

## A CONTRIBUTION TO THE HISTOPATHOLOGY OF PORENCEPHALUS \*

J. H. GLOBUS, M.D.

NEW YORK

Porencephalus is always of interest, partly because of the striking disproportion between the great loss of brain substance and the mild degree of functional disturbance. Unfortunately, however, almost all studies of such brain lesions have been limited to gross anatomic observations. It is hoped that this study adds a few facts to our knowledge of the histopathology of porencephalus. Incidentally it emphasizes the close relationship of such defects to the inflammatory encephalitides.

The term porencephalus was first adopted by Heschl,<sup>1</sup> in 1859, to designate such defects in the brain substance as are characterized by cavity formation in the cerebral hemispheres. Such cavities, to be within the limits of his definition, must communicate either with the subarachnoid or ventricular space. Moreover, the defect might be so pronounced as to lead to intercommunication between the subarachnoid space and the ventricular cavity.

Heschl assumed that this loss of brain substance was the result of faulty development. Some injury had occurred during the intra-uterine life to the anlage of certain parts of the brain cortex, resulting in failure to develop, leading also to malformation of remote and dependent fiber tracts. He drew his conclusions from gross anatomic studies of a fairly large number of porencephalic defects.

Later <sup>2</sup> he admitted that porencephalus might be due to a regressive, destructive process occasioned by occlusion of cerebral vessels. He found histologic evidence of degenerative changes, which he interpreted as being vascular in origin and perhaps syphilitic in character.

Kundrat,<sup>3</sup> in 1882, made a further study of porencephalic brains. He reexamined all of Heschl's specimens and added about twelve of his own. His observations, limited mainly to gross anatomic studies, can be summarized as follows:

---

\* From the Department of Pathology, Mount Sinai Hospital, New York.

\* Work carried out during the tenure of a Fellowship in neuropathology.

\* Presented before the New York Neurological Society, April 5, 1921.

1. Heschl: *Gehirndefect und Hydrocephalus*, Prag. Vrtljschr. f. pract. Heilk. **61**:1859.

2. Heschl: *Neue Fälle von Porencephalie*, Jubelaums band der Vrtljrschr. **100**:40, 1868.

3. Kundrat: *Die Porencephalie*, Eine anatomische Studie (monograph).

1. Most of the porencephalic defects are congenital, although infrequently they may be acquired later.
2. Hemorrhage, thrombosis, embolism, violent uterine contractions, hydrocephalus, anemia and psychic disturbances occurring to the mother during the period of pregnancy, are etiologic factors.
3. The porencephalic loss may be so pronounced that the life of the individual is early terminated, or the destructive process, extensive as

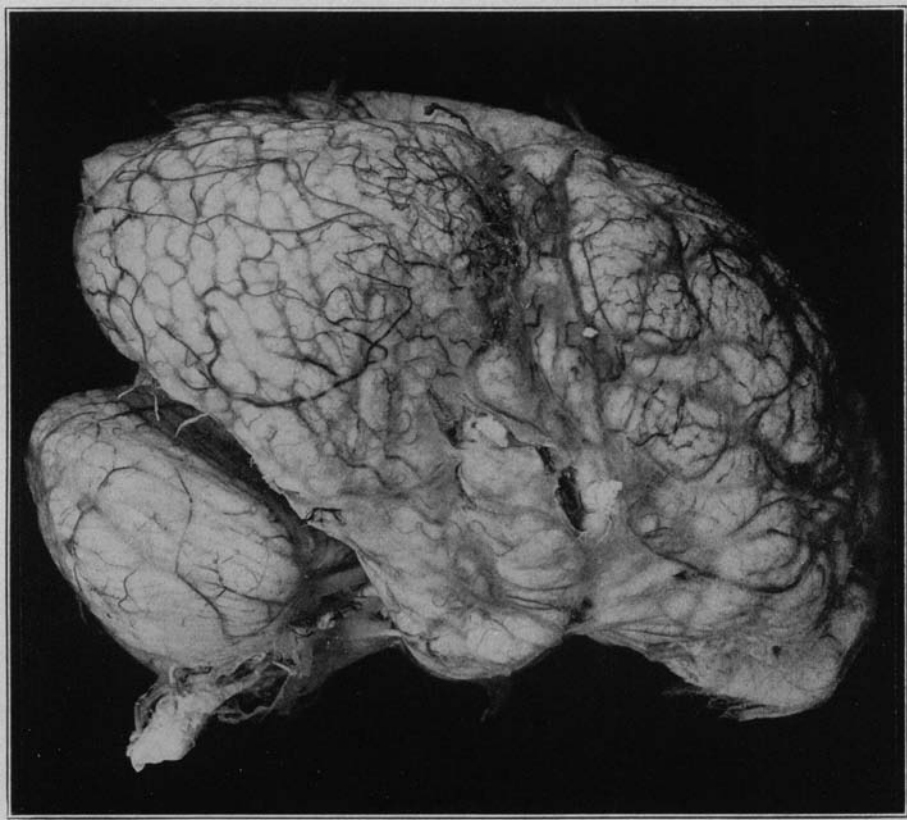


Fig. 1.—Right surface of the brain, showing thickening of the leptomeninges, atrophy of the parieto-occipital lobes, and loss of normal cerebral topography. The irregularly stippled and corrugated surface is particularly noticeable in the region of the parieto-occipital lobes.

it may be, not involving any vital centers, permits the individual to mature, although physical and not infrequently mental deficiencies may be striking.

4. Destruction or atrophy of part of a hemisphere may be compensated for by relative hypertrophy of the opposite hemisphere.

