HISTOLOGIC STUDIES OF THE BRAIN
FOLLOWING HEAD TRAUMA

IV. LATE CHANGES: ATROPHIC SCLEROSIS OF
THE WHITE MATTER

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In three previous communications4-6 we have described our interpretation of the mechanism by which certain early traumatic lesions of the central nervous system are produced: cerebral edema, petechial and massive hemorrhages in the central areas of the brain, and infarction of several of the major cerebral arteries.

It is the purpose of the present paper to report our findings in a series of cases displaying late histologic changes in which were found smaller and larger areas of atrophic sclerosis of the white matter, and to discuss the pathogenesis of these lesions.

PRESENTATION OF CASES

Case 1. Short period of unconsciousness following a head injury. Development of sulfathiazole nephrosis with death at the end of 12 days. Autopsy showed the presence of nephrosis and, in the brain, multiple areas of softening.

History and Course. H. W., a 56-year-old colored male, was admitted to the hospital unconscious shortly after having been struck by a bus. The significant findings were a laceration over the left eye, a fractured mandible, and fracture of the sixth and seventh ribs. Save for loss of consciousness, which was regained shortly after admission, neurologic examination was negative. He was placed under observation and, because of the scalp wound and jaw fracture, sulfathiazole therapy was instituted. For nine days he improved, then there occurred elevation of temperature and an increase in the pulse and respiratory rates. It was thought possible that a subdural clot had developed but exploratory burr holes revealed none.

The next day red blood cells were found in the urine and sulfathiazole therapy was stopped. However, it soon became apparent that uremia was developing. The blood urea nitrogen concentration rose to 130 mg., and then to 200 mg. per 100 cc. of blood. Cystoscopic examination and ureteral drainage showed no sulfathiazole crystals, so that it was concluded that he was suffering from sulfathiazole nephrosis. He died 12 days after admission.

Neuropathic Findings. These, exclusive of those in the nervous system, were sulfathiazole nephrosis, acute cystitis, urethral strictures, and fracture of the left temporal bone, the left mandible, and the third and fourth ribs on the right.

Gross Anatomic Observations. The dorsal surface of the brain was flattened, and the leptomeninges were slightly thickened. The undersurface of the brain appeared normal. The blood vessels at the base were soft save for scattered areas of mild sclerosis. On coronal section there were found multiple scattered areas of petechial hemorrhage, chiefly in the white substance. No areas of massive hemorrhage or grossly visible softening were present.

Microscopic Observations. Blocks were taken from various areas of the cerebral cortex, from the basal ganglia, and the hypothalamus. There were found diffusely scattered small areas of softening and vascular alterations.

The areas of softening varied greatly in size and shape, and consisted of accumulations of compound granular cells. Some scavenger cells contained blood pigment. Occasionally larger
areas of softening were seen in which gitter cells and newly formed blood capillaries replaced the destroyed brain tissue. Some of the foci of softening were in the vicinity of blood vessels which disclosed definite signs of stasis and congestion (Fig. 1). The smaller veins and capillaries appeared distended and engorged with blood, and in some of the congested veins the walls were undergoing disorganization and necrosis. Some of them were surrounded by distended perivascular spaces filled out with large accumulations of red blood cells. Occasionally they contained small numbers of gitter cells. Congested veins were present throughout the entire hemisphere, especially in the white matter. Some were surrounded by perivascular hemorrhages, or by circumscribed areas of edema and rarefaction of the adjacent tissue.

Case 2. Head injury from blunt object. Previous injury 17 years earlier. Recent blow was at

![Fig. 1. Case 1. Small area of softening in which gitter cells and newly formed capillaries replaced the destroyed brain tissue. Note the tremendous distention and stasis of the smaller veins. Hematoxylin and eosin (x105).](image)

site of old decompression. Flaccid hemiplegia led to exploration for subdural clot; none found. Intracerebral clot later evacuated. Staphylococcus septicemia secondary to carbuncle. Death in 50 days. Extensive changes in the vicinity of the intracerebral clot.

History and Course. R. H., a 36-year-old colored male, was admitted to the hospital about two hours after being struck in the left parietal region with a blunt object. Seventeen years earlier he had sustained a head injury in the treatment of which a large parietal decompression was made.

