A STUDY OF

CEREBRAL CICATRIX

A STUDY OF CEREBRAL CICATRIX

by

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1 9 3 7

From the Department of Neurology and Neurosurgery.

ἐγκέφαλον δὲ τρωθέντα
εἴδομεν ἰαθέντα

" But I have seen a severely
wounded brain healed "

(from Galen's commentaries on
the Aphorisms of Hippocrates)

The ceiling of the entrance hall.
Montreal Neurological Institute.


ΤΑ·ΕΓΚΕΦΑΛΟΝ·ΔΕ·ΤΡΩΘΕΝΤΑ·ΕΙΔΟΜΕΝ·ΙΑΘΕΝΤΑ

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PREFACE

Among the regulations concerning theses intended for presentation to the Graduate School Faculty of McGill University is the following: ".....Scientific theses should also contain an introductory historical statement of previous work or investigation,....." and, ".....There should be a clear statement of the claim of original work or contribution to knowledge made by the author".

Within recent years there has developed an increasing tendency in pathology to interpret lesions in terms of the mechanism of their production, so that somewhat less emphasis is now laid on purely descriptive morbid histology. The present study reflects this tendency. We have attempted to show that the diverse, late, histological lesions found in the brain after apparently unrelated insults - vascular occlusion, intracerebral hemorrhage, and cerebral contusion and laceration - should not be looked upon as unrelated lesions, but as expressions of varying degrees of the same functional disturbance - an interference with normal cerebral circulation. This approach is, so far as we are aware, new to the American literature on cerebral pathology; though somewhat of the same method of handling has been employed by Friedrich Hiller in the German literature.

The tendency in the past to discuss the above conditions individually has made it impractical to present a review of the literature as an introductory historical statement, and the literature bearing on each phase of the work is

treated as an integral part of each chapter. Because of the very broad scope of the subject it has been impossible to review the work of all previous investigators on each phase of the problem. The bibliography appended to the thesis is however, so far as we are aware, representative of the best work that has been done.

The portion of this thesis which can make chief "claim of original work or contribution to knowledge made by the author", is the chapter dealing with cerebral arterial occlusion, for, as far as we know, the experimental work, both in its technical details and in its results, is new. Furthermore, the clinical application of the findings is, we believe,of considerable significance for it separates an important group of cases from the general group of "birth injury", and serves to emphasize one of the possible grave consequences for the infant of prolonged asphyxia during birth. The as yet undetermined frequency of incidence of epilepsy in these cases is a matter for further study. But even here the "claim of original work" is not wholly individual for the author owes much to his two collaborators on this phase of the problem, Doctor Donald McEachern and Doctor J. Norman Petersen.

As far as we know, no one has before described the late histological changes which follow the injection of blood into the cerebral hemisphere. Our own observations are then perhaps unique - and serve to show the essential similarity between such lesions and the changes which Cajal found surrounding massive hemorrhage following cerebral laceration.

In the final chapter appear certain results of clinical significance, to which little claim for originality can be made: demonstration of the mechanism underlying the shifting of the ventricular system sometimes seen in atrophy, the arguments relating to the effect of cicatricial pull versus shifting due to atrophy, etc. Finally, the insistence on preservation of vascular supply in carrying out the procedure of cerebral scar excision, while not a new idea, has its rationale given in a more detailed and logical fashion than heretofore.

However, these are all considerations of very minor moment. When an author reviews his notes on the literature after completing his own work, he cannot but be impressed with the fact that many ideas have unconsciously slipped from the literature into his own thoughts, to reappear in his argument as original conceptions. This is even more true of ideas acquired during association with others - which makes proper acknowledgement of the help gained from many sources particularly difficult. The author is sure that much of what follows represents accretions gained in particular from two individuals with whom he has long been associated, Professor Wilder Penfield and Associate Professor William Cone.

Doctor Penfield's interest in the problems of epilepsy lay behind the suggestion that this work be undertaken, and it is because of his provision of facilities and his constant encouragement that completion of this work had been possible. Doctor Cone, as director of the laboratory of neuropathology,

has given invaluable help. To them both the author gives sincere thanks.

