CONGENITAL HYDROCEPHALUS WITH DEFECTIVE DEVELOPMENT OF THE CEREBELLAR VERMIS (DANDY-WALKER SYNDROME)

Clinical and Anatomical Findings in Two Cases with Particular Reference to the So-called Atresia of the Foramina of Magendie and Luschka

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Several reports of malformations affecting only or chiefly the cerebellar vermis can be found in the literature. As a rule the vermis has not been fully developed, particularly its posterior part, and it is a striking feature that this defect has usually been combined with internal hydrocephalus. It appears from the descriptions given in the literature that these cases have been remarkably similar in their pathology as well as in their clinical manifestations and course. We have been able to record altogether 30 human cases, namely those of Fusari (1891-92), Rossi (1891 and 1892, two cases), Woskressenski (1911), Dandy and Blackfan (1914), Dandy (1921, two cases), Lyssenkov (1931), Pines and Surabaschwilli (1932), Castrillon (1933), Scarff (1933), Sahs (1941), Cohen (1942), Taggart and Walker (1942, three cases), Shryock and Alexander (1943), Walker (1944), Brodal (1945), Sidenberg, Kessler, and Wolpaw (1946), Coleman and Troland (1948, two cases), Schwarzkopf (1950), Benda (1954, three cases), Maloney (1954, two cases), Gibson (1955, two cases). Similar malformations have been reported in animals by Lesbre and Forget (1905, calf), Bertrand, Medynski, and Salles (1936, dog), Dow (1940, two cases in dogs), Verhaart (1942, cat), Brodal, Bonnevie, and Harkmark (1944), and Bonnevie and Brodal (1946, in a strain of mice).

In spite of the similarity of the findings in these cases we disagree with regard to the mechanism underlying the development of the anomalies, which by some is held to be a congenital atresia of the foramina of Magendie and Luschka. This problem will be discussed in the present paper with reference to the findings in two cases together with observations made in a strain of mice presenting a hereditary type of the same malformation (Brodal and others, 1944; Bonnevie and Brodal, 1946).

Case Reports

Case 1.—A.B.G. A girl aged 4 years, was born on September 24, 1945, and died on September 12, 1949. (R.H. 861/49, O. 224/49, H.I. 14/49.)

History.—The patient was born five weeks prematurely, and weighed 2,000 g. at birth. The delivery was uneventful. Growth was slow until she was 6 months old, but since then her development has been in all respects satisfactory.

During the six months before admission her mother had noticed that the child had occasional fits, in which peculiar movements of the eyes, staring gaze, and dilated pupils were associated with absent-mindedness, though she replied when spoken to.

Since July 8, 1949, she complained of headache and abdominal pain, usually accompanied by nausea and vomiting. After July 20 she became drowsy and responded poorly when spoken to. Her gait grew unsteady; twice there had been signs of diplopia. From July 17, she had increasingly frequent seizures, up to nine in 24 hours, each lasting for two or three minutes. During these she displayed opisthotonus with extension of the legs and flexion of the arms which showed rhythmic, jerking movements. She appeared to be unconscious during these seizures, which were regularly followed by sleep.

Clinical Examination.—On admission to the Neurological University Clinic, Oslo (July 26, 1949), the patient was drowsy and unresponsive. Her head was retracted and tilted to the left. The head circumference was 51 cm. (average for her age 49 cm.). The frontal and parietal tubera were large. Body weight was 12 kg., height 122 cm.

There was bilateral papilloedema and swelling of the optic discs of 4 and 3 diopters. There were no ataxia or spontaneous movements, no involuntary movements, but slight muscular hypotonia. Kernig and Brudzinski signs were positive. Tendon reflexes were weak but symmetrical, except for the patellar reflexes which were both absent. Abdominal and plantar reflexes were

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normal. A general examination, including laboratory tests of blood and urine, gave normal results. The Wassermann test was negative in blood. A radiograph of the skull showed wide coronal sutures.

Since a medulloblastoma of the cerebellum was suspected, the patient was given daily x-ray treatment starting on July 28. On September 6 ventriculography was done and 250 ml of cerebrospinal fluid was removed, which had a normal content of cells, protein, and glucose. The ventriculograms showed enormously dilated lateral ventricles (Fig. 1), a large third ventricle, and a markedly dilated aqueduct of Sylvius. The contours of the fourth ventricle could not be made out, but there was a large air-filled space under the elevated tentorium cerebelli, suggesting a defect in the cerebellum.

