ANENCEPHALY AND RHACHISCHISIS POSTERIOR, WITH THE DESCRIPTION OF A HUMAN HEMICEPHALUS OF 18 MM.

By W. F. H. STRÖER and A. van der ZWAN

From the Anatomical Laboratory and the Department of Neurology and Psychiatry of the University of Groningen, Netherlands

INTRODUCTION

The malformations of the central nervous system, known as anencephaly, hemicephaly, rhachischisis posterior, spina bifida, etc., may take their origin in two different ways.

(1) They may originate from a non-closure of the neural plate. The persistence of the neural plate condition may involve the whole length of the nervous system, or it may be localized in some definite region, e.g. in the anterior head region (Fig. 1A), or in more posterior parts of the brain or spinal

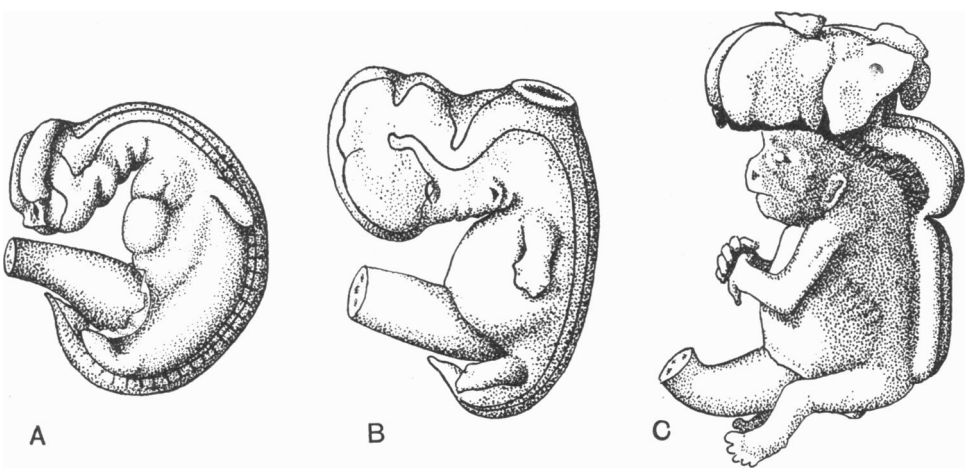

Fig. 1. Three embryos, showing: A, a normally closed central nervous system, with the exception of the head region (pig of 8 mm., after Baxter & Boyd); B, the same for the upper region of the spinal cord (human case of Sternberg); C, central nervous system open over entire length (human embryo of 22 mm.).

cord (Fig. 1B). Fig. 1C shows an example of a rare case of non-closure of the neural tube over its whole length.

In later stages of development, the part of the central nervous system in which fusion fails, shows a tendency to disappear. Lebedeff (1881) and

Sternberg (1929) have illustrated this gradual disappearance. The degeneration of the central nervous system occurs only after the medullary plate has given rise to the peripheral nerves. As a result a full-term foetus may develop in which these parts of the brain or spinal cord are absent, while the peripheral nerves are well developed. Belonging to this category are several types of abnormality described as anencephalus, hemicephalus, spina bifida, rhachischisis posterior, etc.

The question arises—what factor is responsible for the closure of the neural tube? By experimental research it has been shown that the underlying mesoderm (the "Urdarmdach") plays an important role in the formation of the neural plate and its further development. On the other hand, a defective condition of the underlying mesoderm leads to a defect in the development of the central nervous system: Lehmann (1926, 1938) has demonstrated that, if parts of the presumptive mesoderm are extirpated before invagination, those parts of the central nervous system lying above these artificial defects of the organizer show corresponding deficiencies. As a consequence, besides the malformations of the central nervous system, abnormalities may be expected in the underlying skeleton and musculature which take their origin from the mesoderm of the organism. These latter abnormalities should be considered as the primary cause of the deformities of the central nervous system.

As to the aetiology of the disturbance in the "Urdarmdach", with its manifold consequences, we can only say that, at least in some cases, a hereditary factor is involved. Cases are known of familial occurrence of synostosis of cervical vertebrae combined with spina bifida (malady of Klippel-Feil), and also of spina bifida with vertebral defects in other regions (Schwarzweller, 1937). De Vries (1915) also mentions some families with anencephaly as a hereditary factor.