Other members of the staff have also aided notably, Doctor Petersen, Doctor McEachern, and Doctor Arthur E. Childe, roentgenologist to the Institute. Miss Catherine Dart, R.N., has rendered invaluable help in assisting at all the operative procedures and in supervising the care of the animals. The photographs are the work of H.S. Hayden, F.R.P.S. Likewise, help has been given generously by the secretarial and technical staff of the Institute. All of this help the author gratefully recognizes.

I. INTRODUCTION.

The purpose of this study is to review and to correlate the factors involved in the scarring of cerebral tissue. Such a review of cerebral cicatrix in its manifold forms and causations should help in an understanding of the histological processes involved. Furthermore, careful analysis and the application of experimental methods should help to differentiate and to identify the late changes which follow cerebral insults of one form or another. Finally, a clearer understanding of the mechanism of production of the various end results of cerebral insults may guide the way to improvement in therapeutic measures, both medical and surgical.

The work included in this report has been carried on over a period of five years. At the outset the attack was made upon the isolated problem of post-traumatic cerebral cicatrix and an effort was made to determine what factors governed healing, so that one might employ methods of scar excision which would permit of the surgeon leaving less scar than the one which he was removing in the effort to cure the patient of his post-traumatic epilepsy.

The first step in broadening the scope of the investigation came on the finding in the brain of a monkey at autopsy, of a particularly benign-looking area of cerebral destruction - with none of the characteristics of post-traumatic cicatrix. This area of destructiom obviously resulted from an accidental interruption of branches of the middle cerebral artery at

operation nine months earlier. This chance finding suggested that here might lie the answer to cerebral scarring - that if tissue were rendered completely anemic (as was then thought) by interruption of its blood supply, all tissue elements, including those capable of proliferating scar tissue, would undergo necrosis in the involved zone, and that if the interruption of blood supply were only partial, nerve elements might die but tissues with scar potentialities might proliferate abundantly and form cerebral cicatrix - with the meninges implicated or not depending on whether they were or were not involved in the original insult.

To test this hypothesis the middle cerebral artery of the monkey has been clipped at various points. In general - as will be detailed later - the results have been confirmatory of the hypothesis (work done in collaboration with Dr. Donald McEachern). Then a group of three clinical cases was studied and the lesions compared with experimentally produced ones (in collaboration with Dr. J. Norman Petersen) and from this work further deductions concerning vascular occlusion, with particular reference to slow occlusion of vessels, were made.

The next step in the development of the general outline was suggested by the finding, on histological study, of a similarity of some of the lesions produced by experimental arterial occlusion, to those produced by experimental stripping of the arachnoid with resultant local interruption of blood supply, and also to lesions found in certain cases of cerebral contusion. It seemed possible that all of these

lesions might be correlated on a vascular basis and that the late histological changes in cases of cerebral contusion might be regarded as resulting from disturbances in blood flow-- 1) as the result of mechanical interference with circulation because of "brain swelling", or 2) because of rupture of vessels, or 3) because of functional vascular disturbances occurring locally, or 4) because of a combination of these factors. This argument will be elucidated further in the proper chapter.

Similarly, a consideration of the literature on cerebral hemorrhage - with its present-day insistence on the importance of functional vascular disturbance - suggested that an attempt to produce late results of "experimental hemorrhage" might be of value in interpreting the late changes of cerebral hemorrhage, and might cast further light on the process of cicatrization. Accordingly a number of animals have had intracerebral injection of whole blood made. In the past such experiments, as far as we are aware, have not been followed beyond the three week stage. The resultant histological picture will be described later.

Finally, then, we were brought back to the starting point, that of meningocerebral cicatrix, but equipped, as a result of the study, with a better understanding of the morbid physiological processes involved and, hence it is hoped, with a more understanding approach to the medical and surgical principles essential to intelligent application of therapeutic measures.