After ventriculography she deteriorated, her temperature rose, and on the sixth post-operative day reached 41.3° C. She died the same afternoon.

**Anatomical Investigation.**—Necropsy was performed by Dr. J. Cammermeyer. Pathological findings were confined to the brain.

The leptomeninges appeared to be somewhat thickened. The cerebellar hemispheres were separated by what appeared to be an enormously enlarged fourth ventricle covered by a membrane uniting the cerebellar hemispheres. The brain, including the cerebellum, weighed 900 g. After fixation in formalin it was sent to the Anatomical Institute for further examination.

The cerebral hemispheres appear grossly normal except for some flattening of the convolutions and ventriculostomy wounds in both occipital lobes. The floor of the third ventricle bulges considerably.

Coronal sections reveal severe internal hydrocephalus (Fig. 2) most marked on the left. The third ventricle is abnormally wide, the interventricular foramina of Monro and the aqueduct are dilated, the thalamus and basal ganglia are displaced laterally and appear flattened and somewhat reduced in size.

The thickness of the cerebral cortex is reduced throughout, the corpus callosum has a maximal thickness of 2.5 mm. and the anterior, posterior, and habenular commissures appear as cords.

From the posterior aspect (Fig. 3a and b), the two cerebellar hemispheres are separated by a wide cleft bridged by a thin ruptured membrane (Fig. 3a). Anteriorly the membrane bears a tongue-like structure, consisting of some transversely running cerebellar folia.

Retraction of the two halves of the membrane exposes the floor of the fourth ventricle (Fig. 3b). Posteriorly no trace of a vermis is seen, but anteriorly it is represented by an unpaired prominence (x in Fig. 3b), convex in the rostro-caudal as well as the lateral direction but having a small transverse furrow (y in Fig. 3b). The under surface of this prominence can be followed rostrally to the caudal opening of the aqueduct, while its upper surface is covered with cerebellar folia. The most posterior of these form the tongue-like mass of folia which can be seen from the outside (V in Figs. 3a and b). These relationships become clearer after the cerebellum and brain-stem have been cut mid-sagittally (Fig. 4). Upon careful dissection, the folia of the preserved anterior part of the vermis can be identified by their connexions with parts of the hemispheres (see below). Extending from the anterior part of the vermis the folia is a thin anterior medullary velum which is attached to the brachia conjunctiva.

The ventricular surface of the vermis (x) is separated on each side by a shallow sagittal sulcus from a smooth, somewhat smaller prominence facing medially (z in Figs. 3b and 4) which macroscopically belongs to the hemisphere. This smooth prominence fuses ventrally with a bulging produced by the brachium conjunctivum (Bc in Fig. 4), posteriorly it extends onto the medial surface of the hemisphere. The hemispheres are smaller than normally, but all lobules can be identified. The upper surface of the cerebellum is more anterior than normally, and the vermis overlies the superior colliculi.

The membrane covering the fourth ventricle is thin, more or less translucent, and contains fine vessels. It appears to be attached to the cerebellum along a laterally curved line which passes approximately in a rostro-caudal direction on the dorsal (posterior) surface of each hemisphere (Figs. 3a and b and 5). When followed in a rostral direction, the line of attachment bends medially and ultimately reaches the tongue-like extension of cerebellar folia. Caudally the line of attachment also bends medially to the medial surface of the hemispheres, to reach the flocculus (Figs. 3b and 5), below which its most anterior point is found. Here a foramen of Luschka is present on each side, through which a tuft of the choroid plexus (Figs. 5a and b) protrudes. From the region of the foramen of Luschka the attachment of the membrane passes just inferior to the flocculus in a medial direction, reaches the lateral border of the medulla oblongata and follows this caudo-medially to meet its fellow from the other side in the midline caudal to the fourth ventricle. This line of attachment of the membrane is somewhat more lateral on the surface of the medulla than the tenia of the fourth ventricle in a normal brain.

On the ventral surface of the caudal part of the membrane, which extends across the cleft between the two cerebellar hemispheres, several distinct ridges of a choroid plexus are seen on both sides, coursing in a longitudinal direction (Fig. 6). From the caudal end of the lateralmost of these ridges a well developed strand of choroid plexus extends anteriorly, a few millimetres medial to the line of attachment of the membrane to the cerebellar hemispheres. The most anterior part of this plexus protrudes through the foramen of Luschka on both sides (Fig. 5a and b).