(2) Malformations of the central nervous system of the second type arise from an early local or general hydrops. In these cases the closure of the neural tube is normal, but after closure an excessive collection of cerebro-spinal fluid in the tube causes local enlargements (types of hydrocephalus, myelocele, spina bifida).

Kr. Bonnevie has shown that an excess of the fluid may escape through the ependymal roof of the fourth ventricle, either by passing through the thin wall or through foramina. In this way blebs are formed which shift along the surface of the body of the embryo to different places where their effect becomes manifest in malformations. If the excess of fluid is not able to leave the ventricles of the brain, it gives rise to a swelling of the neural tube, and a thinning of the wall. The thinning of the wall may lead to its degeneration, giving rise to the appearance of a partly open tube, such as has been described in the first category. The aetiology of the excess of fluid in the neural tube is not known, but it appears that hereditary factors play an important role, as has been shown by the experimental work of Kr. Bonnevie (1934, 1935).

MATERIAL

The embryo to be described was presented to the Anatomical Institute of the University of Groningen by Prof. Deelman several years ago. As far as is known, it was one of a series of abortions of one woman. When received, it was preserved in 10 % formalin. Ordinary photographs, stereophotographs and drawings were made. Subsequently it was embedded in celloidin and cut into transverse sections (25 μ thickness) which were stained with haematoxylin-eosin. From a histological point of view the material was not ideal, but the different tissues and organs could be well distinguished. Both graphic reconstructions and wax models were made to clarify the more difficult relations. We here express our thanks to one of our students, Mr Rinsma, who made a wax model of the greater part of the axial skeleton.

SURFACE ANATOMY

The crown-rump length of the embryo is 18 mm. Externally several abnormalities are observable. The most striking of these malformations is

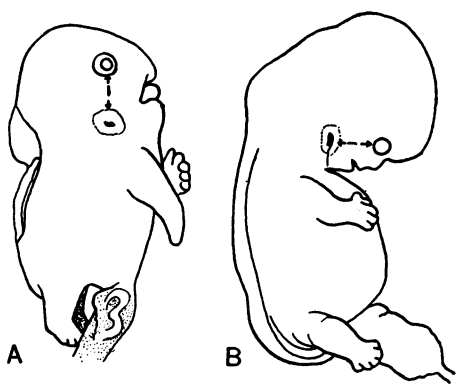

Fig. 2. Lateral view of the anencephalic embryo (A) and of a normal embryo of the same length (B, after Keibel & Elze).

found in the mid-dorsal region, stretching from the neck to the pelvic region (Fig. 5). Here the skin and subcutaneous tissue are absent, and there are exposed to view a median blood vessel and on either side a row of spinal ganglion. The spinal cord is absent. Rostrally, two larger masses of brain tissue are present (Fig. 5).

Apart from the rhachischisis, the whole appearance of the embryo is abnormal, showing the typical features of anencephalus (Fig. 2). The extremities are well developed with the normal number of digits. A hare-lip is present on the right side.

MICROSCOPICAL ANATOMY

(1) *Central nervous system*

The microscopic sections show that in the abnormal dorsal region the spinal cord is absent, and confirm the identification of the spinal ganglia. The masses present in the cranial region (Fig. 5) are brain tissue which continues rostrally in the cranial cavity. These are the only remnants of the central nervous system.

Three parts of the brain can be distinguished, two lying antero-laterally (Fig. 6) and the other in a postero-median position. The first two represent the cerebral hemispheres, of which apparently a great part of the lateral wall and the roof are lacking (Fig. 6). This defect is due to an early non-closure of the neural tube as represented in Fig. 3. Instead of a closure, an

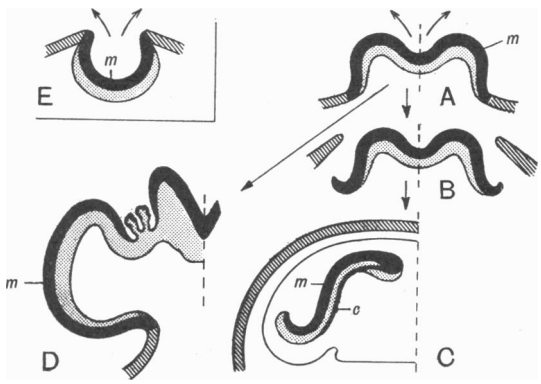

Fig. 3. Diagrams explaining the method of eversion of the medullary plate. From the normal E, through eversion, A is formed; from A, D may follow (Hunter's case), or B and C (our case). A, D and E after Hunter.