The main contribution of Kundrat was extension of the term so as to admit other cerebral malformations, which, while not presenting typical cavity formation, are nevertheless characterized by extensive loss of brain substance and by other pathologic features similar to those recognized in the typical form of Heschl. Another suggestion of doubtful value is that "anemic encaphalitis" is responsible for the defect in instances showing no evidence of trauma or changes in the

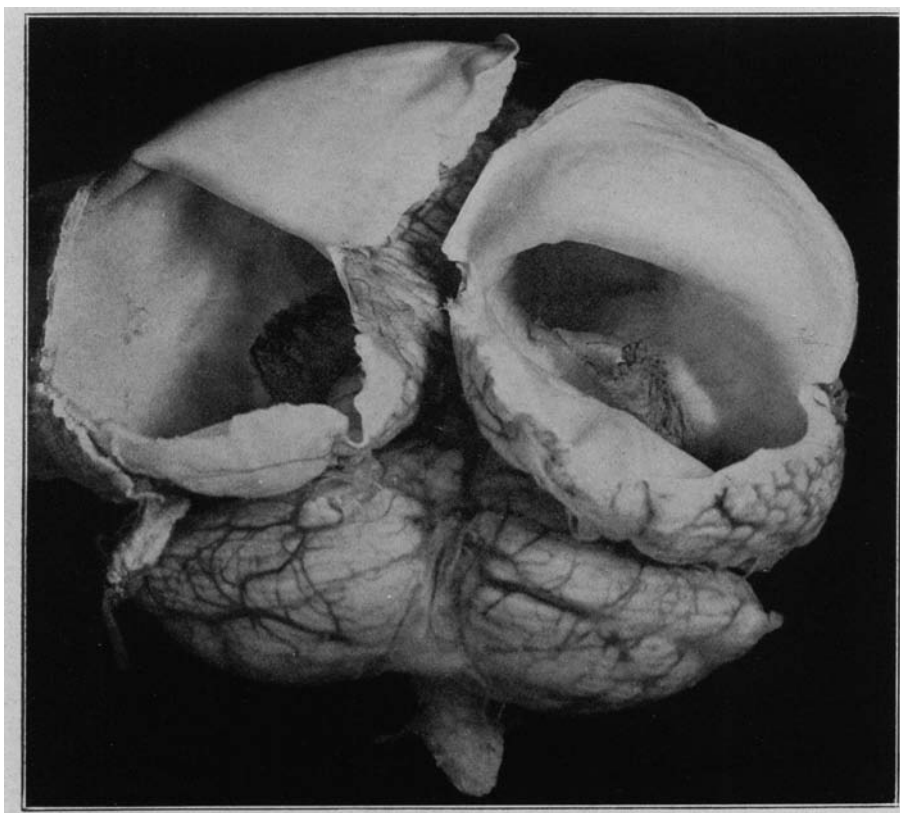


Fig. 2.—Extreme distention of the lateral ventricles and marked thinning of the cerebral hemispheres.

blood vessels. He finds an analogy in the ischemic softening of senile persons without demonstrable changes in the cerebral vessels.

Soon after Kundrat, Schultze<sup>4</sup> suggested that porencephalus may be due to infectious encephalitis. He criticizes Kundrat for failure

4. Schultze, F.: Beitrag zur Lehre von den Angeborenen Hirndefecten (Porencephalie). 58 Versammlung Deutscher Naturforscher und Aerzte in Strassburg, 1885.

to study his material microscopically and denies the possibility of anemic encephalitis. He found microscopic evidence of inflammatory changes, probably of infectious origin. He further concluded that the destructive changes began during intra-uterine life.

That prenatal encephalitis is possible is shown by the observations of Virchow,<sup>5</sup> who established the existence of congenital encephalitis as the result of an infection in the mother. He says: "It is conceivable

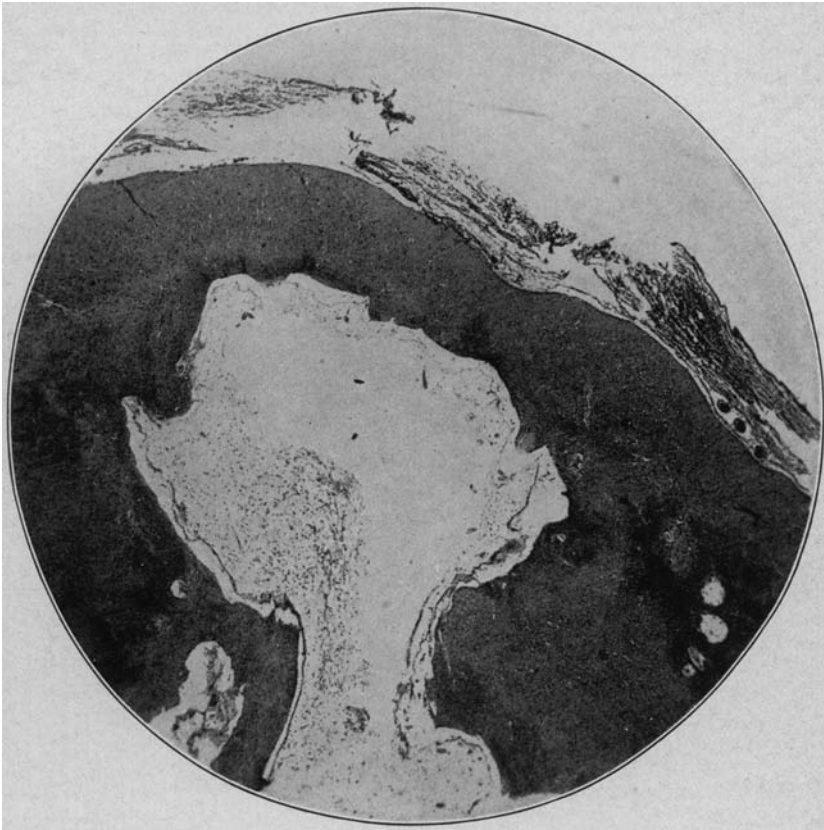


Fig. 3.—A porencephalic defect opening into the lateral ventricle. Smaller defects are seen in the vicinity of the porencephalic cavity. The pia-arachnoid is thickened and fibrous in structure. Photomicrograph;  $\times 17$ .

that such encephalic and myelitic affections are not always fatal and that instances occur where healing takes place, although this fact is yet to be established by further research. . . . It is most probable

5. Virchow, R: Congenitale Encephalitis und Myelitis, Virchows Arch. f. path. Anat. **38**:129, 1867.

that many cases of idiopathic and deuteropathic paralyzes of the infant and many instances of idiocy can be traced back to such encephalitic changes."