The pons and medulla oblongata show minor changes. The medulla is transversely flattened but all normal structures can be identified. The pons is somewhat flattened, but is otherwise normal. In the mesencephalon the cerebral peduncles appear small, and the aqueduct is dilated. The cranial nerves are all present and appear normal.

**Microscopical Investigation.**—Pieces were removed for histological study from the membrane covering the fourth ventricle and from its line of attachment to the cerebellum and stained with haematoxylin-eosin. The left half of the cerebellum and the entire medulla oblongata and pons were embedded in paraffin and sectioned serially in the transverse plane. The right half of the cerebellum was cut in serial sections in the sagittal
CONGENITAL HYDROCEPHALUS

FIG. 1

FIG. 1.—Case 1: Ventriculogram showing dilatation of lateral and third ventricles and a large collection of air in the posterior cranial fossa below an elevated tentorium.

FIG. 2.

FIG. 2.—Case 1: The posterior part of the cerebral hemispheres seen from the anterior aspect following a transverse section at the plane of the mammillary bodies. The corpus callosum is reduced in thickness. The posterior and the habenular commissures extend across the dilated third ventricle.

FIG. 3.

FIG. 3.—Case 1: The cerebellum seen from behind, showing in (a) the ruptured membranous covering of the fourth ventricle. The line of attachment of the membrane on the left cerebellar hemisphere is indicated by arrows. In (b) the membrane is pulled aside to expose the fourth ventricle. In the midline is seen the ventricular surface (x) of the anterior part of the vermis. V: posterior part of vermis. To: tonsilla. Z and y: see text.

FIG. 4.

FIG. 4.—Case 1: The right half of the cerebellum and brain-stem. The upper part of the membrane is kept raised by means of a pin to expose the smooth ventricular surface of the cerebellum with its prominences (z and Bc) described in the text. F.p.: primary fissure. To.: Tonsilla. Y: Sulcus corresponding to the fastigium.
FIG. 5.—Case 1: (a) Anterior view of the cerebellum and brain-stem to show the relations of the membrane and the patent foramina of Luschka. The line of attachment of the membrane on the left is shown by arrows. Pins are placed in the foramina of Luschka. Fl.: Flocculus. Pl.: Choroid plexus. (b) Enlarged view of the area outlined in (a) showing the choroid plexus (Pl.) protruding through the right foramen of Luschka.

FIG. 6.—Case 1: The posterior part of the translucent membrane drawn backwards (cf. Fig. 3b) to expose its inner surface with the ridges of choroid plexus (Pl.).

FIG. 7.—Case 1: Sagittal section through the vermis of the cerebellum. The folia and lobules of the anterior lobe in front of the primary fissure (F.p.), and the folium-decline-tuber (Fdt.) have an approximately normal configuration. The pyramis (Py.) and particularly the uvula (U) are elongated in the sagittal plane and not subdivided in their peripheral portions as usual. The nodulus (N) is flattened and extends as fragments of cerebellar tissue on the outer surface of the membrane. The eversion of the vermis leaves a faint groove only, indicating the fastigium (F), corresponding to the sulcus y in Fig. 4.
plane. Every tenth section was mounted and stained with cresyl violet.

Microscopically the membrane covering the fourth ventricle is covered by ependyma on its ventricular surface and by loose connective tissue with small vessels on its outer surface. The ependymal cells are in places cuboidal, elsewhere flattened. Occasionally small tufts of connective tissue covered by ependyma protrude on the inner surface of the membrane. From the line where the membrane is attached to the cerebellar hemispheres (Fig. 3a and b) the ependymal lining of the membrane continues in a ventral direction and covers the medial surface of the cerebellar hemisphere, but is separated from this by a thin layer of connective tissue, which can be followed ventrally to the region where the folia of the hemisphere disappear. The outer, connective tissue layer of the membrane is continuous with the pial covering of the cerebellum.

The choroid plexus appears normal except that its arborizations are fewer and more slender than normal.