In an effort to simplify and clarify the problem a deliberate exclusion has been made of developmental anomalies, and of infectious and degenerative conditions (including arteriosclerosis). Such omissions are obviously open to grave criticism but they are believed warranted, if only because of the magnitude of the problem as already delineated, and there is much evidence to suggest that the principles developed in the course of the following argument may justly be applied as a partial solution at least of the cerebral scarring occurring in infections and degenerative conditions.

An even more important omission, perhaps, is a consideration of the role played by venous obstruction in cerebral cicatrix. This has not been touched on by us experimentally and will, therefore, not be included in this presentation. Fortunately Putnam and his co-workers are at present actively engaged in an experimental approach to this problem and in general it may be said that the characteristics of their lesions are such as not to lead to ready confusion with those described in the pages that follow. (vide Putnam, 1935).

II. THE CEREBRAL CIRCULATION AND ITS ALTERATIONS IN CERTAIN PATHOLOGICAL STATES.

The investigations of Pfeifer (1928) and particularly of Cobb (1931) and his school have necessitated a complete revision of the old conceptions of cerebral circulation. From a purely anatomical point of view Pfeiffer has conclusively shown that the arteries within the brain substance are not end arteries as was argued by Conheim from pathological material. Pfeiffer's views have been abundantly corroborated by Cobb and Talbott (1927) so that Cobb (1936) has made the statement, "the capillary bed of the whole cortex is an endless network, in which a red cell might start in the olfactory bulb and travel to the occipital lobe".

The presence of extensive anastomoses among the vessels making up the pial-arachnoidal circulation was affirmed by Heubner in 1872 and since that time has been denied and reaffirmed by various authors. Testut (1929) and Poirier and Charpy (1921) record the anatomical work from which have been drawn these discordant conclusions. But the presence of pial-arachnoidal anastomoses is now generally accepted as an anatomical fact. With the knowledge of these two extensive anastomotic networks, meningeal and cerebral, a reinterpretation of the pathological changes resulting from vascular disturbances becomes desirable. In reviewing the matter it is imperative to bear in mind that the efficiency of the collateral channels established after the occlusion of a main arterial trunk may not be so great as that of the

original pathway so that, as pointed out by Ley (1932), there exists a certain autonomy in the distribution of the major vessels. Thus, for example, if the middle cerebral artery is occluded a degree of collateral circulation becomes established in the more peripheral area of supply of the middle cerebral artery, the collateral circulation being dependent upon the circulation in the unobstructed anterior and posterior cerebral arteries. The degree of collateral circulation established must depend on the relative amount of available minute flow of blood that can be delivered through the capillary anastomotic network between the obstructed and the unobstructed arterial beds, as compared with the available minute flow delivered under normal conditions.

If the cross-sectional diameter of all the vessels making up the anastomotic pathways is less than that of the usual vessel of supply the minute volume of blood delivered will obviously be less than normal. Other factors, such as the resistance of the vessel walls, capillary permeability, vasomotor control, etc., enter into the problem and make it one of extreme complexity.

An experimental approach to the problem has been made by Evans and Petersen (1937) and Evans and McEachern (1937) who have studied the pial-arachnoidal circulation following the placing of a clip upon the middle cerebral artery of the monkey. Following the clipping there can be observed in the distribution of the clipped vessel pallor of the brain, loss of arterial pulsation, diminution in venous pressure, and diminution in rate of blood flow in the vessels which are

Fig. I.

Brain injected with bismuth solution shortly after the placing of three clips on branches of the middle cerebral artery. Two of the clips can be seen. The third is hidden under the extravasated bismuth near the origin of the right middle cerebral artery. Note that bismuth has extended , via collateral channels, to the distal side of the clip in all three instances.

Fig. 1.

