician's direction, it had been put on a variety of changeable diets.

Present Illness.—Four months ago the child, then a seemingly normal baby of only eight weeks, awoke early one morning evidently suffering from some derangement of acute onset. This was followed an hour later by a severe convulsion which produced unconsciousness. On the following day there occurred four or five other convulsions, and again three weeks later still another of the same character, though there had been none in the interval. For several days and nights after the onset the child was feverish and screamed constantly. The eyes are said to have become crossed, the neck stiff and the head drawn back. There was no continuous eruption; no herpes.

The child had been treated during these four months by various physicians for pneumonia, muscular rheumatism, indigestion, intestinal rickets, etc.

In addition to the notes on the child's physical condition given above, a blood examination was made after entrance showing white blood corpuscles 17,000, polymorphonuclears predominating; red blood corpuscles of variable size; none nucleated.

March 22.—Lumbar puncture No. 2 was performed, only 2 c.c. of fluid being obtained: no evident increase of tension. Fifteen c.c. of antimeningitis serum (Flexner) were injected, causing evident discomfort. Microscopically the sediment of the centrifugalized fluid showed no organisms and hardly any cellular elements—only a few leucocytes were found. The cultures remained sterile, confirming the observation made on the fluid removed the day before at *Lumbar Puncture No. 1.*

March 24.—Child seems somewhat better, taking nourishment well. Fontanelles remain less tense than when first seen, that is, before first ventricular puncture. Child lies quietly on its side with head retracted and eyes widely open. Does not appear to see, though pupils react to light.

March 28.—The tension has gradually increased until the fontanelles have become fully as tight as on admission; circumference of head 46.5 cm. *Ventricular Puncture No. 2.* No anæsthesia; needle introduced through outer angle of fontanelle into left ventricle, presumably through second frontal convolution. Clear fluid, unstained with blood, rose in capillary tube to height of 95 cm., though child was quiet without crying or straining. Tube was lowered and 150 c.c. of clear, limpid fluid containing a few flucculi were slowly withdrawn; 15 c.c. of antimeningitis serum were then injected. Child's condition was unaffected one way or another; no vomiting followed the puncture as on the first occasion.

The fluid contained intra- and extracellular diplococci in considerable numbers. There was a diffuse growth on glycerine agar from two loops of the centrifugalized sediment.

The rectal temperature rose, after the puncture, to 101.2°, but the general condition on the following day seemed somewhat inproved.

March 30.—After atropine instillation a satisfactory view of the eye-grounds was obtained for the first time on this day, Dr. Bordley finding a choked disc of at least 3 D. on the right and 2 D. on the left, with extremely large and tortuous veins near the discs.

March 31.—Ventricular Puncture No. 3. Though the fontanelles are somewhat less tense than before and the child evidently gaining, the puncture was repeated; ventricular tension was not measured; 100 c.c. of fluid were withdrawn from the right ventricle and 15 c.c. of antimeningitis serum introduced.

The head measured 46 cm. before tapping, and 45.5 cm. afterwards, showing its ready collapsibility.

The fluid obtained was clear, though yellowish in tint, evidently stained by serum. A centrifugalized specimen showed diplococci in undiminished numbers, though possibly there were more intracellular and fewer extracellular organisms than before. Smears from two loops of the sediment again gave a diffuse growth on glycerine agar.

For two hours after the tapping clear fluid leaked from the puncture wound; the bandage and pillow were stained yellow and it was thought that much of the serum might have been lost. The head became so greatly collapsed that the thin shells of bone overlapped at the sutures.

April 1.—The general condition seems much improved; cheeks and body in general seem to be filling out. Actual gain in weight, however, is not great, possibly owing to loss of fluid. Head gradually refilling.

April 3.—Child irritable; crying much; head again tense, measuring 46.5 cm. *Ventricular Puncture No. 4.* Fluid rose in capillary tube only 50 cm.; 60 c.c. removed and 15 c.c. of antimeningitis serum introduced through needle.

The fluid was clear with no trace of color to suggest serum, much of which may have leaked out after the injection of March 31st. Smears showed diplococci both in and out of cells though greatly diminished in number. On culture two loops of the centrifugalized sediment gave isolated colonies instead of a diffuse growth as before.

April 5.—The rectal temperature again showed a transient rise to 101.8° after the puncture of two days ago. General condition, however, seems to be much improved. Weight 3,970 grm.