Study of the sagittal series of sections through the right half of the cerebellum establishes that all lobules of the vermis are present. But, while the lobules of the anterior lobe appear to be normally developed, those of the posterior lobe are more or less reduced in size (Fig. 7) and are abnormal in shape. In particular the nodulus is very irregular and flattened; in part it is stretched out on the outer surface of the membrane (Fig. 7). The fastigium is very faintly marked (F in Fig. 7) and corresponds to the fissure y seen on gross examination (Fig. 3b). The flattening of the ventral surface of the vermis is due to the elevation of the posterior part of the cerebellum above the floor of the fourth ventricle.

The cortex of the cerebellum is of normal structure apart from some minor aberrations in the malformed nodulus. On the ventricular surface the ependyma in some places shows the picture of “granular ependymitis”.

The intracerebellar nuclei when studied in serial sections show some irregularities. The dentate nucleus is situated closely beneath the ependyma, underneath the prominence labelled z in Fig. 3b. Its regular band is not everywhere clearly outlined, and medially its band-like structure is lost. The medialmost cell aggregates of the intracerebellar nuclei may represent part of the dentate nucleus, but may also be rudimentary parts of the fastigial, globose, and emboliform nuclei which cannot be identified.

Histological sections through the pons and medulla show no substantial abnormality. The inferior olive, studied in detail, showed a possible reduction in size of the rostral part of the medial accessory olive.

Case 2.—R.S., a girl aged 7½ years, was born on October 12, 1942, and died on August 31, 1950. (R.H. 556/50, O. 208/50, H.I. 7/50.)

History.—The child had been in good health and developed normally until February, 1950, when she began to complain of pains and stiffness in her neck and had a fit during which her body grew stiff and her gaze was staring. There were no convulsions. During the following three weeks she had moderate fever. In April the same symptoms recurred but again disappeared after some weeks. In July she again had two fits with stiffness of the body and extension of fore- and hindlimbs without loss of consciousness. She was admitted to the Paediatric University Clinic on July 15, from which she was transferred on July 31 to the Neurosurgical Division of the Neurological University Clinic.

Clinical Examination.—On admission the girl complained of headache, and particularly of pain in the neck on movements of her head. The neck was stiff and a “cracked pot” note was heard on percussion of the head. Both optic discs were choked with engorged veins, protruding some 4 diopters. There was paresis of the right abducent nerve, and signs of affection of both oculomotor nerves. There was general muscular weakness and atrophy with some spasticity in the legs, and signs of cerebellar ataxia. The tendon reflexes in the legs were very brisk, the abdominal reflexes weak and the plantar reflexes inverted. Laboratory tests of urine and blood were normal apart from an increased blood sedimentation rate. A chronic otitis was found on the right.

At ventriculography 200 ml. of cerebrospinal fluid was removed. Its protein content was normal but glucose and cells were slightly raised. The ventriculogram (Fig. 8) showed great dilatation of the lateral and third ventricles. In the posterior fossa below a markedly elevated tenorialum was a large air-filled space. The cranial sutures were widened.

After ventriculography cerebrospinal fluid leaked through the left burr hole, and on the second postoperative day her temperature rose suddenly. In spite of treatment with aureomycin and penicillin her condition continued to deteriorate until she died 13 days later.

Anatomical Investigation.—Necropsy was performed by Dr. J. Cammermeyer. Apart from the brain no pathological alterations of significance were noted. The weight of the brain was 1,050 g. After fixation in formalin the brain was referred to the Anatomical Institute for further study.

On gross examination the leptomeninges over the base of the brain and medulla are covered with pus.

Fig. 8.—Case 2: Ventriculogram showing essentially the same features as in Case 1 (see Fig. 1).
thickened and their vessels prominent. On transection of the cerebral hemispheres the lateral and third ventricles are considerably enlarged, although less than in Case 1. The commissures and the massa intermedia are elongated transversely. The aqueduct is dilated rostrally to the inferior colliculus where it is narrowed. Otherwise the appearances of the cerebrum are as in Case 1.

The cerebellar hemispheres are driven apart, and connected rostrally only by what appears to be a reduced vermis (Fig. 9). The right hemisphere is a little smaller than the left, particularly in the region of the tonsil, which on the right shows indistinct foliations. The pathological alterations are otherwise in principle similar to those described in Case 1. The two cerebellar hemispheres are caudally connected by a membrane which is considerably thicker and more vascular than that in Case 1. Its torn ends can be brought together, and there can be no doubt that the membrane has originally covered the fourth ventricle. Its line of attachment to the hemispheres is approximately as in Case 1. However, from the right rostrolateral part of the membrane, caudal to its attachment to the vermis rudiment, a sac-like evagination extends in a rostral direction to the under surface of the corpus callosum. Above this evagination a vermis of reduced size connects the two cerebellar hemispheres. On the inner surface of the caudal part of the membrane is a somewhat underdeveloped choroid plexus. On account of the thickening of the membrane and meninges the foramina of Luschka cannot be identified.