"extroversion" (Hunter, 1934–5) has occurred; as a result the inner layers are turned outside (from E to A). This process may lead to a condition represented in Fig. 4D (case of Hunter, 1934–5, and of Baxter & Boyd, 1938); in our own case it leads to a condition represented in Fig. 4C. Though the presumptive material for the lateral wall and roof is present, it does not reach its normal position. The free border of the lateral wall, showing signs of degeneration, is the place of former contact with the ectoderm. The interpretation here given is confirmed by the histological structure of the brain wall with its matrix, its intermediate layer and cortical layer (Fig. 6). It must be mentioned that the cortex is lacking in the ventral and lateral part of the hemisphere (Figs. 6 and 3C). No plexus chorioideus and no foramen Monroi can be observed; the falx cerebri is found in a normal position between the rudiments of the hemispheres.

The central portion of brain tissue contains many loose fragments (Fig. 6),

probably portions of the wall of the diencephalon and mid-brain; they are difficult to identify.

The hypophysis consists of a thick-walled pocket of tissue ending in two short posterior offshoots, as is normal for the adenohypophysis. The neurohypophysis is absent; no connexion of the hypophysis with brain tissue could be found. The glandular hypophysis is connected with the roof of the mouth

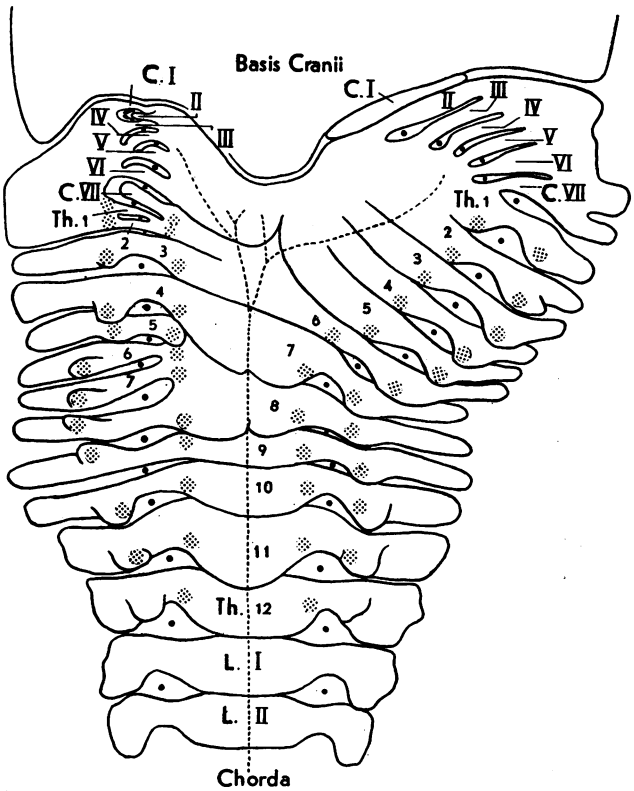

Fig. 4. Drawing of the wax model of the vertebral column. *L*, lumbar; *Th*, thoracic; *C*, cervica vertebra. Foveae costarii: stippled; spinal nerves: large dots.

cavity by means of a long but narrow stalk, running through the cartilaginous base of the skull.

The two internal carotid arteries run laterally of the pituitary body where they branch off into blood vessels and plexuses.

(2) *Peripheral nervous system*

(*a*) *Cranial nerves.*

(i) *Olfactorius.* This nerve is well developed on both sides. Coming from the mucous membrane of the olfactory sacs, nerve fibres can be traced over a certain distance. There is no olfactory bulb or tractus.

(ii) *Opticus.* On both sides optic nerves emerge from the eyeballs and run in postero-medial direction (Fig. 6, *n. II*). They both end near the optic foramen outside the chondrocranium.