On admission he was unconscious. In the old decompression area were found two superficial abrasions and a large subgaleal hematoma. There was a right-sided flaccid hemiplegia. Because of the hemiplegia, exploratory burr holes were made on the first hospital day in search of a possible subdural hematoma. None was found. On the third day ventriculograms gave evidence of a left frontal lobe hemorrhage. A small bone flap was reflected, and 35 cc. of blood were evacuated from the left frontal lobe. He improved gradually following this procedure,
but remained severely dysphasic. A carbuncle developed in the right shoulder and septicemia followed, from which he died on the 50th hospital day.

**Gross Anatomic Changes.** Figure 2 shows the general nature and extent of the destructive lesion in the left fronto-parietal region. There were large areas of tissue softening, surrounded by a thin margin of golden-brown discoloration. The area involved extended deep into the white matter and measured in its greatest diameter $5 \times 2$ cm. The leptomeninges over the area of destruction were thickened and stained yellowish-brown.

Transverse sections through the pons and cerebellum showed discrete areas of diffusely scattered diapedetic hemorrhages.

**Microscopic Observations.** Blocks were taken from the left fronto-parieto-temporal region and were stained with hematoxylin and eosin, and phosphotungstic acid. Frozen sections from

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Fig. 2. Case 2. Large areas of tissue destruction in the left fronto-parietal region, associated with intracerebral clot.
the same region were impregnated by the Hortega silver carbonate and the Cajal gold chloride methods.

Examination showed slight fibrous thickening of the parietal leptomeninges which contained numerous macrophages filled with blood pigment. The pial vessels were congested and surrounded by large masses of extravasated red blood cells. The principal alteration within the brain itself consisted in numerous areas of tissue destruction typical of far advanced softening. The greater part of the cortex appeared completely destroyed and replaced by large masses of gitter cells in a dense network of newly formed capillaries. It was of interest that in areas distant from the softening the vessels appeared congested and disclosed signs of stasis and prestasis. The perivascular spaces were distended and the adjacent tissue appeared rarefied and edematous. Many of the nerve cells were lost while others showed severe cell changes and ischemic degeneration.

Sections stained with phosphotungstic acid disclosed an increase in fibrous tissue outlining the greater portion of the area of softening. In addition there was a slight increase in glial fibers, more particularly toward the surface of the destroyed area. There was some increase in the subpial glial tissue. The blood vessels in the region adjacent to the area of softening showed an increase in adventitia. No definite sclerosis or thrombus formation was seen in any of the vessels. There was a striking increase in microglia throughout the areas adjacent to the softening (Fig. 3).

In sections prepared by Cajal's gold sublimate method, many hypertrophied astrocytes were seen in the outer border of tissue around the area of softening (Fig. 4). Here, in the area of tissue destruction, many of the astrocytes displayed clasmatoendothrosis. Obviously the bulk of these changes was the result of the 50-day-old injury, rather than that sustained 17 years earlier, though some of the glial hypertrophy may have been longstanding.


History and Course. J. B. was first admitted to the hospital in 1935 at the age of 49, an
indefinite period of time following an injury to his head. He was restless and somewhat stuporous. There was found an old non-infected healed scalp laceration. Neurological examination showed no localizing signs. The cerebrospinal fluid was grossly bloody and the pressure was reported as "increased." The blood and cerebrospinal fluid Wassermann reactions were negative, and the gold curve was reported as 0. On bed rest he improved rapidly and was discharged on the 13th day.

In 1937 he was readmitted because of left-sided convulsive seizures associated with transient post-convulsive left hemiparesis. The diagnosis of arteriosclerotic heart disease was made at this time. There followed a series of admissions because of recurrent seizures. Pneumoencephalograms in 1939 showed evidence of diffuse cerebral atrophy, far advanced in the right hemisphere. There was displacement of the third ventricle to the right, but a focal contracting lesion was not demonstrable. When placed on dilantin he showed temporary improvement, but on October 8, 1941, he was brought to the hospital because of rapidly repeated left-sided Jacksonian seizures. Death followed four days later.

Postmortem examination showed bronchitis, lobular pneumonia affecting both lower lobes, and arteriosclerosis of the aorta.