Microscopical Examination.—This shows heavy infiltration of the leptomeninges, chiefly with polymorphonuclear and some mononuclear leucocytes. There is some perivascular cuffing of the pial arteries. In the right cerebellar hemisphere a well circumscribed abscess is found, measuring $2 \times 1 \times 1$ cm. It is surrounded by a marginal zone of leucocytes and “foam cells”. The abscess destroys part of the dentate nucleus in addition to white matter. Sagittal sections through the vermis show that all lobules are present, but as in Case 1 those of the posterior vermis are underdeveloped and abnormal. In sections through the pons and medulla oblongata the configuration of the major nuclei and tracts appear largely normal. A detailed study of the particular tracts and nuclei was not made.

The chief anatomical findings in these two cases may be summarized as follows: The entire ventricular system is considerably dilated. The tentorium cerebelli is elevated. The cerebellar hemispheres are separated caudally by a broadened fourth ventricle; rostrally they are connected by a vermis, which is somewhat everted and displaced rostrally. The vermis of the anterior lobe is normal, while posteriorly the vermis is underdeveloped. While all the usual lobules can be identified, the uvula and particularly the nodulus are smaller than normal and also have an abnormal configuration.

The caudal part of the roof of the fourth ventricle is formed by a thin membrane of connective tissue (pia mater) covered on its inner surface by ependyma. Its line of attachment to the brain-stem corresponds to that of the normal tela choroidea, while its attachment to the cerebellum on macroscopical examination is found on the dorso-medial surface of the hemispheres. On microscopical examination, however, the ependyma on the inner surface of the membrane continues on the medial aspect of the hemispheres to the region where these join the vermis, but is separated from the cerebellar hemispheres by a layer of connective tissue. This is continuous with the pia on the dorsal aspect of the hemispheres and with the connective tissue on the outer surface of the membrane. In the caudal part of the membrane a plexus choroideus is present, but it is smaller and less branched than normal. In Case 1 the foramina of Luschka are patent, but the foramen of Magendie cannot be identified. In Case 2, in which there is severe leptomenigitis and an abscess in the right cerebellar hemisphere, none of the foramina can be found.

Discussion

The pathological changes in the brains in our two cases betray striking similarities to those found in most cases described in the literature. The chief common features have been a generalized hydrocephalus, an underdevelopment of the cerebellar vermis, particularly of its posterior parts, and anomalies in the roof of the dilated fourth ventricle, which has been covered by a thin membrane of a much larger size than the normal posterior medul-
lary velum and the tela chorioidea. But certain variations in the intensity of the changes have been noted in the cases described. Thus the degree of concomitant alterations in the cerebellar hemispheres as well as the anomalies in the vermis have varied. According to some reports the vermis has been entirely absent, but in some of these it can be seen from the illustrations that a reduced vermis has, nevertheless, been present. In spite of these and other variations there can be no doubt that all these cases represent one type of developmental disturbance. Since little information of value can be gained from an analysis of the presumably secondary changes in other parts of the brain, for example, the nuclei of the brain-stem, these changes will not be discussed. Nor is analysis of the clinical features of importance.

Several attempts have been made to explain the developmental disturbances which produce this type of malformation. In recent years most authors have regarded atresia of the foramina in the roof of the fourth ventricle as the primary defect (Dandy and Blackfan, 1914; Taggart and Walker, 1942; Walker, 1944; Coleman and Troland, 1948; Maloney, 1954; Gibson, 1955, and others). This atresia is assumed to give rise to a hydrocephalus which in turn is responsible for the anomalous development of the vermis. However, for reasons which will be given below, it is here concluded that a retardation or failure of development of these foramina is not an essential factor in the production of the anomalies.