(iii) *Eye muscle nerves.* Of the eye muscles the four recti and the obliquus inferior are present bilaterally. Of the associated nerves the n. oculomotorius and the n. abducens were observed. They pass caudalward, medial to the ganglion Gasseri and terminate behind the otic capsules in darkly stained masses of tissue containing no gray matter. The m. obliquus superior and its nerve are absent.

(iv) *Nervus trigeminus.* This nerve is well developed on both sides. The three chief rami with their different branches could easily be traced. The Gasserian ganglion is well developed. A motor root is present and its fibres lead to the primordia of the masticating muscles.

The connexion of the r. ophthalmicus with the Gasserian ganglion and the presence of the sympathetic ganglion ciliare cannot be established with certainty. The connexions of the maxillary and the mandibular nerves with the ganglia are quite apparent. Small nerve bundles pass to the sphenopalatine and otic ganglion. A strand of nervous tissue originates dorsal of the Gasserian ganglion, connecting the ganglia of the Vth, VIIth and VIIIth nerves.

(v) *Nervus facialis and nervus acusticus.* Both are present with their associated ganglia. The n. petrosus superficialis can be identified. The main trunk of the facial nerve cannot be followed within the mass of nerve and muscle fibres through which it passes. The eighth nerve is seen within the labyrinth capsule. The previously mentioned strand of nervous tissue which connects the different ganglia (of nerves V, VII and VIII) ends on same level as the foramen endolymphaticum.

(vi) The *ganglia* of the *ninth, tenth* and *eleventh nerves* form a complex gradually passing over into series with the cervical ganglia. One strong band of nerve fibres rises from this complex, finding its exit through the foramen lacerum posterius where it splits up into its different branches; in this region the sympathetic cervical ganglion is seen.

(vii) *Nervus hypoglossus.* It is present on both sides and finds its exit through the hypoglossal foramen (Fig. 6). It can be followed readily into the muscles of the tongue.

(*b*) *Spinal ganglia.*

All the spinal ganglia are evident.

The innervation of the musculature of the arm and leg is normal; the brachial and lumbar plexuses show their usual structure and relationships.

(*c*) *Sympathetic trunks.*

These are well developed bilaterally and can be followed along the vertebral column, showing the typical praevertebral enlargement in the region of the kidneys (plexus renalis and plexus coeliacus).

(3) *Sense organs*

The *nose* is well developed on both sides, but as previously mentioned, a hare-lip is present on the right side. The primordia of maxillo- and ethmoturbinale I and II are present on both sides (Fig. 6, *E.t.* and *M.t.*).

The eye. Both eyes are present; the lenses are well developed but show signs of degeneration (Fig. 6). Both the tapetum and retina are well formed. The latter is thrown into numerous large folds.

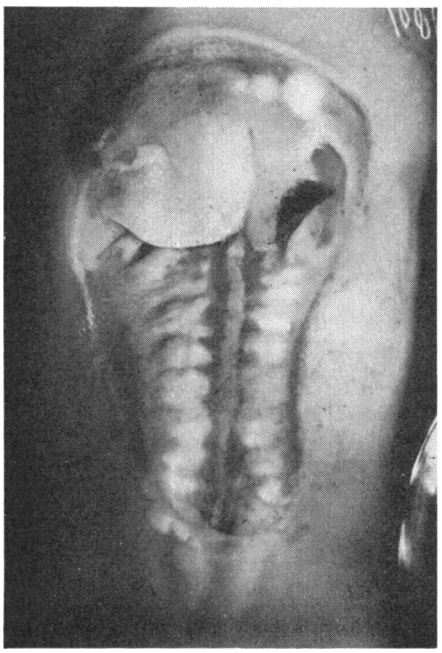

Fig. 5. Photograph of the rhachischisis posterior.

Labyrinth. The histological structure of the inner ear is too poor to be able to discern the different parts. A large saccus endolymphaticus is present.

(4) *Skeleton*

For the interpretation of the skeletal relations of skull, vertebral column and thorax, it proved necessary to make a wax model.

First of all attention should be paid to a feature, present in all the vertebrae, and also in the skull: they are defective on the dorsal aspect. All the vertebrae are flattened in lateral direction. In the skull this results in the absence of the tectum posterius.

The formula of the vertebral column is normal.