Strümpell<sup>6</sup> studied acute encephalitis in the infant, clinically and anatomically, and concluded that many porencephalic defects are due to encephalitis.

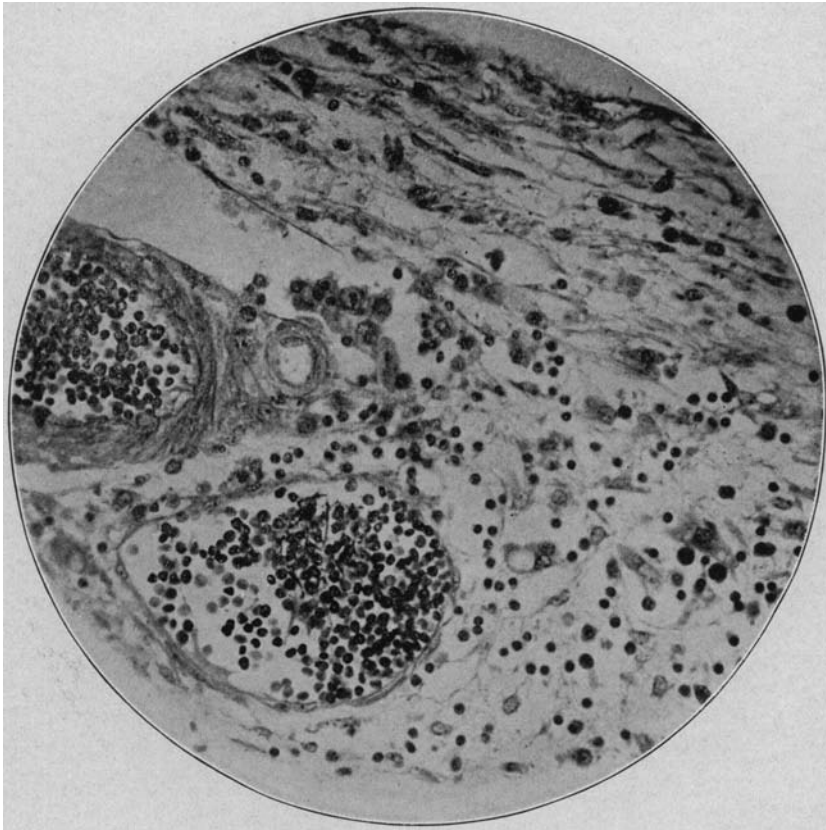


Fig. 4.—Section from the leptomeninges of the central gyrus of the frontal lobe, showing distention and infiltration of the pia-arachnoid space; vacuolated macrophages, small lymphocytes, large mononucleated leukocytes and fibroblasts. The vessels are distended and engorged with blood. The adventitia is thickened and infiltrated. Photomicrograph;  $\times 300$ .

More recently Limbeck,<sup>7</sup> who studied four cases of porencephalus, has supported the views of Strümpell.

6. Strümpell: Ueber die Acute Encephalitis der Kinder, *Jahrb. f. Kinderh.*, 1884, vol. 22.

7. Limbeck: Zur Kentness der Encephalitis congenita in ihrer Beziehung zur Porencephalie, *Ztschr f. Heilk.* **7**:1886.

Sachs and Peterson<sup>8</sup> say: "Porencephalus is a secondary condition and although much has been written on the subject, we know little of its origin. We are willing to concede that some of the many cases of atrophy or sclerosis may have been due to polioencephalitis, but it

