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BRAIN.

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THE STRUCTURAL BASIS OF TRAUMATIC EPILEPSY AND RESULTS OF RADICAL OPERATION.[1]

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EPILEPSY is a specific reaction on the part of the central nervous system to a noxious stimulus. It may be called focal when it is possible to determine a circumscribed area upon which the stimulus first acts. Thanks to recent advances in neurophysiology and in neurosurgery it is now possible to include in the group of focal epilepsy many cases formerly considered to be generalized. In addition to the march of crude motor phenomena characteristic of Jacksonian epilepsy, alterations in the directions of gaze, turning of the head and certain sensory auras may serve to point to the focus from which an epileptogenic stimulus is derived.

Even in traumatic epilepsy, however, where the irritative focus may be easily localized there are other factors to be considered. In addition to the irritative stimulus the occurrence of a convulsion depends upon the irritability and the susceptibility of the brain to such stimulus. Further, there are certain general influences which though they operate from a distance directly influence the production of convulsions. There can be little doubt but that epilepsy is an active stimulation process and not a release phenomenon, although release phenomena may be observed during and following an attack.

Exploration of the human cerebral cortex, both in normal and

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pathological areas in well over 100 cases under local anæthesia, has made it possible to outline certain definite epileptogenic cortical areas (Foerster [4]). The areas in the human cortex are analogous to but not identical with the areas outlined by Vogt in monkeys. The movement patterns which follow such stimulation experiments provide a local sign which often makes it possible to localize the irritating focus of an epileptic discharge, even where there are no physical signs to suggest this localization.

Quantitative stimulation in the post-central field (3, 1, 2) (fig. 1)

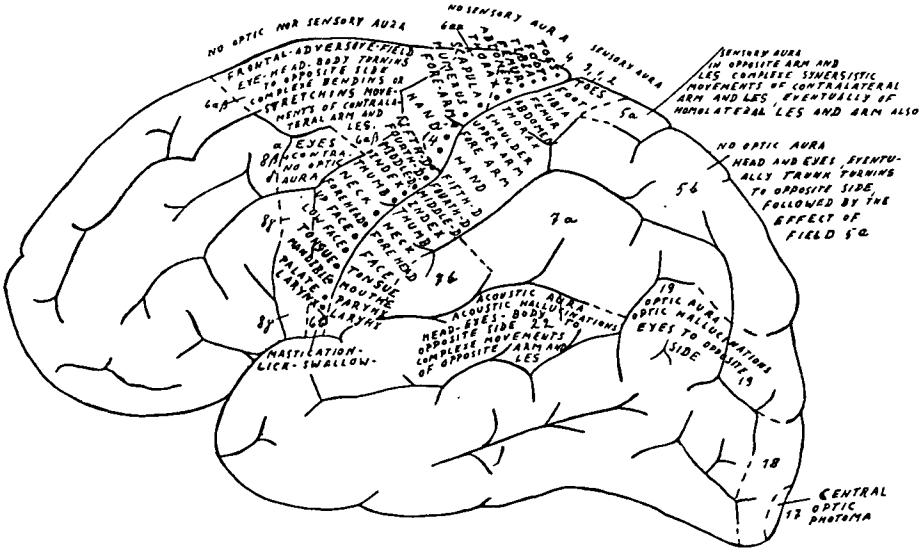

FIG. 1.—Epileptogenic cortical areas in the human brain. The outlines indicate roughly the initial movements and auræ which follow direct stimulation of the cortex by an electrical current sufficient to produce an epileptic seizure.

requires a considerably larger amount of current to bring on an attack than in the pre-central (4 + 6a α). The clonic convulsion produced by stimulation in either area appears to be about the same. If it arises, however, behind the central fissure the attack is preceded by a sensory aura which begins in the part first affected and often spreads like a wave over that side of the body.

Stimulation in the frontal adversive field (6a β) (fig. 1) produces turning of eyes, head and body to the opposite side, followed by clonic or tonic movements of the contralateral arm and leg. These movements take place without any aura. Below this field the frontal eye field may give rise to a convulsion initiated by isolated clonic turning of the

eyes to the opposite side without any optic aura. Following this the attack takes on either the characteristics of a frontal adversive field attack, or a simple pre-central attack, depending upon the direction in which the stimulus spreads.

Stimulation of the occipital pole in area 17 produces an attack which is ushered in by an optic aura such as light, flames, stars, &c., usually in the opposite visual field. Stimulation farther forward (area 19) causes a change in the direction of the gaze to the opposite side associated with an optic hallucination, such as a figure in the opposite visual field. A stimulus in the parietal adversive field (5b + 5a) produces turning of the eyes, head and body to the opposite side and movements of the opposite limbs. If it be in the anterior portion of this area (5a) the movements of the head and eyes may be absent, but there is a sensory aura of discomfort in the arm and leg of the opposite side followed by leg and arm movements. As indicated in fig. 1, a stimulus in the posterior temporal region is likely to produce an acoustic aura. Lesions affecting the operculum centrale (area 6b) cause grunting, licking, swallowing or some such movement of the mouth and pharynx, associated usually with a sensation in this vicinity and also singultus.