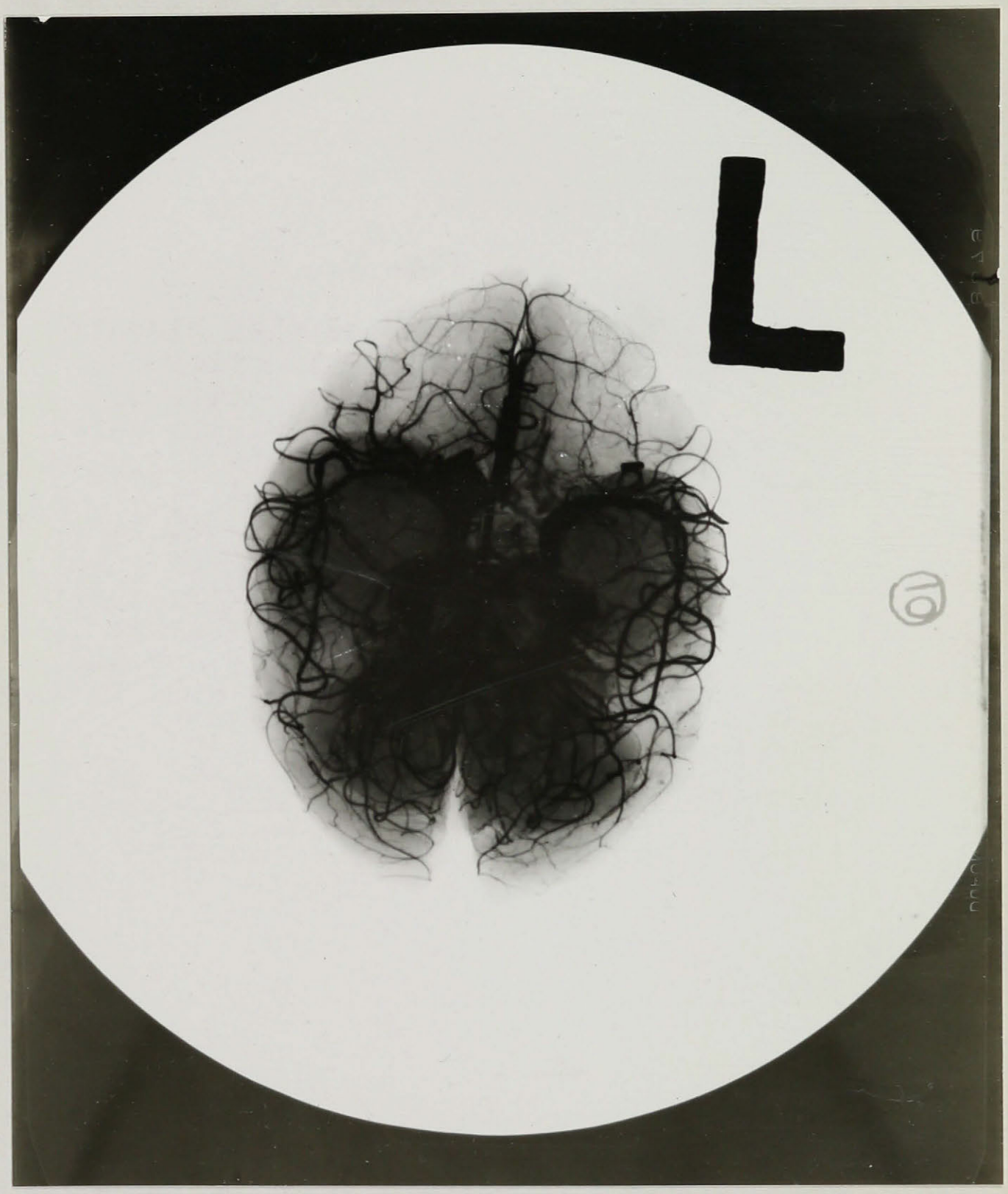