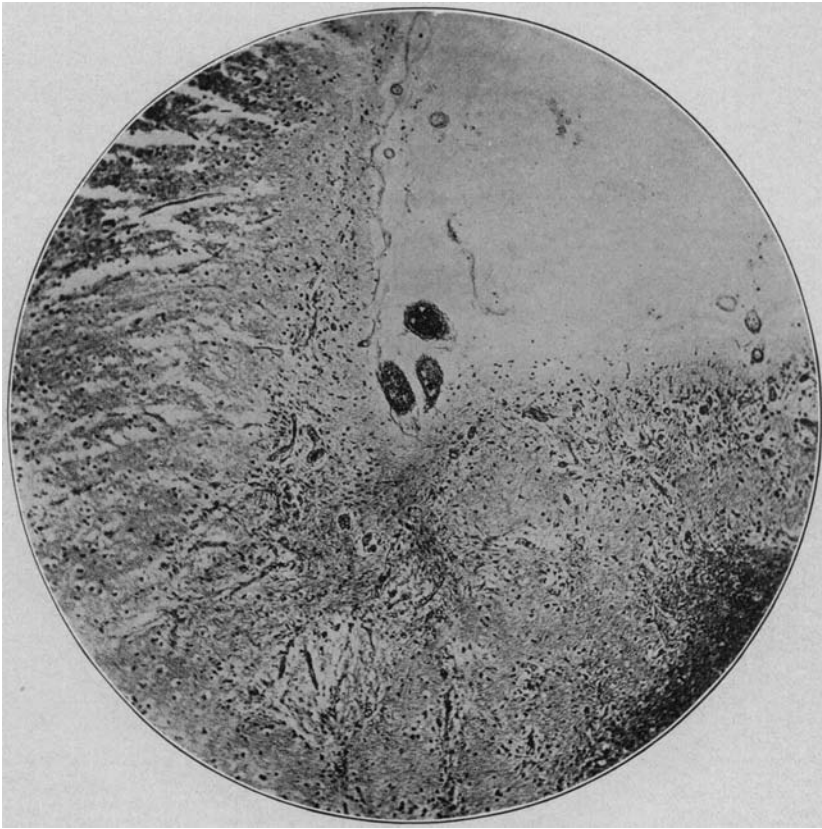


Fig. 5.—Note the marked thickening and fibrous character of the pia-arachnoid covering the parietal lobe. The underlying cerebral cortex is replaced by sclerotic patches. While the vessels on the surface are distended and engorged with blood, the vessels in the cortex are obliterated and represented by fibrous bands. Photomicrograph;  $\times 70$ ; Bielschowsky-Alzheimer-Mann stain.

is unfortunate for Strümpell's theory that all of the necropsies after death have shown other conditions but not encephalitis."

8. Sachs and Peterson: A Study of Cerebral Palsies of Early Life based upon an Analysis of One Hundred and Forty Cases, *J. Ment. & Nerv. Dis.* **17**:319, 1890.

## CASE REPORT

*History.*—G. N., 11 months of age, the first child, was born after a full term pregnancy and normal delivery. There was no evidence of syphilis in the parents, who gave a negative blood Wassermann reaction. At birth the patient was well formed, and he developed normally until the age of 4 months when it was noted that he did not progress mentally and acted as though he were blind and deaf. Aside from a small head, the child showed no physical maldevelopment.

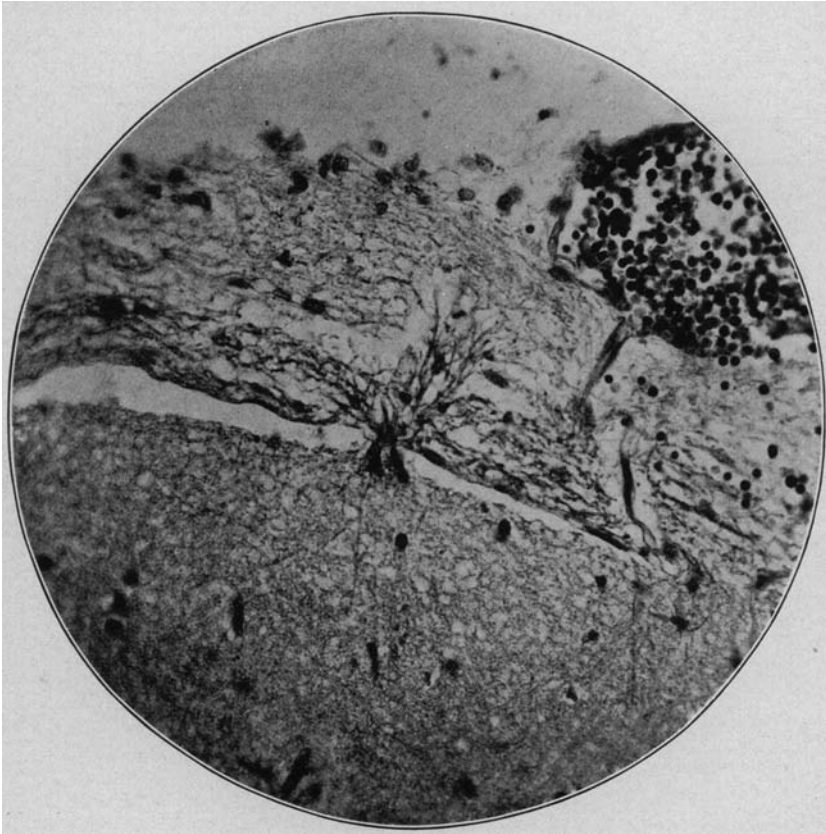


Fig. 6.—Glial cells are seen sending out their processes into the pia-arachnoid, bridging over the sub-arachnoid space. Photomicrograph;  $\times 300$ .

*Examination.*—On admission to Mount Sinai Hospital the following findings were recorded:

Child well nourished and well developed. Head small; fontanelles closed. Pupils regular, react to light and accommodation, no nystagnus. Upper extremities spastic and in flexion. Lower extremities spastic; all deep reflexes exaggerated. Temperature irregular ranging from 99.5 to 102 F.

*Treatment and Course.*—The diagnosis was congenital microcephalus, and bilateral subtemporal decompression was advised, which was performed four days later. After operation cerebrospinal fluid escaped from the wound, but the

patient's condition was unchanged. A high variable temperature continued. On the eighth day the child had several attacks of generalized convulsions, grew rapidly worse and died the same day.

*Necropsy.*—Heart, spleen, liver, and suprarenal glands showed no gross or microscopic lesions. The lungs, with the exception of some emphysema, were normal. The kidneys showed a mild degree of cloudy swelling.



Fig. 7.—Glia cells are seen in large numbers streaming into the pia-arachnoid alongside vessels that are still patent in their meningeal course, but hardly penetrating the cerebral cortex. Camera lucida drawing (Zeiss ocular 6  $\times$  objective 3).

The brain was rather small and apparently somewhat collapsed due to postoperative escape of cerebrospinal fluid. The meninges over the dorsolateral surfaces of the cerebral hemispheres were thickened in some areas and firmly adherent to the underlying cortex; in other areas they were greatly distended by fluid. The meninges at the base were normal.