In any case of focal epilepsy where there is a reasonable suspicion of a cerebral lesion, *encephalography* should be employed to demonstrate any gross cerebral abnormality. If operation be then undertaken a careful electrical exploration of the cortex under local anæsthesia serves to prove whether or not the suspected focus is actually the site of the initiation of the discharge.

The radical excision of a lesion, even though it is obviously the focus for epileptic discharges, can only be a rational procedure if the lesion produced by the excision be a more innocent one than the original focus. A comparison of the results of cerebral laceration and excision has been made the subject of a series of experiments by Penfield [1] which indicate a striking difference in the end-result of excision from that of laceration.

If a wound be made in the brain and the damaged cerebral tissue is not removed there forms rapidly a scar which contains connective tissue and fibrous astrocytes, and which is densely attached to the overlying meninges. A very rich plexus of new-formed vessels appears in the scar. This plexus anastomoses on the one hand with the extra-cerebral blood supply of meninges and scalp, and on the other hand with the vessels of the brain. The cicatrix contracts steadily over a period of years. There results a very considerable pull upon the vaso-astral framework of the

brain. This framework is made up of the blood-vessels and attached fibrous astrocytes. The pull exerts an influence on the whole hemisphere and, in fact, upon the whole brain.

The effect of such a pull after a brain injury has been pointed out by Foerster [2]. He noted that there was a "wandering" of both lateral and third ventricles towards the site of such a lesion. The cause of this phenomenon is now apparent, as will be pointed out below. The displacement is due to cicatricial *pull* probably associated with the atrophy which takes place in the brain about the cicatrix.

Excision of cerebral tissue, however, produces a different result. There is no organization of connective tissue. Instead of that there appears a fluid-filled space with a very small amount of gliosis about it, without a plexus of new-formed vessels and without evidence of cicatricial pull upon the surrounding brain. Thus the results of brain injury and brain excision are structurally quite different.

Nevertheless, in the last analysis of course, the wisdom of substituting a non-contracting fluid-filled space for a contracting cicatrix in these patients must be judged on a human empirical basis.

The cases to be reported below provide an opportunity for studying the result of the excision of cerebral cicatrix in epileptics and the mechanism involved. In the group of cases selected the gunshot wounds of the brain are of long duration and the birth injuries of still longer. Consequently the excised tissue offers a remarkable opportunity to study the late results of cerebral trauma histologically.

Case Reports.

Case 1.—In 1914 the patient received a gunshot wound in the left parietal region. This was followed by twelve hours of unconsciousness and a hemiparesis and hemi-ataxia of the extremities of the right side. Ataxia and intention tremor have persisted in the right arm together with loss of cortical sensibility. The patient learned to write with his left hand. The onset of Jacksonian epilepsy involving the right side began in 1920, i.e., six years after the trauma.

Encephalography in 1925 showed some enlargement of the left lateral ventricle and a displacement of both lateral and third ventricles towards the side of the lesion (fig. 2).

Operation, 1925.—A large parietal craniotomy was carried out and dura mater was found to be densely adherent to an underlying brain scar. Within the scar was a large cyst which did not communicate with the ventricles. Electrical exploration showed the lesion to lie just posterior to the motor area for the fingers. A wide excision was carried out as indicated by the broken line in

fig. 3. The bone flap was not replaced. The patient made a good recovery and in the five years following the operation up to the time when last heard of he was quite free from convulsive seizures.

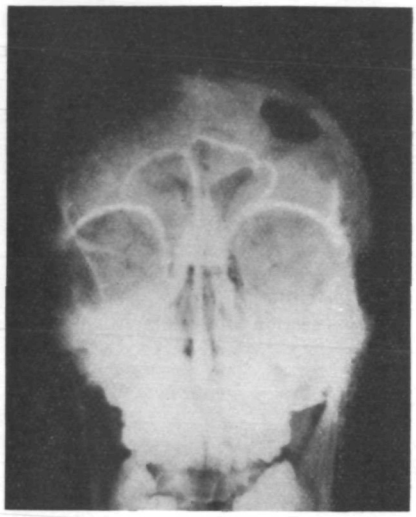

FIG. 2.—*Case* 1. Encephalogram (brow up) eleven years after gunshot wound of left parietal region. Cranial defect is shown and lateral ventricles pulled towards it.