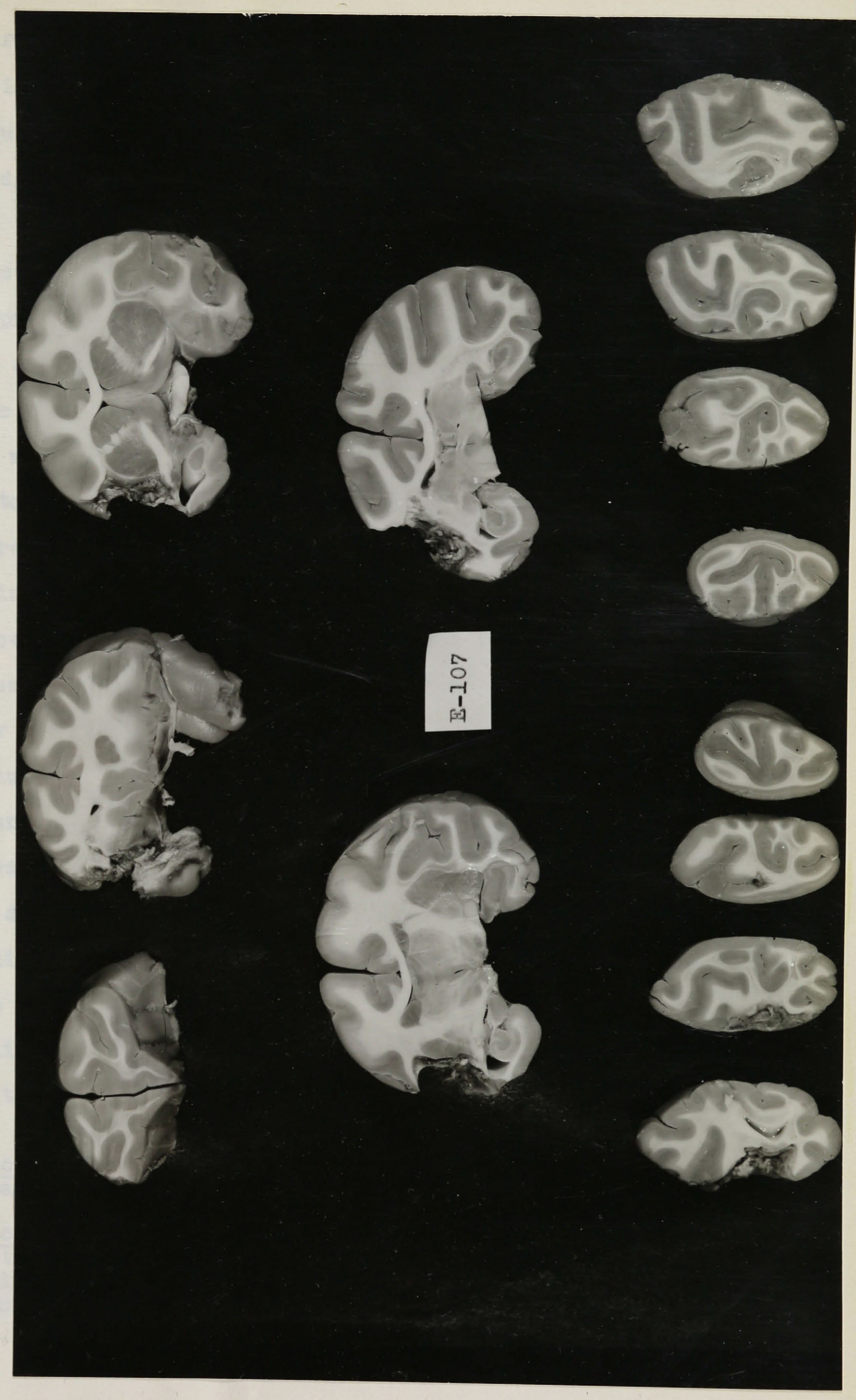