A second abnormal characteristic of the vertebral column consists in a

tendency for doubling in all cervical and most of the thoracic vertebrae. This deformity is due to a splitting in an early stage of the chorda dorsalis, which has led to many complications. Fig. 4 shows that the caudal thoracic vertebrae (Th. 9–12) are complete single vertebrae. All the other cranial vertebrae are

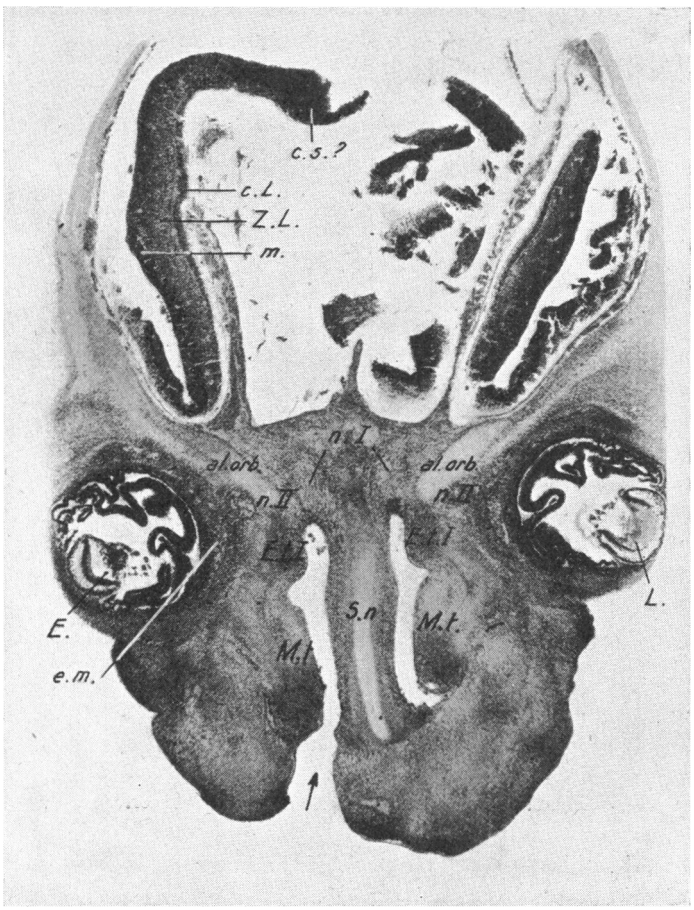

Fig. 6. Photograph of a section through the head. *al.orb.* ala orbitalis; *c.L.* cortex layer; *c.s.* corpus striatum; *E*, eye; *e.m.* eye muscles; *E.t.I*, ethmo-turbinale I; *L*, lens; *m*, matrix; *M.t.* maxillo-turbinale; *S.n.* septum nasi; *Z.L.* intermediate layer.

abnormal. They consist of two *or more* half vertebrae, fused together in an irregular way, e.g. no. 8 consists of four right half vertebrae, and one left half vertebra. The enumeration was made possible by considering the attachment of the ribs and counting the spinal ganglia. It is noteworthy that, in spite of the irregular mode of fusing of the vertebral components, the number of ribs and spinal ganglia, as well as the number of foramina intervertebralia, is normal.

Thorax. The wax model shows that on both sides twelve ribs are present which articulate with the thoracic vertebrae. Of the two longitudinal bars which later form the sternum, the right is connected with the cranial four ribs and the left one with the cranial three ribs. In general the ribs are well developed.

Scapulae and *clavicles* are present and normal in shape.

The *arm skeleton* is normally developed.

Skull. The splanchnocranium as well as the neurocranium are normal, save that the hind part remains open dorsally. No remains of the notochord could be found in the basal part.

(5) *Heart, lungs, intestine and uro-genital organs*

All these organs are present and show no features of special interest. The suprarenal bodies are well developed.

(6) *Trunk musculature*

The trunk musculature seems, when compared with a normal embryo, to be poorly developed.

DISCUSSION[1]

In the introductory section we indicated two categories of malformations of the central nervous system.

The anomaly described in this paper is an example of the first category. The greater part of the central nervous system has disappeared, yet we may conclude from the occurrence of its derivatives (peripheral nerves) that it must have been present in earlier stages.