April 6.—Weight 4,150 grm. Child doing splendidly; sleeps well, takes nourishment greedily. Head less tense than on any previous occasion 48 hours after puncture. Condition thought to be so favorable that the contemplated retapping of the ventricle was postponed.

April 8.—During the early morning hours, from some unaccountable cause, the patient became cyanotic and developed Cheyne-Stokes respiration. When seen at 7:30 A. M. the baby was in a state of collapse; in a cold sweat; eyes sunken; pulse weak and hardly perceptible; respiration gasping.

The fontanelles had become tense during the night, and as a last resort a *ventricular puncture* (No. 5) was made, in the hope of relieving the pressure symptoms; 140 c.c. of clear, slightly yellowish fluid were removed. The child's condition was not appreciably changed by the procedure, and in spite of stimulation the pulse and respiration gradually grew weaker and the child died six hours later. The rectal temperature did not rise above 99°.

Cultures taken in the routine fashion (two loops of centrifugalized sediment on glycerine agar) from the fluid at this last tapping gave only eight to ten colonies. The smears showed a great diminution in the number of organisms. Some polymorphonuclear leucocytes contained indistinctly staining Gram-negative diplococci; there were very few extracellular organisms to be seen.

Comment.—It has been our impression that the fatalities in many of the cases of cerebrospinal meningitis that we have seen during the past few years have occurred through the medium of cerebral pressure rather than as the result of an overwhelming intoxication or terminal infection. Although not fully dwelt upon in the autopsy notes of each case, in most instances nevertheless the existence of a ventricular dilatation has been recorded. Unfortunately it has not been an invariable custom to harden the brains in situ, and consequently the full extent of the pyo-hydrops ventriculorum may in some cases have escaped notice.

As early as 1898 attempts were made in the Johns Hopkins Hos-

pital to treat some of the more desperate cases of cerebrospinal meningitis by surgical measures. At that time a few patients[2] were subjected to a lumbar laminectomy and a permanent drain was established after washing out the subarachnoid space as thoroughly as possible by retrograde irrigation. One of these patients recovered from the meningeal infection to die of pyo-nephrosis some two months later; another after a period of apparent improvement succumbed to the infection, and the meningeal spaces and basal cisternæ were found post-mortem so occluded with a fibrinoplastic deposit leading to an internal hydrocephalus that it was impossible to conceive of a lumbar drain helping the condition in any way.

In view of these and similar experiences a median suboccipital drainage with opening of the exposed posterior cistern has more recently been adopted and has seemed to promise more than did these lumbar operations; nevertheless, even in these cases, an obstructive hydrocephalus may develop. For this reason during the past two years a number of patients with evident ventricular obstruction have been subjected from time to time to ventricular aspiration. Some few of them have for the time being been markedly improved, although without exception they were all practically in extremis at the time of the operation. The brief history of one of these cases may be cited in illustration.

The patient, a sailor, was brought to the Johns Hopkins Hospital from a North German Lloyd steamer on January 19, 1907. During the voyage another sailor had died from meningitis. The patient was exceedingly ill with the characteristic symptoms of cerebrospinal fever. From the time of his admission to February 7 repeated lumbar punctures—twelve in all—were performed. After the earlier punctures there was considerable improvement; after the later ones none, and finally no further fluid could be obtained. A double choked disc appeared, complete nerve deafness, strabismus, delirium, etc. A cranial operation with puncture of the lateral ventricle at Keen's point of election was performed by Dr. Sowers. There was an almost immediate and a very marked improvement in the patient's condition; he regained consciousness, the choked disc and headache subsided, the temperature became normal, and there were no further untoward symptoms until February 15, when there was a sudden and unexpected exodus.

At the autopsy it was evident that the infection had largely subsided, leaving,

[2] Some of these cases were recorded by Dr. Osler in his Cavendish Lecture. *West London Medical Journal,* 1899, iv, 145.

however, a thick membrane which effectually closed the outlets for ventricular fluid in the neighborhood of the fourth ventricle. The lateral ventricles which were considerably dilated (Fig. 3) contained sero-purulent fluid. The lining surface, particularly of the left ventricle, showed the characteristic granular ependymal inflammation.

Before the days of serum treatment the experiences with lumbar puncture, as in this instance, usually proved symptomatically beneficial up to a certain period of the illness, at which time the punctures would often fail even temporarily to give relief, supposedly owing to the small amount of fluid, if any, which could be obtained. Since the serum injections following lumbar puncture have become a routine with us in the treatment of this disease, its course has almost always been less severe and it seems unquestionable that there has been less of a fibrino-plastic exudate than in the cases which were treated in earlier days by a lumbar puncture alone. This would make it seem probable that under the serum treatment there is a lessened likelihood of the particular complication we are considering.