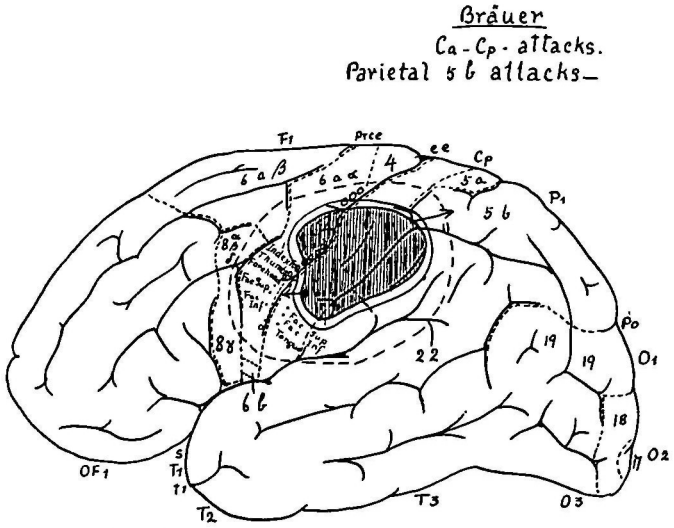

FIG. 3.—*Case* 1. Shaded area shows the position of the lesion at operation and the second line the extent of operative removal. The pattern of the attacks indicated that the stimulus might arise in front of or behind the lesion, as indicated by the arrows.

The gross specimen showed considerable thickening of the dura. A bit of bone was embedded in the cicatrix and bands of fibrous tissue could be seen passing downwards into the brain (fig. 4).

Microscopical examination shows the connective tissue to be entering the brain scar in more or less parallel lines (fig. 5). Closer examination shows these bands to be made up of blood-vessels and sturdy collagen fibres. When stained so as to demonstrate both collagen fibres and neuroglia fibres, it is seen that the two types of fibres are more or less intermingled and parallel as though they were strands in a rope. Deeper in the brain neuroglia fibres are found

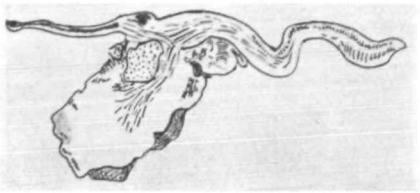

FIG. 4.—*Case* 1. Cross section of cicatrix attached to thickened dura.

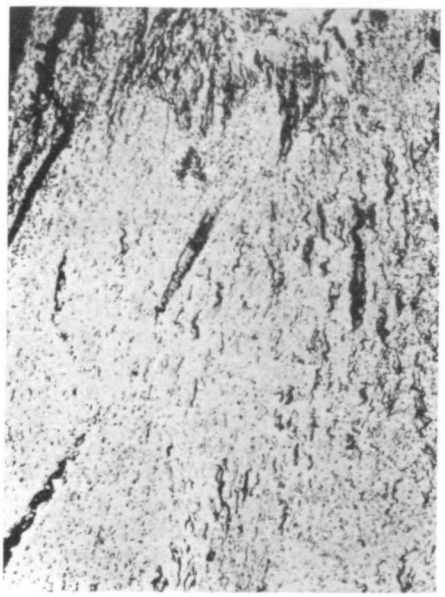

FIG. 5.—*Case* 1. Connective tissue and vessels entering the brain scar in parallel strands. Silver carbonate collagen stain.

lying in parallel lines, pointing upwards towards the meningo-cerebral adhesion (fig. 6).

In one sense this tissue can no longer be called cerebral tissue inasmuch as it no longer contains either nerve-cells or nerve-fibres. A very occasional nerve-fibre may be found in these areas of gliosis.

It seems obvious from the structure of this tissue that it is quite capable of transmitting the pull which the contracting cicatrix must have exerted

FIG. 6.—*Case* 1. Parallel neuroglia fibres oriented in the direction of the cicatricial pull. Silver carbonate astrocyte stain, Hortega.

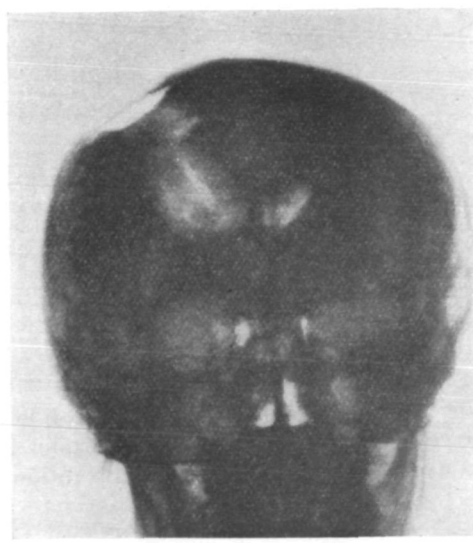

FIG. 7.—*Case* 2. Encephalogram (brow up), fourteen years after gunshot wound of right parietal region; shows cranial defect, the underlying brain cyst, enlargement of right lateral ventricle and pulling of all three ventricles in the direction of the defect.

upon the brain itself, as evidenced by the migration of the ventricles towards the side of the lesion.