Gross Anatomic Observations. The right hemisphere was smaller throughout than the left. The undersurface of the right frontal lobe showed loss of substance and brownish discoloration.

The coronal sections are shown in Fig. 5. The loss of bulk in the right hemisphere and the compensatory dilatation of the right ventricle are evident.

Microscopic Observations. Blocks were taken from the right frontal region (upper, lower, mesial, and lateral surfaces), right centrum semi-ovale, right ventricular wall, and hypothala-
mus. They were stained with hematoxylin and eosin, and phosphotungstic acid, and by the Loyez and Bodian methods. Frozen sections were taken from the right frontal region and prepared by the Cajal gold sublimate and the Hortega silver carbonate methods.

In the dorso-lateral portion of the right frontal lobe were several abnormalities. The subarachnoid spaces were distended and showed moderate connective-tissue proliferation. The cortical ribbon was relatively well preserved, though small areas of glial scarring were evident.

The most striking changes were in the white matter, which disclosed throughout the sections an increase in astrocytic nuclei. In some regions the glia appeared as an extensive scar. These changes were especially prominent in the regions in which the parenchymatous cortical changes were slight or absent. It is of interest to note that the nervous tissue adjacent to some of the blood vessels disclosed a high degree of rarefaction amounting to perivascular cystic formation (Fig. 6). These zones often contained pigment-bearing macrophages.

Sections stained with phosphotungstic acid showed diffuse proliferation of glial fibrils throughout the white matter. The fibrils in the gray matter appeared fairly well preserved except in the molecular zone, where they were increased and some appeared thicker than normal.

In sections stained by the Loyez method, there was found diffuse loss of myelin in the white matter with sparing of the cortical ribbon. In some areas the "u" fibers as well as the fibers adjacent to the ventricular wall appeared relatively well preserved. Under higher magnification the myelin sheaths displayed various types of destruction: swelling, beading, and fragmentation.

Sections impregnated by the Bodian method disclosed a moderate degree of axis-cylinder

![Fig. 5. Case 3. Diffuse loss of bulk in the right hemisphere with dilatation of the right ventricle.](image_url)
damage in the form of bead-like swelling, slight tortuosity, and occasional fragmentation of the affected axones.

The dorso-mesial portion of the right frontal lobe disclosed findings in the gyrus cinguli similar to those described above. It is of interest to note that the adjacent areas in the corpus callosum and mesial portions of the frontal cortex were fairly well preserved, suggesting that any changes due to circulatory disturbance were not the result of disturbance in the supply of the anterior cerebral artery, but rather were of local character.

In summary the changes consisted of sclerotic atrophy of the entire right frontal lobe with compensatory dilatation of the right lateral ventricle. There was proliferation of fibril-

![Fig. 6. Case 3. Perivascular tissue rarefaction amounting to small cyst formation. Note the increased amount of glial nuclei throughout the white matter. Hematoxylin and eosin (X195).](image)

ary astrocytes throughout the centrum semi-ovale of the right frontal lobe, associated with a diffuse demyelination and mild degenerative changes of the axis cylinders. The cortical ribbon escaped significant change except in the basilar gyri where presumably it was subjected to direct contusion and laceration.

Case 4. **Severe head injury followed by a three weeks' period of unconsciousness.** Development of signs of dysphasia led to evacuation of a subdural hematoma. Lung abscess developed. Death occurred three years later. Brain showed extensive old damage of the left hemisphere.

**History and Course.** P. L., a 54-year-old colored male, had enjoyed apparently excellent health until about September 1, 1939, when he was struck by a bus, rendered unconscious, and taken to another hospital. There he lay unconscious for three weeks. Roentgenograms showed an occipito-temporal fracture on the right, running into the basilar region. At the end of the second week, lumbar puncture was done. It was reported that there was no blood in the cerebrospinal fluid. The cerebrospinal fluid Wassermann was positive, and a paretic gold curve was found. Further data were not obtained. By the end of the fifth week he had improved somewhat, but was thought to be psychotic. Therefore he was transferred to the
Psychiatric Service of the Cincinnati General Hospital, where he was admitted on October 5, 1939 with the diagnosis of general paresis.

It was soon appreciated that he was not demented but dysphasic; and a lung abscess was found.