It seems permissible to make the following generalizations. Cases of "rhachischisis posterior" are not only characterized by a "schisis" of the vertebrae, accompanied by defects of the central nervous system, but also by a disturbance of the vertebral column and dorsal musculature lying underneath these defects. The back region is always shortened as a result of the defective mesodermal inductive mechanism and its defective derivatives, as was experimentally proved in amphibians by Lehmann (1926, 1938). These defective derivatives cause the typical appearance of all these cases. We may conclude that the defective underlying mesoderm is the primary cause of the abnormal development of the central nervous system, which is extroverted and partly open; this, again, is the cause of the non-closure of the neural arches of the vertebrae in the dorsal mid-line.

Quantitatively these defects show great differences. Minor vertebral defects, sometimes of a hereditary character, may not be accompanied by

[1] We herewith express our thanks to Prof. J. J. Th. Vos of the Pathological Department, who kindly put his valuable collection of anencephali at our disposal.

evident abnormalities of the central nervous system. It is interesting to note that in some families individuals occur with vertebral defects, sometimes with and sometimes without accompanying abnormalities of the central nervous system (Schwarzweller, 1937).

SUMMARY

1. Two types of congenital defects of the central nervous system are ascribed to (*a*) a defective underlying inductive mechanism, and (*b*) an abnormal equilibrium of the cerebro-spinal fluid.

2. As an example of the first category the description of a human hemicephalic embryo of 18 mm. is given; the malformation of the central nervous system in this case is due to the abnormal character of the underlying structures.

REFERENCES

BAXTER, J. S. & BOYD, J. D. (1938). "Abnormal development of the brain in an 8 mm. pig." *J. Anat., Lond.*, vol. LXXII, pp. 422–9.

BROEK, A. J. P. v. d. & DAM, S. VAN (1938). "Een geval van rhachischisis anterior en posterior." *Ned. Tijdschr. Geneesk.* pp. 3666–73.

BONNEVIE, KR. (1934). "Embryological analysis of gene manifestation in Little and Bagg's abnormal mouse tribe." *J. exp. Zool.* vol. LXVII, pp. 443–520.

—— (1935). *Vererbarre Missbildungen und Bewegungsstörungen, auf embryonale Gehirnanomalien zurückführbar.* Der Erbarzt.

BROUWER, B. (1916). "Klinisch-anatomische Untersuchung über partielle Anencephalie." *Z. ges. Neurol. Psychiat.* Bd. XXXIII, S. 164–89.

HARRISON, R. G. (1904). "An experimental study of the relation of the nervous system to the developing musculature in the embryo of the frog." *Amer. J. Anat.* vol. III, pp. 197–220.

HUNTER, R. H. (1934–5). "Extroversion of the cerebral hemispheres in a human embryo." *J. Anat., Lond.*, vol. LXIX, pp. 82–6.

KERNAN, J. P. (1916). "The chondrocranium of a 20 mm. human embryo." *J. Morph.* vol. XXVII.

LEBEDEFF, A. (1881). "Über die Entstehung der Anencephalie und Spina bifida bei Vögeln und Menschen." *Virchows Arch.* Bd. LXXXVI, S. 263–99.

LEHMANN, F. E. (1926). "Entwicklungsstörungen in der Medullaranlage von Triton erzeugt durch Unterlagerungsdefekte." *Roux Arch. Entw. Mech. Organ.* Bd. CVIII.

—— (1938). "Regionale Verschiedenheiten des Organisators von Triton, insbesondere in der vorderen und hinteren Kopfregion, nachgewiesen durch phasenspezifische Erzeugung von lithiumbedingten und operativ bewirkten Regionaldefekte." *Roux Arch. Entw. Mech. Organ.* Bd. CXXXVIII, S. 106–58.

SCHWARZWELLER, F. (1937). "Der angeborene Schulterblatthochstand und seine Beziehungen zu den Misbildungen der Wirbelsäule." *Z. menschl. Vererb. Konstit.* Bd. XX, S. 350–80.

STERNBERG, H. (1929). "Über Spaltbildungen des Medullarsrohres bei jungen menschlichen Embryonen, ein Beitrag zur Entstehung der Anencephalie und der Rhachischisis." *Virchows Arch.* Bd. CCLXXII, S. 325–75.

VRIES, E. DE (1915). "Beschreibung eines Anencephalen." *Psych. Neurol. Bladen*, S. 1–22.