Case 2.—The patient received a gunshot wound in the right parietal region in 1914, which was followed by hemiplegia of the extremities on the left side. The hemiplegia, which has only partially disappeared was followed in 1919 by Jacksonian epilepsy of parietal field type (see legend with fig. 8).

Encephalography in 1928 showed the right lateral ventricle to be considerably enlarged. The air entered a cyst just beneath the cranial defect which was due to the wound. Both lateral ventricles and the third ventricle were deviated across to the right side and the right ventricle upward toward the defect (fig. 7).

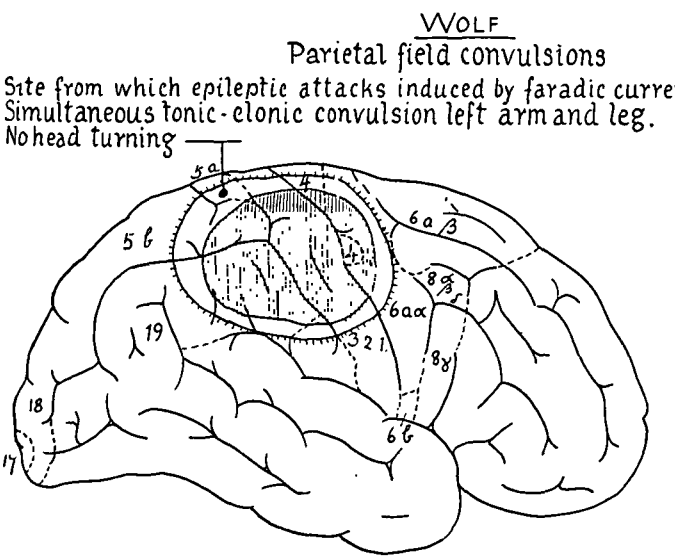

FIG. 8.—*Case* 2. Diagram from operative exposure. Jagged line indicates extent of cicatricectomy. Spontaneous attacks were preceded by sensory aura in the left leg or simultaneously in left leg and arm followed by head, eyes and body turning to left with tonic-clonic spasm of left arm and leg and rapid spread to extremities of right side.

Craniotomy in April, 1928.—Underneath the defect the dura was adherent to a cerebral scar; in the anterior part of the scar was a cyst. Posterior to this the tissue was hard and rather grey. Electrical stimulation near this indurated area produced a convulsion characterized by almost simultaneous movements of the left arm and leg, without head turning (fig. 8). A radical incision was carried out as indicated. Since the operation up till the present time (April, 1930) he had no more attacks.

The gross specimen showed dense adhesion of firm tissue to the under surface of the dura, and a large vessel near the point at which the stimulus had produced the convulsion.

Microscopical examination showed that the indurated areas contained

strands of connective tissue and blood-vessels passing downward from the dura. Some of the vessels were surrounded by sclerotic rings of fibrous neuroglia. There was progressive destruction of tissue taking place as evidenced by pigment-laden cells around certain of the vessels, and also by isolated areas in which the microglia had undergone a partial alteration in the direction of compound granular corpuscles.

Case 3.—The patient received a gunshot wound in the right occipital region in 1914. A preliminary operation was done at once but the patient suffered from headaches and vertigo for some time, and he has had a left-sided homonomous hemianopsia since that time.

In 1916 epileptic seizures appeared, each attack being ushered in by a

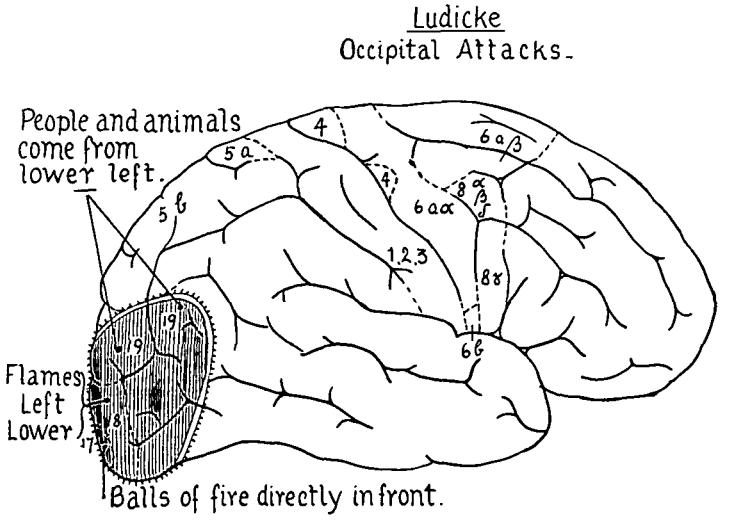

FIG. 9.—*Case* 3. Area of lesion seen at operation indicated by shading. Dots show points stimulated by electrode. The symptoms experienced by the patient following each stimulus are indicated on the chart.

sensation of light in the left visual field. This was followed by turning of the eyes to the left, followed by turning of the head to the left and convulsive movements of the limbs of the left side, ending eventually in loss of consciousness.