On palpation the hemispheres fluctuated due to marked increase of cerebro-spinal fluid in the ventricles, and particularly because of thinness of the walls. Right Hemisphere: The sylvian fissure was well developed at the base but rather wide and shallow in its posterior part. It lodged the middle cerebral artery which ran its normal course over the frontal lobe and for some extent over the parietal. The frontal and parietal opercula were poorly developed, exposing the island of Reil, while the temporal operculum was normal. The convolutions of the frontal lobe could be made out although the fissures were

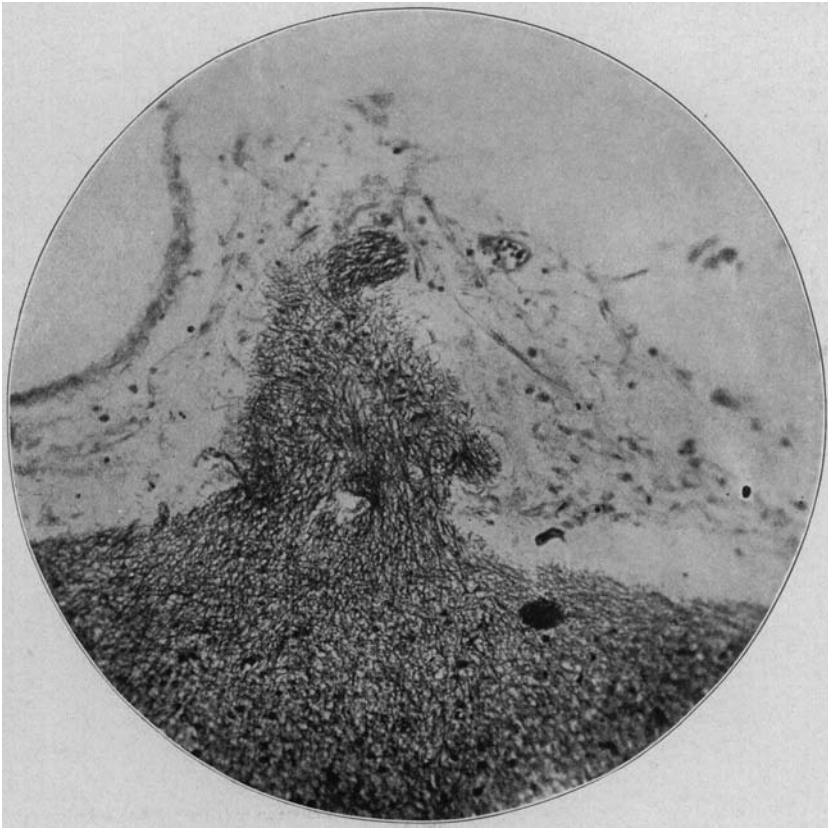


Fig. 8.—Section from the pons. Here a more massive migration of glial elements leads to protrusion of neuroglia into the pia-arachnoid. Photomicrograph;  $\times 180$ .

shallow and the gyri extremely flat. The precentral gyrus was fairly well defined from the postcentral area by a deep central sulcus. The gyri in front of the precentral sulcus were indistinct because of meningeal thickening, adhesions and atrophy of the gyri. The postcentral gyrus was poorly defined and the parieto-occipital lobes were markedly atrophied. Here the normal markings of the cortex were entirely lost. Instead there was a stippled, corrugated, granulated hob-nail surface. The vessels were freely movable

over the surface (Fig. 1). On incision the cortex of the occipito-frontal lobe was found to be only about 2 to 3 mm. thick. At the occipital pole it was reduced to parchment-like thinness (Figs. 2 and 3).

Left Hemisphere: This was similar to the right. The sylvian fissure was well defined but shallow, exposing a poorly developed island of Reil. The middle cerebral artery was in the sylvian fissure and appeared to be patent throughout. There was no first or second frontal convolution but the third was present. The portion corresponding to the first two presented a granular, stippled surface

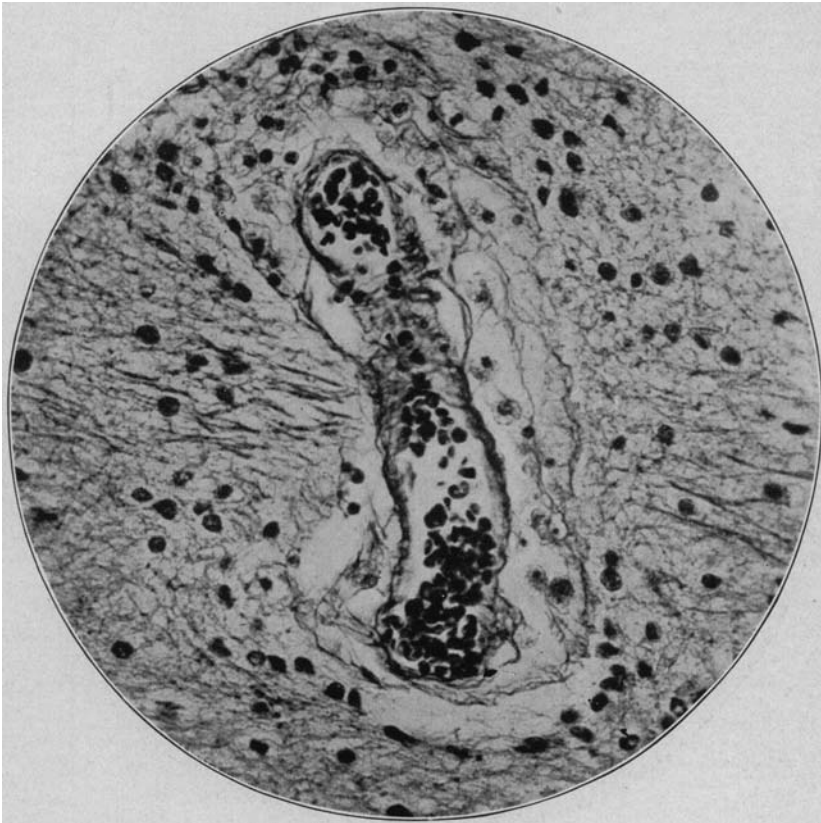


Fig. 9.—Section from the precentral convolution of frontal lobe showing marked distention of the adventitial space of the blood vessel. The granular (Gitter) cells found in the adventitial space point to a still active destructive process. Photomicrograph;  $\times 400$ .