Fig. 2.

Extensive cerebral destruction found 118 days after occlusion of the right middle cerebral artery. Monkey

Fig. 2.



observed microscopically. X-rays of post-mortem injections of bismuth into the brains of these animals show that the opaque material finds its way through collateral channels to the distal side of the clip (Fig.1).

Were it possible to observe the cerebral vessels directly there would with certainty be found comparable changes, for preliminary observations made with blood flow thermocouples have shown a decreased rate of blood flow, and in most instances there has been observed on post-mortem examination of the brain many weeks later, extensive cerebral destruction (Fig.2) similar to that noted clinically by Foix and his pupils.*
The reservation "in most instances" should be noted carefully for in the brain of one monkey whose middle cerebral artery had been completely occluded there was found no gross anatomical defect. In other words, there exist circumstances under which collateral circulation can be very effective. Inasmuch as there was no evident anatomical variation to account for this finding there probably exist certain physiological conditions which determine the establishment of a high degree of collateral circulation.** It is of interest in this connection that Ley (1932) has seen rare clinical cases in which obliteration of the artery of supply by embolism or by thrombosis has occurred without softening resulting and without there being found an arterial anomaly

* Footnote No. 1: For a complete bibliography of the work of Foix and his school see Ley (1932).

** Footnote No. 2: We have sought in conjunction with this study to determine some of the factors which may improve collateral circulation. These findings will be presented in a separate communication by Dr. Donald McEachern.

to account for the lack of softening. His cases three and four are examples and he cites other instances from the literature.

The subject of vasomotor control of the cerebral vessels is naturally of great importance in considering the present problem. The physiological investigations of Cobb and his school* have shown that there are three influences affecting the caliber of the arterial vessels: vasomotor, chemical, and systemic. Of these, the last two are the most important, as far as normal physiology is concerned. Of the two vasomotor functions, constrictor and dilatator, Wolff (1936) says the following: "The constrictor vasomotor apparatus of the brain probably acts primarily to keep the cerebral vessels in the proper state of constriction and to aid them in regaining their normal caliber after vasodilatation. Also, the vasoconstrictor apparatus acts as a fine adjuster, regulating blood flow within the head more precisely than the powerful hydrostatic and chemical forces. This function of fine adjustment, rather than obliterative constriction, would appear to be the chief purpose of cerebral vasoconstriction. Apparently the prime function of neurogenic cerebral vasodilation is that of compensation, reducing the peripheral resistance of the cerebral vascular tree during periods of depressor reflex action".

Forbes, Finley and Nason (1933) have emphasized that the relatively unimportant vasoconstrictor activity observed in the cerebral vessels (usually not causing more than

* Footnote: A detailed bibliography on the cerebral circulation may be found in the review by Wolff (1936).

a ten per cent decrease in the caliber of the vessels studied) could, conceivably, under pathological conditions, become hyperactive. They further point out that under their experimental conditions vasoconstrictor activity is probably somewhat reduced (chiefly by the anesthetic) and furthermore, that there must be borne in mind the high metabolic rate of brain tissue. "Especially in such active tissues as the cortex, any reduction in blood flow, such as that accompanying even a mild constriction of the cerebral arterioles, is of far greater importance than a similar reduction in a tissue of low metabolism (e.g., the skin). Even though the blood supply to the nerve cells is abundant and the flow more rapid than elsewhere, a sudden reduction in oxygen content or in rate of flow results immediately in symptoms of oxygen lack".

Experimentally Florey (1925) has produced marked vascular constriction in the pial vessels by means of mechanical, chemical and thermal stimuli applied directly through the pia-arachnoid.

What evidence is there of extreme vasoconstrictor activity under pathological conditions? Hiller (1936) has covered this question in great detail in his chapter in Bumke and Foerster's Handbuch and it is hardly necessary to review here all the evidence. Firm support for the conception of a functional vascular change as being responsible for organic change was provided by the work of Spielmeyer (1930) on the late changes found in the Ammon's horn of epileptics. But more impressive are two carefully controlled observations

reported by Penfield, the first (1933) dealing with a series of cases, the second (1934) with a single case. In the first of these papers Penfield reports the vascular changes observed by direct vision to occur in twenty-six out of forty-three cases of epilepsy whose cortex was stimulated electrically at operation. In thirteen cases no response to stimulation was obtained and in these there were no arterial constrictions, areas of anemia, flushing, or other evidence of vasomotor disturbance. In twenty-six of the thirty remaining cases there was evidence of vasomotor disturbance and in six of these there was a constriction of one or more pial arteries, which constriction interrupted blood flow entirely. Such constrictions have been observed to persist for fifteen to thirty minutes, disappearing gradually. These extreme ("bologna-like") constrictions are a clean-cut phenomenon which offer no room for misinterpretation.