Encephalography was carried out in 1927. This showed the posterior horn of the right lateral ventricle to be somewhat enlarged, to be displaced to the right and evidently to communicate with a cyst in the vicinity of the cranial defect. Both ventricles, even as far forward as the thalamus, were displaced somewhat to the right.

Occipital craniotomy was carried out in January, 1927. The dura was found to be densely attached to the cerebral cicatrix in the occipital lobe. Electrical stimulation of field 19 (see fig. 9) caused people and animals to be

seen in the left field, and flames or balls of fire were produced by stimulation in field 18 nearer the occipital pole.

The whole area was radically excised; the epileptic seizures became less

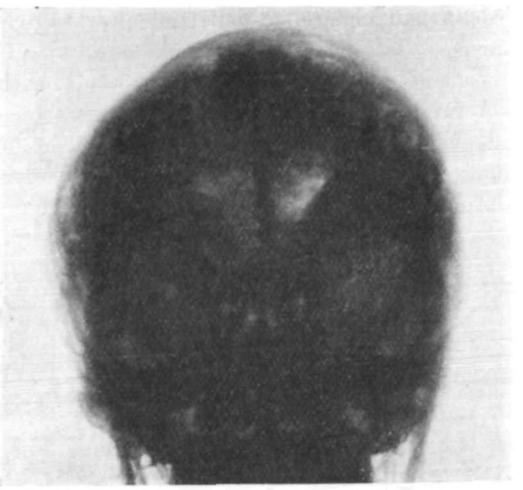

FIG. 10.—*Case* 4. Encephalogram (brow up) eleven years after shell wound of right frontal lobe. Lateral ventricles pulled to right and upwards towards the scar. The radiogram has been reversed in reproduction.

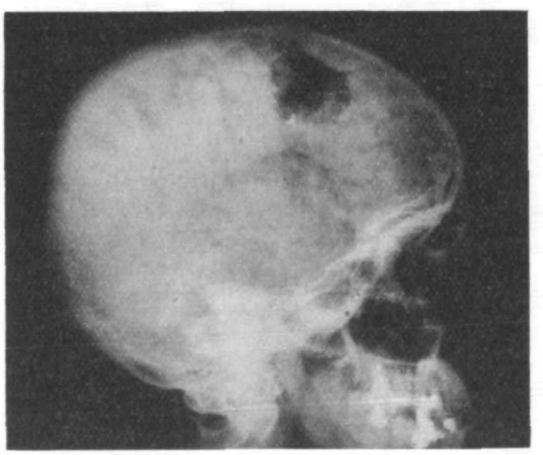

FIG. 11.—*Case* 4. Encephalogram (right side of head up) showing cranial defect with enlargement of anterior horn of the right lateral ventricle, and deflection upward of parts of both anterior horns.

frequent and less intense but did not disappear entirely. One complicating factor in this case is the fact that the patient acquired syphilis in the year following the onset of his epilepsy.

In the excised cerebral cicatrix were two pieces of bone and a remarkable amount of connective tissue.

Case 4.—In 1914 the patient received a shell wound in the right frontal lobe. There was apparently no loss of consciousness and an immediate operation was performed. One year later the cranial defect was closed. At the end of four years, in 1918, the patient began to suffer from epileptic attacks which were of the type of those arising in the frontal adversive field. The eyes and head turned to the left without any sensory aura. This was followed by movements of both the left extremities.

Encephalography which was carried out in 1925 showed that the right lateral ventricle was somewhat larger than the left and was displaced upward

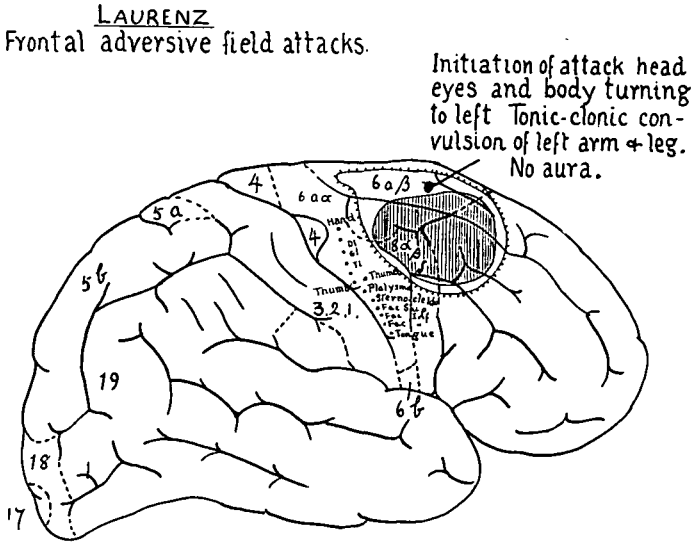

FIG. 12.—*Case* 4. Lesion as seen at operation. Motor response to galvanic stimulation indicated by small dots. Point at which convulsion was induced by faradic stimulation indicated by large dot.

and laterally. The third ventricle was displaced to the right and the left lateral ventricle seemed to be tipped, as though there had been a pull upward toward the cranial defect in the right upper frontal region (fig. 10). In the lateral view (fig. 11) the enlargement and upward deviation of the right lateral ventricle is easily seen.