It was thought that post-traumatic cerebral atrophy was a more likely diagnosis than subdural hematoma, but in view of the localizing sign of dysphasia, a left-sided burr opening was made and “a moderate amount of thin, slightly yellowish, discolored fluid under moderate pressure” was evacuated. The brain was depressed about one-quarter of an inch from the calvarium. Similar findings were made on the right side. He improved very little following the evacuation of the hematomata; his pulmonary condition became more severe and he was bronchoscoped without benefit. Because of his mental status (due in large part, no doubt, to his dysphasia), arrangements were made for his commitment to the State Psychiatric Hospital. At this time lumbar puncture revealed an initial pressure of 0 (sic), the total protein was 22 mg. per cent, the cerebrospinal fluid Wassermann and gold curve reactions were negative. Shortly before his discharge, he had a number of ill-defined convulsive seizures, and was placed on dilantin.

Death occurred about three years following his discharge from the General Hospital and about three years and four months following his injury. An interim history is not available, nor have we information concerning the general findings at autopsy.

**Gross Anatomic Changes.** The undersurfaces of both leaves of the dural cap showed traces of the old hematoma membrane. There was extensive atrophy of the left hemisphere, particularly in the peri-Sylvian region where a strip of destruction, 3 cm. wide and 5.5 cm. in length, extended along the course of the Sylvian vessels. The vessels at the base of the brain were thin-walled and the configuration of the circle of Willis was normal.

The brain stem and cerebellum revealed no gross abnormalities.

**Microscopic Observations.** Blocks were taken from various areas of the left hemisphere. There were large areas of old cystic softening involving chiefly the gray matter. These probably were the result of local damage, though since knowledge of the mechanism of the injury and early clinical data are lacking, this cannot be maintained with complete assurance.

The change of particular interest, however, was the diffuse sclerosis of white matter similar to that described in Case 3. The entire centrum semi-ovale showed a diffuse increase in astrocytic nuclei. In some areas, well beyond the obvious gross changes, the glia appeared as an extensive scar. Dense fibrillary glia was present throughout the white matter adjacent to the lateral ventricle. It should be emphasized that these glial changes were seen in regions where the cortical ribbon did not appear severely damaged.

Case 5. **No history. Death twelve days after admission to hospital. Autopsy showed signs of old post-traumatic cerebral damage.**

**History and Course.** T. B., a 63-year-old white man, was picked up intoxicated and unconscious by the police. No history could be obtained. The positive physical findings were: blood pressure 180/110, flaccidity of the left side including the face, hyperactive tendon reflexes on the left, positive Hoffmann and Babinski responses bilaterally, and evidence of early cardiac failure.

He was digitalized and given general supportive treatment and sulfathiazole. He gradually regained consciousness, but remained aphasic. During the twelve days of his hospital stay, his blood urea nitrogen level rose from 19 to 242 mg. per 100 cc., and his clinical course paralleled the rise in the blood urea nitrogen. The sulfathiazole level was 15.9 mg. per 100 cc. for four days before his death. The urine on one occasion showed a few sulfathiazole crystals, but never any red blood cells. He expired on the twelfth hospital day.

It was thought at the time of his death that he had suffered massive cerebral hemorrhage on the right (having had a probable old hemorrhage on the left), and that he had hypertensive cardiovascular disease. The question of kidney damage from sulfathiazole was raised.

The present interest centers chiefly about the fact that the autopsy findings indicated an old head injury, a history of which was not elicited.

**Gross Anatomic Changes.** The ventral surface of the brain showed several changes of
interest. In the region of the left Sylvian fissure there was extensive superficial loss of tissue with thickening of the leptomeninges and a golden-brownish discoloration. This discoloration extended across the Sylvian fissure and involved the anterior portion of the second temporal gyrus. The undersurface of the frontal lobe near the midline also showed a golden-brown discoloration and there was a small area of destruction in the right frontal lobe just beneath the olfactory bulb.
Horizontal sections through the hemispheres demonstrated diffuse loss of substance in the left frontal and parietal lobes (Fig. 7). In addition there was a recent softening in the distribution of the right middle cerebral artery extending downward throughout the island of Reil and across the external capsule to involve a small portion of the lateral extent of the putamen.