covered in places by thickened meninges. The first temporal gyrus was well developed; the second and third were absent, the latter being replaced by the granular cortical structure. The gyri on the base of the temporal lobe were absent, but the hippocampal gyrus was normal. The parieto-occipital lobes were similar to those on the opposite side. The orbital surface of the frontal lobe was normal.

The cranial nerves were normal.

The ventricles were markedly distended in all their divisions and with the exception of the frontal lobes left nothing but a shell of the cerebral hemisphere. The basal ganglions were well developed; the corpus callosum was present; the septum pellucidum was thin, stretched and fenestrated. The mesencephalon, pons, medulla and cerebellum appeared to be normal. The hypophysis was small, the sella shallow; the blood sinuses and middle ear were normal.

*Microscopic Findings.*—The thickening of membranes over the dorso-lateral surface varied. Thus, over the frontal lobes where the leptomeninges were

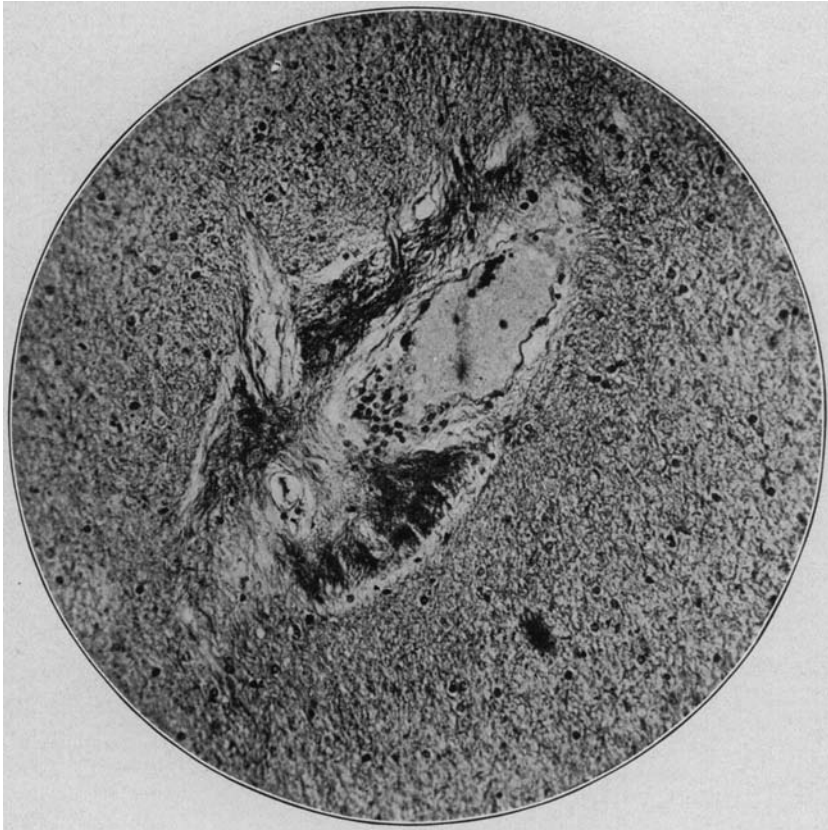


Fig. 10.—Vessel surrounded by a zone of dense gliosis. The adventitial wall of the vessel is infiltrated by small lymphocytes. Photomicrograph;  $\times 200$ .

edematous, the subarachnoid space was distended and infiltrated with elements characteristic of a subacute inflammatory process. The changes in the pia-arachnoid, pointing to a more or less recent inflammatory process, were characterized by macrophages with or without enclosures and with or without vacuolated cytoplasm. Endothelial cells grouped in fairly large numbers about blood vessels constituted an important feature in the cellular infiltration. They were recognized by their large vesicular nuclei, poorly staining chromatin material and abundance of cytoplasm. Small lymphocytes were also seen

in fairly large numbers. Fibroblasts giving off delicate processes formed in places a delicate network. Plasma cells with eccentric nuclei, deep staining chromatin and faintly staining cytoplasm were rare. The blood vessels were much dilated and congested and showed thickening of the adventitia (Fig. 4).

A striking change in the leptomeninges was seen in the wide parieto-occipital area. The transition from the subacute inflammatory process in the frontal meninges to the chronic fibrous thickening over the parieto-occipital area was abrupt. About 5 mm. posterior to the central fissure the leptomeninges were



Fig. 11.—Section from the midbrain at the level of the inferior quadrigeminate bodies showing extensive adventitial infiltration of the vessels with mononuclear elements. Photomicrograph;  $\times 240$ .

represented by a thick fibrous structure poor in cellular elements in which it was impossible to distinguish the pia from the arachnoid (Fig. 5). In some places extremely short pial processes could be traced into the cortex where blood vessels penetrated, but the majority of cortical vessels were apparently cut off by the meningeal cicatrization; others were strangulated by glial changes at a point just below their entrance into the cortex and in their deeper course were often obliterated and converted into a narrow band of connective tissue.

Strangulation and obliteration of blood vessels led to sclerotic changes in the cortical and subcortical substance. These zones of sclerosis corresponded to the areas supplied by obliterated vessels (Fig. 5).