Frontal craniotomy was carried out in 1925. A dense adhesion between the dura and cerebral cicatrix was found. Electrical stimulation of the brain at the border of the cicatrix (fig. 12) initiated an attack which was quite typical of those from which the patient suffered ordinarily.

The operative recovery was satisfactory, and during the three years which followed the operation there were no further convulsions.

The excised tissue contained yellowish grey gelatinoid material as is usual

in these cicatrices. Two bits of shell were found embedded in the tissue. Histologically there was a large amount of gliosis and remarkable parallelism of the glia fibres. There was a very well-developed vascular plexus entering the scar (fig. 13).

Case 5.—In 1916 the patient received a gunshot wound in the parietal region near the vertex, a little more on the left than the right. An immediate operation was carried out. There followed a bilateral spastic paresis, more marked on the left side and associated with sensory disturbances of both legs.

In 1923 he began to have epileptic seizures typical of those arising in the right parietal adversive field. The head and eyes turned towards the left and

FIG. 13.—*Case* 4. Plexus of vessels and collagen fibres entering brain from overlying cicatrix. Silver carbonate connective tissue stain.

then suddenly simultaneous movements appeared in the left arm and leg, followed quickly by the right leg.

Encephalography showed some enlargement of the lateral ventricles and an upward deviation of the right side.

Parietal craniotomy was carried out and a large meningocerebral cicatrix found. The operation was carried out in two stages. At the first operation during the dissection of the scalp free from the dura, several typical convulsions were produced apparently as a result of the manipulation of the scar.

At the second stage of the operation electrical stimulation of the brain in the vicinity of the scar produced a typical attack. A wide excision was carried out as indicated (fig. 14). The excised tissue showed the usual type of con-

tracting cicatrix. During the four years which have elapsed since operation the patient has been completely free from any attacks.

Case 6.—The patient gave an obvious history of birth injury followed by

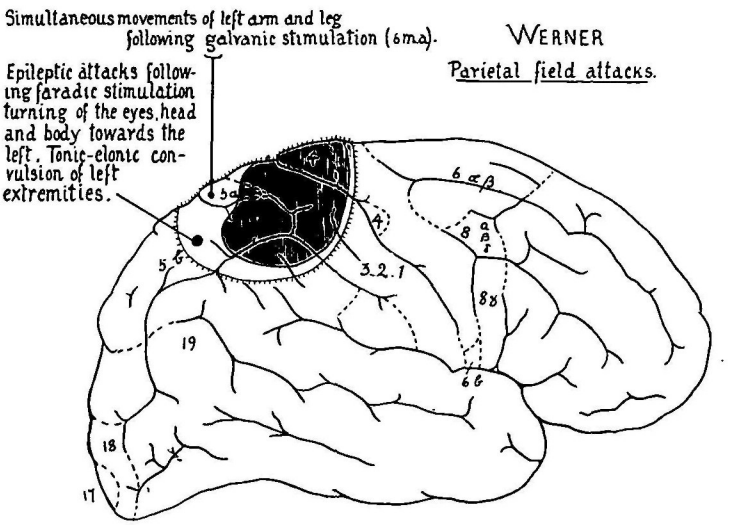

FIG. 14.—*Case* 5. Location of lesion and extent of removal.

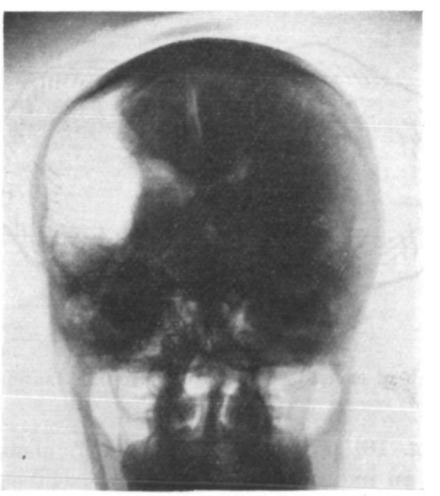

FIG. 15.—*Case* 6. Encephalogram (brow up) nineteen years after birth injury. Cyst of left hemisphere. The radiogram has been reversed in reproduction.

right-sided hemiplegia which gradually improved during boyhood. There was normal mental development up to the age of 12, after which time he was somewhat retarded. At 14 he began to suffer from epileptic seizures which began

Case 7.—This is a second case of cerebral birth injury followed this time by left-sided hemiparesis. At the age of 9 he began to suffer from epileptic attacks typical of those arising in the right frontal adversive field. The head and eyes turned to the opposite side followed by convulsive movements of the opposite extremities. The following year an opening was made in the bone over the right frontal area without entering the dura. This was without effect on the epilepsy.