However, even among our later cases there have been a certain number of fatalities, evidently due to a ventricular block, and in all instances in which an autopsy has been permitted internal hydrocephalus has invariably been found. Such a stasis of ventricular fluid in the closed skull of an adult leads naturally to critical pressure symptoms, and in the reduced physical condition of these patients the complication is often fatal. It is notable too that these signs of cerebral compression—the stupor, increased headache, the choked disc and so on—may supervene with considerable abruptness in the course of an infection which seemed to be progressing favorably, and not uncommonly late in the disease. In an infant, on the other hand, as in this patient the history of whose illness has been detailed, the pressure effects may be warded off through the possibility of cranial enlargement owing to separation of the sutures.

In case, therefore, the acute pressure symptoms can be alleviated, either by operative measures or, in an infant, by the method of relief through cranial distension, it is quite conceivable that the dilated ventricles may continue to hold organisms which remain a menace for a considerable period of time. For this to occur there

presumably must be a discontinuity between the ventricular cavities and the subarachnoid spaces of the brain and spinal cord. So far as clinical evidence can be relied upon, it certainly appears to be conclusively shown in this patient that such a discontinuity existed and that the organisms had completely died out of the spinal meninges and had retained their viability within the ventricles alone.

Late complications, associated oftentimes with a low grade of hydrocephalus and accompanied by irritative symptoms due to cortical changes and to cortico-meningeal adhesions, have in the past not uncommonly been seen after recovery from meningitis—complications which it is to be hoped will be greatly lessened under a more widespread use of serum treatment. It is but natural that they should be seen more frequently after recovery from the disease in childhood than in adult life, and it is well known that a low grade of persistent ventricular distension is not incompatable with subsequent and even unusual mental vigor, provided there has occurred a reopening of the outlets for the escape of fluid.

We have seen a number of cases in which, for some months after the primary infection, symptoms of ventricular distension recurred with a more or less definite periodicity, the pressure symptoms being absent in the interval. In some patients indeed, even after an interval of freedom, they have recurred and persisted. Some of these cases have been subjected to operation and one of them in particular we wish to mention:

The child had been desperately ill for six months during the epidemic of three years ago in New York, and his recovery was long despaired of. Blind and deaf, totally paralyzed for many weeks, there was a gradual slow restoration to fairly normal health. The child, however, began to have frequent convulsive seizures, many of them Jacksonian in character, and also began to fail mentally. An ophthalmoscopic examination showed a low grade of choked disc. A bilateral exposure of the hemispheres disclosed the presence of innumerable fine adhesions between the pia-arachnoid and overlying dura. These adhesions were separated over both hemispheres, the ventricle was aspirated, and at the same moment a lumbar puncture was performed. On lowering the capillary tube used to measure the tension of the fluid in the lumbar region, fluid was withdrawn in large amounts, evidently escaping from the ventricles by this lumbar route, for the somewhat protruding brain subsided markedly. It was the operator's impression that with an open skull the atmospheric pressure against the hemisphere was sufficient to allow a rechanneling of the membranous thickenings over the fourth ventricle, which enabled the pent up fluid to again find

its way from the ventricles into the subarachnoid spaces and thus to escape by its normal channels. The child completely regained its normal health.

This history is cited merely to emphasize the importance of these intracranial complications even in cases of recovery from cerebrospinal meningitis and the possibility of their at least occasional betterment through surgical measures.

Noteworthy in the case the subject of this report are the following facts—namely, the obstructive hydrocephalus; the long-standing ventricular infection with the meningococcus in the presence of sterile fluid in the spinal meninges; and finally the marked diminution in number of the organisms in the ventricles as the result of serum injection even in a case of such long standing.

The case suggests that it may be advisable in other instances of ventricular obstruction in the acute stages of the disease to perform, even in the adult, ventricular punctures and, if organisms are present, to administer serum, with proper precautions, directly into the ventricle.[3] It is possible that in this way the mechanical factors at work in producing the compression may be relieved for a time sufficiently long to tide over the period of plastic inflammation about the brain stem and thus to enable the channels of exit for the fluid from the ventricles again to become reopened.