Microscopic Observations. Blocks taken from the left frontal lobe revealed the leptomeninges to be slightly thickened, but otherwise not remarkable. The cortical ribbon was generally well preserved, except for small circumscribed areas of old destruction. The striking findings were to be seen in the white matter, and consisted of a diffuse proliferation of glial nuclei and fibrils producing a widespread gliosis. In some areas both progressive and regressive glial changes were present, though the former usually predominated. There were dense bands of glial tissue in areas subjacent to the superficial tissue destruction. Regressive glial changes were limited to relatively small areas of the white matter. Oligodendroglial cells occasionally showed acute swelling. The microglia did not appear altered.


Course and History. O. H., a 60-year-old colored male, was readmitted to the hospital because of convulsions. Three years previously he had fallen and struck his head on a sidewalk. Three days following the accident, because of the presence of dysphasia, exploratory trepanation was performed and a left-sided subdural hematoma was evacuated through a subtemporal opening. The cavity left was of about 30 cc. capacity. The underlying brain was "somewhat reddish in color." Following his discharge a month later he was not seen again until the second admission.

Four days prior to readmission he had had a generalized convulsive seizure without apparent precipitating cause. The attacks recurred frequently, several times an hour on one day. Nevertheless, the day before readmission he was up and about, talking rationally and displaying no weakness. That night he had some thirty seizures, remaining unconscious between them. The attacks were said to be generalized, but there was more movement on the right.

He gradually improved and regained consciousness, though he remained mildly disoriented. An occasional convulsive movement was noted in the right hand. Then rather suddenly he developed signs of pulmonary edema, became comatose, and had several convulsive seizures. On the third hospital day sulfathiazole therapy was instituted, and by the seventh day the level had risen to 17 mg. per 100 cc. of blood despite attention to fluid. The blood urea nitrogen rose to 77 mg. per 100 cc. of blood. The urine remained clear save for the appearance of albumin. On the 10th hospital day he died.

Gross Anatomic Changes. The superior surface of the left frontal pole showed massive discoloration and disorganization extending back practically to the Rolandic fissure. The leptomeninges and underlying brain were stained a deep orange-brown, and the meninges were thickened, tough, and firmly attached to the brain. The undersurface of the left frontal and temporal lobes showed similar changes.

The brain was sectioned horizontally. The white matter of the left frontal lobe was shrunkened and destroyed, and the overlying cortex was much depleted (Fig. 8). The anterior horn of the left lateral ventricle was correspondingly enlarged. There was diffuse gliosis at the junction of the gray and white matter. The right frontal lobe showed similar changes. The rest of the hemispheres appeared normal. The vessels making up the circle of Willis appeared normal in structure and distribution.

Microscopic Findings. Blocks were taken from various areas of the left frontal lobes. They revealed cystic softening of the cortical ribbon, seemingly the result of direct contusion and laceration. There were diffuse changes in the white matter, evidenced by proliferation and hypertrophy of the glial elements, particularly the fibrillary and protoplasmic astrocytes. The latter showed definite hypertrophy. The tissue generally appeared somewhat rarefied. No vascular or inflammatory lesions were found.

History and Course. J. H., a 62-year-old white male, was admitted to the hospital on November 22, 1940 in coma. A later history revealed that his past health had been excellent. He had been a heavy drinker for 25 to 30 years and had been on a spree shortly before admission. He was not able to account for the hours immediately antecedent to his arrival in the hospital.

Examination on admission showed a semi-comatose individual with a slightly dilated left pupil, bilateral optic atrophy, left facial paresis, and a left Hoffmann sign. Shortly thereafter a number of convulsive seizures were witnessed. These seemed to be generalized. Lumbar puncture revealed an initial pressure of 130 mm. of water. There were two white blood cells and eleven red blood cells per c.mm. Total protein content was 70 mg. per 100 cc. The Wassermann reaction of the blood was negative, as were also the cerebrospinal fluid Wassermann and gold curve reactions. Blood urea nitrogen was 18 mg. per 100 cc. Roentgenograms of the skull showed a large linear skull fracture in the right parietal region. This was the only frank sign of trauma obtained.

The convulsions ceased shortly after admission. His level of consciousness improved and after two weeks' hospital stay he was discharged with the diagnosis of chronic alcoholism associated with mental deterioration and convulsive seizures.