Encephalography in 1928, at the age of 19, showed enormous dilatation of the right lateral ventricle with some displacement of the third ventricle across

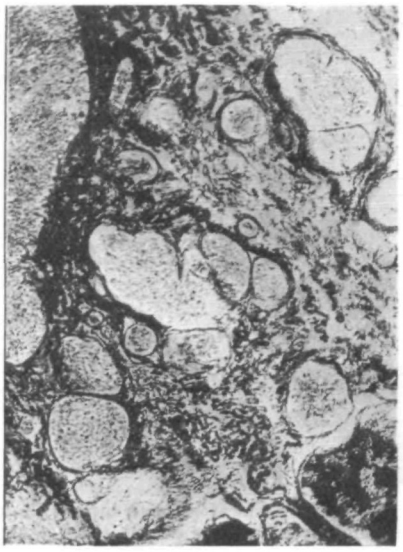

FIG. 21.—*Case* 7. Low-power photomicrograph of strands of cicatrix in cross section. Collagen makes a dark line about each. The dots within are neuroglial nuclei.

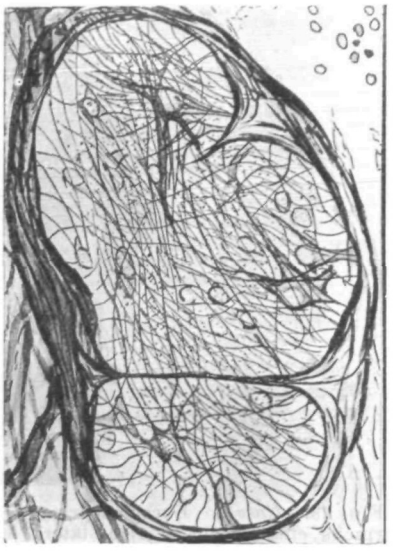

FIG. 22.—*Case* 7. High-power sketch of one of the strands seen in fig. 21. Some of the astrocytes can be seen to apply large processes to the collagen lining. The fine fibres are all neuroglial and arise from these cells. The dots indicate numerous such fibres cut across. Silver carbonate astrocyte stain, Hortega.

to the right side (fig. 19). The enlargement was chiefly in the anterior end of the ventricle (fig. 20).

Craniotomy the same year demonstrated a dense adhesion between the dura and the brain scar. Dissection of the scar produced a typical attack. The lesion was excised, thus removing the lateral wall of the ventricle.

This excised tissue like that examined in the last case contained strands of glial tissue in which no nerve-fibres were to be found. The neuroglia cells were fibrous, containing many long, slender neuroglia fibres. These strands were coated with collagen and the neuroglia cells within were attached by numerous

footplates to the under surface of the collagen covering. This is tissue capable of withstanding a considerable pull. These strands (fig. 21 and 22) were unlike any other type of pathological material. The tissue can hardly be called cerebral tissue in the strictest sense, inasmuch as there are no nerve-cells and no nerve-fibres in it, and although the tubes are composed entirely of neuroglia they have been coated over with collagen, just as nerve-fibres in other portions of the nervous system are invariably covered.

Operative Technique.

The general preparation and pre-operative study are indicated in the outline of the above cases. Operation must be carried out under local anæsthesia. After electrical exploration radical excision is practised.

The removal should go deep enough to carry away all of the injured tissue and is best carried out by passing sutures deep down into the brain and tying them one by one so that the suture itself cuts through the cerebral tissue and procures hæmostasis of the blood-vessels in the pia arachnoid. The defect in the dura should be closed by the insertion of a piece of fascia. Operations that provide for the closure of the bone defect without removal of the scar can hope to accomplish nothing. Likewise dissection of the dura free from the scar and the interposition of an implant should only make matters worse, for no matter what the implant may be, it stimulates the formation of increased amounts of connective tissue. Only radical excision can remove the scar and relieve the abnormal physical strain. Anything less will serve only to increase the cicatrizing process.

There are minor differences in operative procedure as carried out by the two authors. In the neuro-surgical clinic at Breslau the bone is removed permanently over the area of operative exploration, while in Montreal the original procedure has been modified to the extent of replacing the bone flap. The important feature is that the removal is radical, clean, and directed toward the lesion responsible for the attacks.

Discussion.

There were five additional cases included in the original report which will not be cited here; the ones already taken up being sufficient to serve as examples. These cases were selected because they illustrated certain aspects of the problem of traumatic epilepsy. Numerous similar cases could be added from the experience of each of the authors.