The extensive studies of Larsell (see Jansen and Brodal, 1954, 1958) have shown that in all mammals the cerebellum develops principally in the same way. The cell material destined to form the cerebellum migrates from the lateral margin of the rhombencephalon along the two cerebellar commissures which both pass in the thin cerebellar plate, the caudal part of which is continuous with what later becomes the roof of the fourth ventricle. Dow (1940) suggested that the defective development of the vermis in his dogs and in other similar cases might be due to some (unknown) factor which had prevented completion of the cerebellar commissures. This factor might well be a hydrocephalus arising at an early foetal stage (Brodal and others, 1944; Brodal, 1945) since this would produce an extension of the cerebellar plate and impede the cellular migration. Conceivably this might easily be followed by aberrations and distortions in the pattern of the medial parts of the cerebellum and, in more advanced stages, also of the hemispheres. In agreement with this hypothesis in all cases reported the vermis of the anterior lobe has been less affected than that of the posterior lobe, since the migration towards the midline begins rostrally and is completed latest caudally (see, for example, Hochstetter's Figs. 103 to 107). A failure of the foramina of Magendie and Luschka to develop might in this way be assumed to be the primary cause of the pathological changes.

That another explanation is far more likely appears, however, when a comparison is made with the findings in a strain of hydrocephalic mice with defective development of the cerebellar vermis (Brodal and others, 1944). In these mice, as in the human cases, the vermis of the anterior lobe was always less affected than the posterior vermis, and the posterior part of the fourth ventricle was covered by a membrane, consisting on its inner side of ependyma, on its outer side of connective tissue continuous with the pia. The membrane was attached to the brain-stem along the normal lines of attachment of the roof of the fourth ventricle.

Of the mice belonging to this strain only a certain number develop the anomalies under discussion which are due to a monohybrid recessive gene (Bonnevie, 1943)1. In a study of the development of the anomaly in foetal mice (Bonnevie and Brodal, 1946) various stages could be analysed. In embryos younger than the beginning of the eleventh day, no anomalies have ever been seen (Bonnevie, 1944). However, on the twelfth day a striking difference between normal and abnormal embryos appears. This difference concerns the area membranacea anterior of Weed (1917), which is a transitory transparent oval region in the roof of the fourth ventricle immediately caudal to the cerebellar Anlage. It is covered by extremely flattened ependymal cells and situated closely beneath the epidermis. Caudal to the area anterior the choroid plexus develops, the first signs of its development being seen on the eleventh day in normal embryos. In the course of the following two days the area anterior normally disappears and becomes incorporated into the plexus. At the same time an area membranacea posterior appears caudal to the developing choroid plexus, marking the beginning of the future "foramen" of Magendie2. In the abnormal mouse embryos, however, the area anterior is not incorporated into the plexus but persists. It is even enlarged and can be seen to bulge outwards, apparently on account of an increased intraventricular pressure. The whole roof of the fourth ventricle is extended, the median part of the choroid plexus is displaced caudally, separated from the cerebellum by the persisting area anterior, and the cerebellar plate is also changed. Its median thin part is thinner and broader than normal. During the following days the attenuation of the

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1It is interesting in this connexion that two of Benda's (1954) cases were sisters.

2In the mouse embryos the "foramina" of Magendie and Luschka on all stages appear as continuous, though very thin membranes.
cerebellar plate continues. It affects chiefly its median part and is most marked caudally. The formation of the normal vermis is disturbed to a varying extent according to the degree of distension of the roof of the fourth ventricle. The findings thus confirm the hypothesis mentioned above (for particulars see Bonnevie and Brodal, 1946).

With reference to the findings in human cases it is important that in the abnormal mouse brains the hydrocephalic dilation of the ventricles sets in before any “foramina” of Luschka and Magendie are formed and at a stage of development where the median part of the cerebellar plate is still thin, particularly in its caudal third where it has a thickness of a few cell layers only. In man, according to the extensive investigations of Hochstetter (1929), the foramen of Luschka appears at a foetal stage of 195 mm. crown-rump. The appearance of the foramen of Magendie could not be definitely established, but in an embryo of 125 mm. crown-rump Hochstetter found it not developed. Although the term “area membranacea anterior” (Weed) is not used by Hochstetter (1929), this area is described and clearly seen in his illustrations, and, just as in the mice, is gradually reduced in size (see, for example, his Figs. 113, 114, 121, 146, 210 to 215). At a stage of 68 mm. crown-rump it can still be recognized (Hochstetter’s Fig. 215, Pl. 31), but at the 100 mm. stage it has disappeared, and the choroid plexus is found immediately caudal to the nodulus (Hochstetter’s Figs. 216 to 219, Pl. 31). The normal development in this region in man thus appears to be in all essentials similar to that in the mouse. With regard to the question concerning us here, the time of fusion of the paired Anlages of the cerebellum is of importance. According to Hochstetter (1929), this fusion occurs at the stage of 40 to 45 mm. crown-rump. The last part of the cerebellar plate to fuse is the nodulus, which lags considerably behind and at a stage of 120 mm. crown-rump is still a paired structure (Larsell, 1947).