On March 14, 1941 he was readmitted in shock and died two hours thereafter. The diagnosis made at the autopsy table included duodenal ulcer with massive hemorrhage, generalized vascular sclerosis, and recent skull fracture of the right temporo-parietal region with focal extradural hemorrhage and evidence of old extensive brain injury.
**Gross Anatomic Changes.** In the right posterior parietal region there was a thin intradural clot, 3 cm. in width and 8 cm. in length.

The brain itself showed old brown staining over the dorsal surfaces of the frontal poles, and at the tip of the left frontal pole an old area of contusion, measuring 1.5 cm. in diameter. In the very tip of the right frontal pole was a similar change. The lateral surface of the temporal lobes likewise showed old brownish staining and some destruction of the underlying gyri. Similar brownish discoloration was found on the undersurface of the frontal and cerebellar lobes.

**Microscopic Findings.** Blocks from the right temporal lobe were studied. The leptomeninges showed patchy areas of fibrosis, containing fibroblasts, endothelial cells, and pigment containing macrophages. The cortex presented a few small areas of circumscribed tissue destruction. In addition there was found a more general patchy loss of nerve cells, particularly in layers 3 and 5, and here there were evident satellitosis and neuronophagia. Many shrunken and faded cells were seen in these areas.

The most striking changes, however, were found in the subcortical white matter. These consisted of a diffuse increase in glial cells and fibrils, similar to that described in the foregoing cases, resulting in extensive areas of fibrous gliosis.

**COMMENT**

We have been concerned in the present paper with the late atrophic changes that follow brain injuries. The case reports presented have been included chiefly to attest to the validity of the trauma. A number of authors have described the focal changes associated with cerebral cicatrix, notably Foerster and Penfield,9 and Penfield.10,11 Their concern has been with local changes, ours has been with the explanation of the diffuse cerebral atrophy evidenced, for example, by pneumoencephalograms made at various stages following the receipt of trauma.

In earlier papers we have discussed the acute changes following brain injury, emphasizing particularly the vascular alterations which we believe to be so largely responsible for both acute and chronic alterations in structure. Thus we have postulated and brought evidence to support the thesis that the earliest changes following injury consist in the escape of intravascular fluid through the paretic vessel walls with the production of edema. When the vasoparesis is of a severer grade there may occur escape of erythrocytes (and leukocytes) giving rise to perivascular hemorrhages. Both of these conditions cause an increase in fluid content of the affected cerebral tissue and if the process be limited chiefly to one hemisphere, shift of the ventricular system toward the opposite side will result during the acute stage.

Particular emphasis should be laid upon the fact that it is within the deeper structures of the cerebral white matter that these vasoparetic phenomena are believed to take place. And a sharp distinction must be made between the vascular alterations occurring in the deeper portions of the brain and those that are obviously the result of direct contusion and laceration of cerebral tissue at the surface.

It is evident that in instances of acute change, there must occur varying degrees of interference with transfer over the blood brain barrier. We have for facility of reasoning argued in terms of oxygen and carbon-dioxide trans-
port. Actually the problem is no doubt more complex and is related to fundamental cellular metabolism.

The late changes of such disturbed metabolism result, we believe, in the loss of neuronal elements, the severity of which is directly related to the degree of hypoxia (or a more profound metabolic alteration) resulting from the injury. On the other hand, astrocytes, unlike the nerve cells, hypertrophy in response to lesser degrees of oxygen want and disappear only as the oxygen want becomes severe. 2 Hence, in the later stages, as exemplified in the cases here presented, there is extensive neuronal loss, but as an index of the diffuse vascular alteration there occurs a diffuse gliosis which appears to be most severe in that area least well fortified to withstand vascular insults, the white matter. This portion of the brain has numerically fewer vessels and physiologically lesser capacity for the establishment of collateral channels.*

As demonstrated in these cases, direct contusion and laceration of the gray matter may be associated with profound changes in the cortical ribbon. Presumably in these instances the cortical circulation has been grossly and extensively disorganized, but in these same instances there are to be found diffuse glial changes throughout much of the adjacent white matter.