[3] Unusual care, of course, particularly in the closed skull of the adult, must be observed not only in the ventricular aspiration but more particularly in the reintroduction of serum; for it would be even more hazardous in the case of the ventricle than in the lumbar subarachnoid space to introduce more fluid than has been removed. Flexner has wisely cautioned against this.

In the infant the ventricle may be safely entered through the outer angle of the open fontanelle at a point about 2.5 cm. from the median line. In the adult, on the other hand, cranial penetration is necessary, and in all of our cases, except in the instance cited in this report, Kocher's point of election has been chosen (Fig. 3). There is no especial difficulty in the procedure. A small patch of scalp is shaved and a short one-inch linear incision made about 3.5 cm. from the mid-longitudinal line and about 5 cm. anterior to the Sulcus centralis; the bone is exposed and penetrated by a Doyen perforator followed by a burr, which leaves a cup-shaped fossa and gives sufficient exposure of the dura to assure the operator that there is no large underlying cortical vessel. The hollow exploratory needle, which should have a blunted point with openings upon the side, is then gently inserted into the second frontal convolution perpendicular to its surface, and at a depth of from 4 to 5 cm. readily finds the ventricle, particularly if it is distended. (Cf. chapter in Keen's "System of Surgery," 1908, vol. iii, p. 117.)

EXPLANATION OF PLATE XXXI.

FIG. 1. Photograph showing general appearance of the child. Note enlargement of head and dilatation of superficial vessels, the retraction of the neck with no arching of the spine, the hypertonicity of the muscles and tremor of the extremities, the dorsal flexion of the great toes.

FIG. 2. Photograph of top of head showing separation of sutures and widely opened anterior fontanelle containing isolated island of bone. Note dilatations of vessels.

FIG. 3. Showing degree of ventricular dilatation in fatal adult case of cerebrospinal meningitis. Section of brain after hardening in situ by carotid injection of formalin. Arrow shows direction of ventricular aspiration at point of election.

FIG. 1.

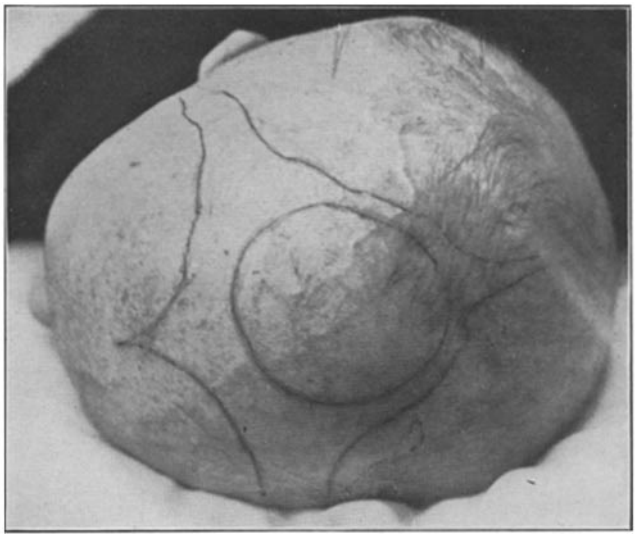

FIG. 2.

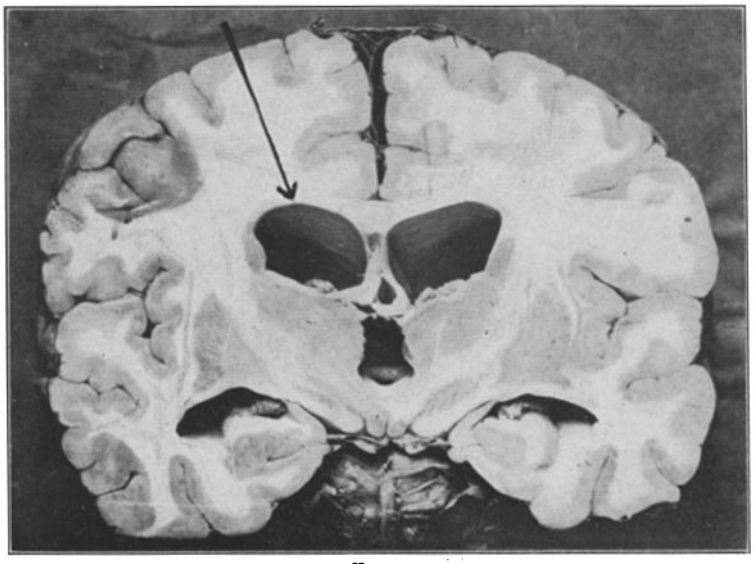

FIG. 3.