In each of the twelve cases studied there was displacement of one or all of the ventricles towards the side of the lesion. In most of the cases there was some degree of enlargement of the ventricle on the side of the lesion. In the two cases of birth injury the enlargement was enormous. That the local atrophy is not the cause of the deflection of the ventricles towards the site of the lesion is shown by the fact that the wandering of the ventricles is not greater in those cases where the atrophy is great. Likewise cases of cerebral thrombosis do not show

FIG. 23.—Schematic drawing of three levels in any meningo-cerebral cicatrix of long standing. Uppermost panel shows blood-vessels and bundles of collagen penetrating the brain beneath the meninges. Middle panel from area farther below surface shows intimate relationship of collagen strands and fine-fibred neuroglia, all parallel and pointing in the direction of the cicatricial pull. Lowermost panel from an area deeper in the brain shows the structure of astrocytes and blood-vessels which make up the vaso-astral framework and transmit the cicatricial pull.

this ventricular displacement and many cases with little or no enlargement of the lateral ventricle may show quite marked ventricular displacement. Instead of wandering of the ventricles the process is really brain-pull or ventricle-pull.

Its seems evident that cicatricial contraction is responsible for the displacement of the ventricles in these human cases just as has already

been demonstrated experimentally. Histological examination of this human material provides eloquent evidence of a long-continued cicatricial traction. There was always fibrous tissue, especially near the surface, and adhesion to the meninges (fig. 23). Thus connective tissue and an astonishingly rich plexus of vessels were invariably present in the scars, intermingled with fibrous astrocytes whose fibres were in general arranged in parallel and extended in the direction of the obvious traction, that is upward toward the cicatrix (fig. 23, middle panel). Deeper down in the brain (fig. 23, lowest panel) the astrocytes and blood-vessels still continue to form the only framework capable of withstanding tension, the vaso-astral framework [1].

In the areas of gliosis nerve-fibres are rare and nerve-cells still rarer. Occasionally localized areas are found in which there are groups of phagocytes containing pigment. Such patches are evidently in the vicinity of blood-vessels which have been shut off and they seem to indicate that the process of cerebral destruction is a long-continued one as they were present twelve and fourteen years after the initial wound. These areas recall the focal perivascular destruction described by Spielmeyer [3] in epilepsy of a different type.

The most extreme degree of progressive scarring is seen in the two cases of birth injury, both of which were of nineteen years standing. In these cases the process of connective tissue invasion and fibrillation of neuroglia had gone to such a point that there were tubes and sheets of neuroglia surrounded by connective tissue sheaths. Even where local atrophy and destruction had given rise to the presence of cysts there was always to be found also an area of grey, gelatinous fibrous tissue, the centre or the focus of concentric traction.

One further convincing evidence of the physical pull which these scars exert is the fact that in one of these cases reported here and in a number of others which we have observed, there was a definite pulling in of the scar which was noted as soon as the bone was removed and the edges of the adherent dura incised. The centre of the scar thus drew itself together, sucking the attached dura inward as much as 1½ cm. as soon as it was freed from the attachment to the overlying skull.

Relationship of Cicatricial Contraction to Traumatic Epilepsy.

An outstanding feature of all of these scars is the rich plexus of newly-formed vessels in and about the cicatrix. This vascular plexus

anastomoses very freely with the large vessels which enter the scar from without. It also anastomoses freely with intracerebral vessels inasmuch as the surface of the dura continues to bleed after it is completely exposed and cut free from surrounding dura. We have already shown [1] also that experimentally this vascular plexus can be injected either by way of the external carotid artery or through the internal carotid.

During the years which follow the infliction of a brain wound there is evidently a progressive increase in the vascular elements of the scar and a progressive decrease in the nervous elements. Associated with these two changes is the steady cicatricial contraction which obviously takes place for an indefinite period.

Now if the stimulus for an epileptic seizure arises in the nervous elements one might expect the attack to begin shortly after the infliction of the wound when these elements are plentiful and undergoing progressive destruction. If, on the other hand, the vascular elements are responsible for the initiation of the process, epilepsy might well be expected to make its appearance later when the vascular plexus reaches its fullest development and nerve-fibres have largely vanished.

In the twelve cases reported, the time between the wound and the onset of convulsion varies between five months and fourteen years, the average period of immunity before the onset of attacks being five years and six months. The acute effect of the injury must have disappeared long before the end of the fifth year. There remains, however, one process progressive through all these years, and that is the cicatricial contraction which gradually draws one or both hemispheres toward the lesion.

We have shown that at operation the focal epileptic attacks may often be produced in two ways: either by electrical stimulation of the brain in the neighbourhood of the wound, or by gently pulling upon the adherent dura. This latter fact may be of considerable significance, for if increase of a pre-existing strain produces an attack it may well be that the pre-existing strain itself is an important factor in the ætiology of spontaneous convulsions.

As pointed out above, the blood-vessels form in one sense the woof of the contracting network. Traction, therefore, upon the vessels must be inevitable. The hypothesis at once suggests itself that a vaso-motor reflex secondary to this traction is responsible for the initiation of the convulsive seizures.

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