We have discussed in detail in earlier papers the nature and pathogenesis of these diffuse alterations in the white matter. By way of recapitulation their hypothetic basis may be described as follows. As the result of injury to the brain, noxious stimuli are transmitted to the vessels of the white matter. These stimuli appear to cause either direct relaxation of the muscular coat of the smaller vessels, or to result in the propagation of vasoparetic stimuli over the neurovascular network to the deeper vessels. It may be, as suggested by Ferris, 8 that the difference between the viscosity of the fluid blood and the fluid matrix of the nervous parenchyma facilitates the production of vasoparesis.

We postulated that the stasis so regularly seen in our cases in the smaller peripheral subdivisions of the vascular tree was the result of vasoparesis, and that the stasis with its associated accumulation of carbon dioxide led to further dilatation, to greater stasis, and eventually to the development of edema. Should the stasis become more severe, actual necrosis and softening of the parenchyma might occur. Should, on the other hand, the inadequacy of blood supply be less severe, and should it be present for a relatively long period of time, the development of atrophic sclerosis of the white matter, as

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* The relatively greater susceptibility of the white matter to lesions caused by circulatory disturbances is a point worthy of additional comment. It has been noted by Bodechtel 1 in two cases of chronic cardiac decompensation, and by Ferraro 2 using as an experimental asphyxial poison sub-lethal doses of cyanide. Both observers found the gray matter essentially normal. Similar findings were observed by one of us (I.M.S.) in the brain of a patient who died of carbon monoxide poisoning, and also in the brain of a child, which showed diffuse sclerosis of the white matter, apparently due to vascular disturbances. A more detailed description of this interesting discrepancy between the reaction of gray and of white matter to circulatory disturbance will be described in detail elsewhere.
described in the cases embodied in this report, might reasonably be expected to occur.

That alterations occur in the gray matter is not to be denied. We believe, however, that the more severe forms of gray-matter disturbance occur as the result of direct contusion, or as the result of grave disturbance in the circulation of major arterial trunks.⁶

We have attempted to correlate our observations with the pneumoencephalograms of patients who have suffered head injury. In our experience in civilian practice diffuse enlargement of the ventricles is a more common finding than focal dilatation of a part of the ventricular system, which we believe correlates well with the more usual gross and histologic changes. In military practice, however, the occurrence of focal lesions is much more frequent, and it was chiefly upon a study of such material that Foerster and Penfield drew their conclusions concerning the wandering of the ventricles toward the site of local injury. They postulated that the shift occurred as the result of contraction of the local cicatrix. That this need not always be the explanation is indicated by the fact that one of us (JPE) has seen appreciable ventricular shift in an experimental animal as early as three weeks following the production of an extensive cerebral wound, before there was time for the development of cicatrization. It would seem that as atrophy of one hemisphere occurs in asymmetrical lesions, there is a tendency for the normal ventricle to shift toward the affected side, helping to fill the vacated space, and resulting in a less great compensatory dilatation of the ipsilateral ventricle than would otherwise occur. Because of the rigid falx of the adult the shifting of the more normal hemisphere is never so great as in the case of an infant, whose falx is relatively mobile up to the age of about one year.

Dyke⁵ likewise believed that local dilatation of a ventricle and shift of the intracranial contents occur in an effort to compensate for loss of brain bulk.

SUMMARY

The pathologic alterations in the brains of seven patients surviving head injuries for variable periods of time up to seventeen years have been analyzed.

We have been concerned not with the focal changes associated with cerebral cicatrix but rather with seeking an explanation of diffuse cerebral atrophy noted following many forms of head injury.

Attention is called to the evidence of stasis in the smaller blood vessels, and the associated edema and perivascular hemorrhages, notably in the white matter. We believe that as a result of these circulatory alterations hypoxia develops. In the cases described the circulatory disturbances have been relatively longer lived and as a result diffuse gliosis of the white matter has developed, since the characteristic reaction of glia to sustained oxygen want of moderate degree is gliosis. That some loss of neuronal elements occurs is true, but the changes are relatively greater in the white matter which is less well equipped to withstand vascular insults.
The resultant pneumoencephalographic changes are discussed and an explanation sought for them. Diffuse atrophy is thought to be a more significant factor than focal cicatrix in the production of ventricular wandering.

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