From these data it is seen that in man the fusion of the two cerebellar Anlages is completed far in advance of the appearance of the foramina of the fourth ventricle. A pathological dilatation of the fourth ventricle, occurring as a consequence of a failure of development of the foramina, would therefore scarcely produce marked changes in the cerebellar vermis, which, by the time of the formation of the foramina, shows all its principal subdivisions (see Jansen and Brodal, 1958). If a pathological dilatation occurs at an earlier stage, however, namely when the “area membranacea anterior” still persists, i.e., before approximately the 100 mm. crown-rump stage, it would probably have a profound effect on the development of the vermis. The splitting of the vermian in two more or less symmetrical halves which has been observed (Brodal, 1945) corresponds to the findings made in the mice and indicates that the distension of the roof has occurred at a very early stage. The fact that the nodulus in some cases (Sahs, 1941; Gibson, 1955), as in our own, or even the nodulus and uvula (Brodal, 1945), is represented by cerebellar tissue covering the rostral part of the membrane (see Fig. 7) also points to a disturbance occurring before the formation of the nodulus is completed. Another finding of relevance is the caudal position and rudimentary development of the median part of the choroid plexus of the fourth ventricle in our cases. In Sahs’ (1941) case and in Gibson’s (1955) case 1 this part of the plexus was absent, likewise in Castrillon’s (1933). While such aberrations might easily be explained by a persistence of the “area anterior”, since the plexus develops caudal to this, it is difficult to see any causal relationship between this feature and the lack of development of the foramen of Magendie.

The above analysis leads us to conclude that the anomalies in the cerebellum and the roof of the fourth ventricle in human cases of the type under discussion arise at a foetal stage considerably earlier than the formation of the foramina of Magendie and Luschka, and are due to an increased intraventricular pressure, the reasons of which remain unknown. The mechanisms at work appear to be essentially similar to those operating in the hydrocephalic mice. If so, the causal role of a possible atresia of the foramina of the fourth ventricle appears questionable. Certain observations may be mentioned which collectively cast doubt on the generally accepted assumption that the type of malformation under discussion is due to an atresia of the foramina of Magendie and Luschka.

It is now generally agreed that these foramina are not artefacts (Dandy, 1921; Alexander, 1931; Barr, 1948; and others), but normal brains have been found in which the foramen of Magendie (Key and Retzius, 1875) or one or both foramina of Luschka (Alexander, 1931; and others) were lacking. Apparently fluid can escape from the ventricular system to the subarachnoid space without such foramina, presumably through the thin roof of the fourth ventricle. On the other hand, in our Case 1 as well as in some others (Castrillon, 1933; Gibson, 1955, Case 2) one or more of the foramina have

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1Bonnevie (1944) has been able to trace the first signs of an anomalous development in the hydrocephalic mice to the blastocyst stage. They first become manifest in the foetal coverings.