There was a transition between these two types of meningeal alteration over the temporal lobe, particularly over the third temporal convolution. There was increase in fibrous elements with moderate mononuclear cell infiltration. Of interest was the fusion of the cortex with the pia-arachnoid alongside closed or partially closed vessels brought about by a most unusual migration of glial

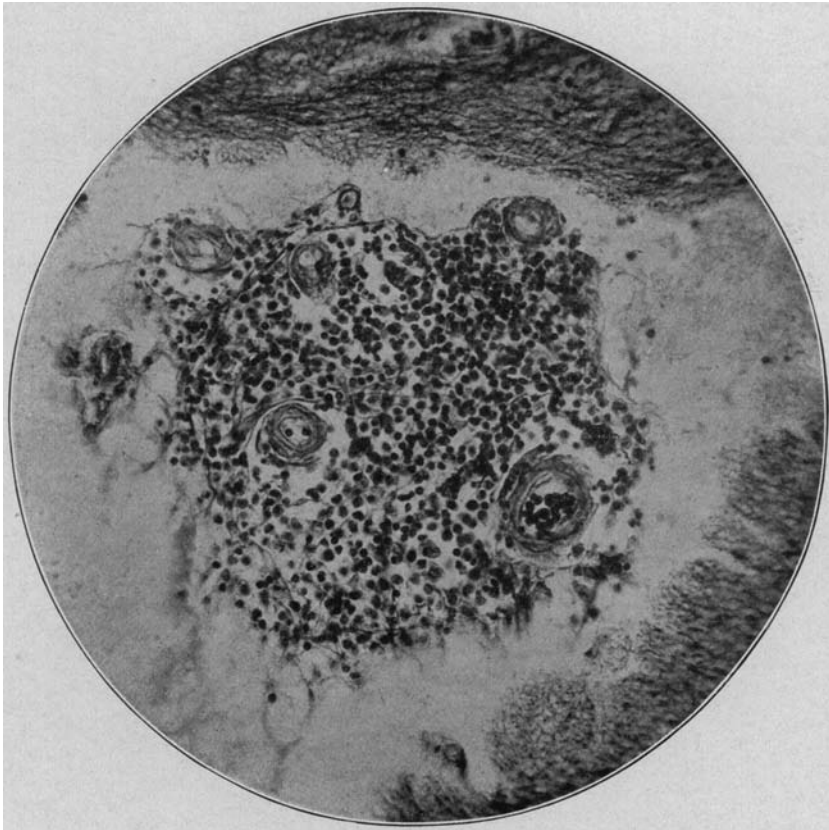


Fig. 12.—Section from the pons, showing a group of small vessels enveloped by a large mass of small lymphocytes. The adventitial walls of the vessels appear to be thickened. Photomicrograph;  $\times 240$ .

elements into the pia-arachnoid. In this way the boundary between the mesodermal pia-arachnoid and ectodermal glia-supporting tissue was effaced. Thus individual glial cells could be seen migrating into the pia-arachnoid, their processes extending over the subarachnoid space while the cell bodies were still in the peripheral zone of the cortex. Also larger groups of glial cells were noted streaming into the pia-arachnoid membrane, alongside a partially obliterated blood cell (Figs. 6 and 7).

This reaction of glial cells to anemic conditions resulting from obliteration of blood vessels is thus clearly demonstrated and is in full accord with the frequently expressed opinion that glial elements usually react to circulatory disturbances in the central nervous system by proliferation.

This feature is most pronounced where the inflammatory process is most recent, as in the pons. There massive migration of glial elements gives rise to herniation of neuroglia into the pia-arachnoid (Fig. 8). Such a process was thought and is still considered by many writers to be impossible. But Saxer,<sup>9</sup>

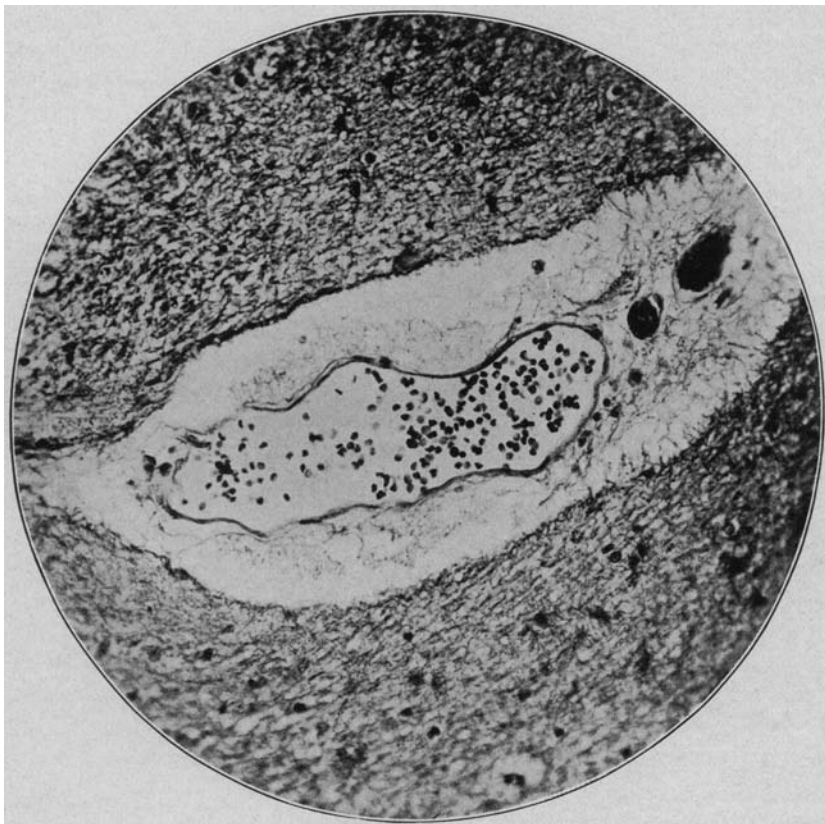


Fig. 13.—Pons; vessels with distended perivascular space filled with serous exudate and a few lymphocytes. Photomicrograph;  $\times 240$ .

in studying syringomyelia, called attention to glial infiltration of the pia. He even described the transformation of glial cells, on reaching the pia-arachnoid, into macrophages and other phagocytic cells. Also Strauss<sup>10</sup> has demonstrated involvement of the pia by an infiltrative subependymal glioma.

9. Saxer: Anatomische Beiträge zur Kenntnis der sogenannten Syringomyelie, Ziegler's Beitr. z. pathologischen Anatomie, **20**:332.

10. Strauss, I.: A Glioma Infiltrating the Pia Membrane, New York M. J. 1908, p. 1079.

Apparently the inflammatory process was primary where it now presents the more chronic features. Next, the inflammatory process involved the temporal lobe and finally the frontal lobes.

**Cortex:** The lesions of the cerebral cortex corresponded to the chronicity and character of the disease in the meninges. In the parieto-occipital lobes, where the meninges were fibrous, the cortex and subcortical substance were only a thin layer of scar tissue. Only here and there one could see a poorly preserved ganglion cell (Fig. 5).

The cortex of the frontal lobe presented an entirely different picture. Here many ganglionic elements were preserved, but the large motor cells were few in number and badly damaged. Important was the evidence of recent degenerative and inflammatory change. Large collections of fat globules crowding the adventitial space pointed to an active destructive process in the brain substance. Vessels with perivascular small round cell infiltration and with gutter cells crowding the adventitial space were further evidence of progressing inflammation (Fig. 9). Of particular interest were the vessels surrounded by zones of marked gliosis (Fig. 10) as well as wedge shaped zones of sclerosis resulting from the strangulation of the blood vessels by the cicatrizing pia-arachnoid.

In the mesencephalon at the level of the trochlear nerve was evidence of recent trouble—vessels with well defined adventitial infiltration. The cells found in the adventitial space were mostly small mononuclears, with a few plasma and endothelial cells (Fig. 11). In the pons was an area in which a group of small, probably newly formed blood vessels was enveloped by relatively large collections of mononuclear cells (Fig. 12); also vessels with serous exudate into the distended adventitial spaces (Fig. 13) and a limited number of perivascular hemorrhages were found.

**Spinal Cord:** Though it appeared that the ventral gray columns on one side were poorer in ganglion cells than on the other, it was difficult to establish a primary inflammatory process in this area.

#### COMMENT

The observations recorded in the foregoing present abundant evidence of an encephalitic process early in the life of the infant. The extensive destruction of the cerebral cortex and eleven months of the post-natal life not marred by any illness lead to the conclusion that the destructive process, resulting in the porencephalic defect, must have begun in the latter part of the intra-uterine life period and remained active and slowly progressive after birth.

That the physical development of the child was practically uninfluenced by the enormous loss of brain structure is most striking. This is best explained by the lack of early disease in the basal ganglions, midbrain, pons and medulla.

The opinion that the process was inflammatory and not traumatic or developmental is well borne out by the microscopic findings. Chronic and subacute lesions were found in the leptomeninges and underlying hemispheres, subacute and more recent lesions in the midbrain, pons

and medulla. Wherever the meningeal lesions were of the chronic fibrous type, complete strangulation of blood vessels resulted in diffuse and pronounced atrophy of the brain. The parenchyma was replaced by wide sclerotic zones, with fibrous bands.

In the temporal region, the pia-arachnoid was in process of fibrinous organization, shown by the presence of many fibroblasts and numerous mononuclear elements. Findings here indicate that wherever circulatory disturbances occur in the brain tissue, the destruction of brain parenchyma is accompanied by proliferation of glial elements. The thickening and cicatrization of the pia-arachnoid lead to strangulation of the blood vessels, producing ischemic zones of softening and sclerosis in which proliferation of glial elements and migration along closed blood vessels in the direction of the pia-arachnoid membrane are readily seen. This unusual process is of interest because it may help to a better understanding of changes that occur in multiple sclerosis, gliosis and scar formation in the central nervous system.

The histologic findings in the more recent lesions, especially in the region of the frontal lobe (mononuclear leukocytes, fibroblasts, plasma cells and macrophages) speak for a still active pathologic process. So probably the disease, started in the parieto-occipital region, spread to the temporal lobe, thence to the frontal region and finally to the mesencephalon, pons and medulla.

Repeated attempts to find the causative agent of the encephalitic process failed. Nevertheless the changes in the brain were clearly inflammatory, placing the case in the Strümpell group, so aptly named by Sachs—polio-encephalitis corticalis cerebri.

#### CONCLUSIONS

1. This case, although characterized by marked atrophy and diffuse sclerosis, can be considered one of porencephalus.

2. The atrophy and porencephalic defect were due to an inflammatory process, beginning as a meningo encephalitis in the parieto-occipital lobes.

3. The meningitic process led to strangulation of the blood vessels, producing anemia, degeneration of the parenchyma, proliferation of glial elements and finally to scar formation in the cortex.

4. Glia cells proliferate whenever blood vessels are occluded and migrate along the closed vessels toward the seat of active inflammatory process.

5. The migration of glial elements into the pia-arachnoid is well established by the findings recorded and supported by the observations of Saxer and Strauss.



6. The inflammatory process, primary in the meninges of the parieto-occipital lobes, slowly progressed to the temporal, then frontal lobes and finally to the midbrain and hind brain.

7. The strangulation of blood vessels causing sclerotic changes in this case is an important finding in relation to the pathology of disseminated sclerosis.