2The recent studies by means of radioactive isotopes on the “circulation” of the cerebrospinal fluid make clear that this problem is far more complex than hitherto believed. Other mechanisms than passage through the roof of the fourth ventricle may well be at work in hydrocephalic brains.
been patent in spite of dilatation of the ventricles and an anomalous development of the vermis. Benda (1954) as well as Walker, according to Benda, observed cases of this malformation in which the foramina were judged to be patent, since dyes passed into the spinal subarachnoid space. Clarke and Laidlaw (1958) report a case which was diagnosed as an example of atresia of the foramina of Magendie and Luschka, in which filling of the ventricular system, including a dilated fourth ventricle, was achieved by air encephalography via the lumbar route. Such observations support the contention that atresia of the foramina of Magendie and Luschka is not the primary factor responsible for the development of the anomalies in the brain in these cases. Furthermore, it appears reasonable that atresia cannot be solely responsible for the clinical symptoms, even if it may be a contributing factor, for many of the patients suffering from so-called atresia of the foramina of Magendie and Luschka have led a fairly normal life for many years. Thus our cases were 4 and 8 years respectively, Brodal’s (1945) 11 years, Maloney’s (1954) 6 and 13 years, Gibson’s (1955) 12 and 13 years, Coleman and Troland’s (1948) Case 2, 17 years, Sahs’ (1941) 16 years, Walker’s (1944) 20 years, Clarke and Laidlaw’s (1958) 36 years, and Castrillón’s (1933) almost 60 years. In most cases the clinical disturbances have been signs of increased intracranial pressure, and occasionally symptoms have been intermittent. It seems likely that patients with this anomaly are prone, sooner or later, to encounter difficulties in the escape of cerebrospinal fluid from the ventricular system, but in most the reasons for this remain obscure. In some cases a slight “serous” meningitis might have been responsible, in others physical exertions seem to have provoked acute symptoms. It is conceivable that a meningeal infection or oedema might endanger a cerebrospinal fluid circulation which is already impaired by occluded foramina of the fourth ventricle, but no entirely satisfactory explanation can at present be given of the curious fact that patients affected with this anomaly may live for years without signs of increased intracranial pressure.

Some favourable results of operative intervention in cases like those described here have been reported (Sahs, 1941; Cohen, 1942; Walker, 1944; Coleman and Troland, 1948; Maloney, 1954). The establishment of an opening between the dilated fourth ventricle (commonly, but erroneously referred to as a “cyst”) and the cisterna magna may well be of importance in relieving the symptoms due to increased intracranial pressure when these occur. It will be of practical importance, therefore, to be aware of such cases which clinically, as recently suggested by Benda (1954), may properly be referred to as presenting the Dandy-Walker syndrome. A diagnostic finding of value is the raising of the transverse sinuses, which can be recognized on a radiograph of the skull and indicates an elevation of the tentorium, although this sign may be absent, as in Coleman and Troland’s (1948) cases. Additional clues are given by an enlarged head, particularly an elongated occiput (Benda, 1954). When found in patients presenting signs of rather rapidly increased intracranial pressure, such findings should arouse suspicion, and a ventriculograph, or in some cases even an air encephalograph via the lumbar route, will clinch the diagnosis.

**Summary**

The clinical and pathological anatomical findings in two cases of the “Dandy-Walker” syndrome are described. The patients were two girls, aged 4 and 7½ years, respectively, who had presented signs of increased intracranial pressure for relatively short periods before they succumbed. Ventriculography showed a generalized hydrocephalus, with a large air-filled space in the posterior cranial fossa, indicating a cerebellar defect.

The chief anatomical findings, apart from a generalized hydrocephalus, were the following: The posterior part of the cerebellar vermis was underdeveloped, and was continuous caudally with a membrane consisting of ependyma and connective tissue which represents the extremely enlarged roof of the fourth ventricle. In Case 1, the foramina of Luschka were patent. The median part of the choroid plexus of the fourth ventricle was underdeveloped and displaced caudally. A comparison with the findings made in adult and foetal brains belonging to a strain of mice affected with a similar type of malformation (Brodal and others, 1944; Bonnevie and Brodal, 1946) and a consideration of data from the normal development of the human brain make clear that the anomalies in the human cases originate at a stage before the foramina of Luschka and Magendie develop. This, as well as other data, for example, the occurrence of the anomalies and symptoms in cases with patent foramina, show that the atresia of the foramina found in many cases cannot be an essential factor in the production of the anatomical (and clinical) disturbances in cases of this type.

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*Benda (1954) also has recently opposed the view of the causal role of the atresia of the foramina of Magendie and Luschka in this type of hydrocephalus, but is inclined to consider the anomalies as belonging to the group of rachischisis malformations.*
REFERENCES

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Brodal, A. (1945). Ibid., No. 3.

CONGENITAL HYDROCEPHALUS WITH DEFECTIVE DEVELOPMENT OF THE CEREBELLAR VERMIS (DANDY-WALKER SYNDROME): Clinical and Anatomical Findings in Two Cases with Particular Reference to the So-called Atresia of the Foramina of Magendie and Luschka

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*J Neurol Neurosurg Psychiatry* 1959 22: 99-108
doi: 10.1136/jnnp.22.2.99