In the second paper Penfield called attention to the possible significance of such spasms, describing progressive degeneration of an occipital pole in an epileptic patient who, with succeeding attacks, suffered a progressive loss of vision in the homonomous half fields and who at operation was found to have an extensive degeneration of the occipital lobe.*

* Footnote: Penfield's interpretation of the degeneration as being due to anemia consequent upon recurrent vasospasm has been questioned on the ground that organic disease of the posterior cerebral artery was not excluded. This would seem a valid objection and in an attempt to answer it we have reviewed the microscopic preparations of the amputated occipital lobe. There is present in the vessels an extensive vascular reaction, many of the arteries and capillaries being obliterated. This evidence does not, however, exclude Penfield's interpretation from consideration, for the organic vascular changes could be secondary to functional disturbance in the circulation.

Fig. 3.

Diagrammatic representation of Ricker's theory of vaso-paresis. (Bauman, 1931).

Fig. 3.

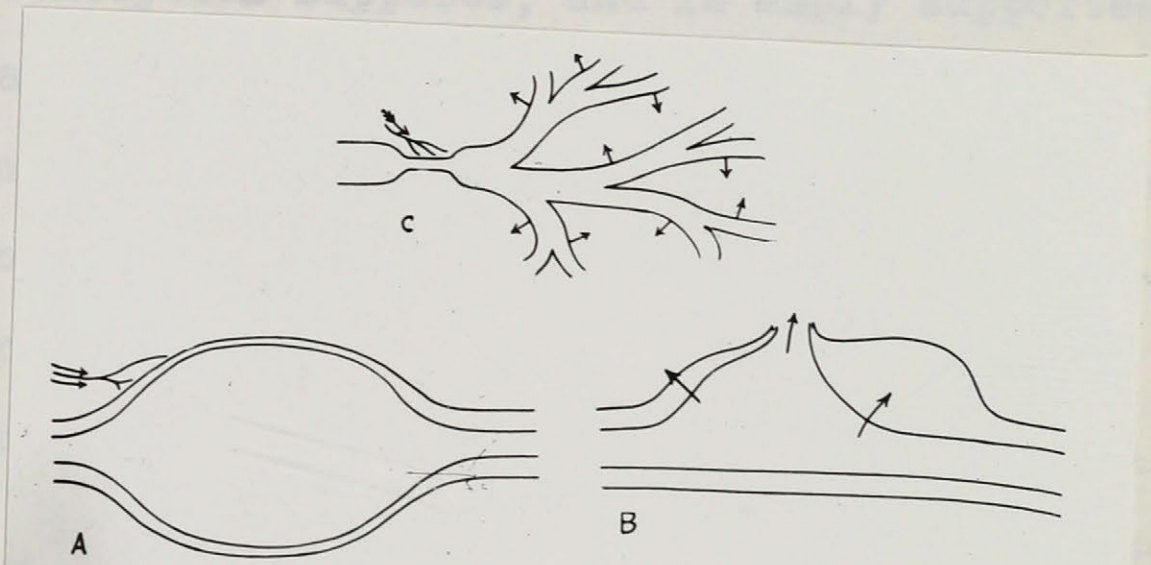


Fig. 3.—*A*, excessive neural impulses may paralyze the vessel wall; the vessel dilates. *B*, if the blood pressure has not decreased, the liquid movement in the wall itself is suppressed. The wall degenerates and the blood may pass through it (Ricker). *C*, neurogenic spasm of an arteriole causes reflex dilatation of its capillaries, stasis and hemorrhage by diapedesis. If blood from the surrounding vessels enters the area of the diseased vessel, a circular hemorrhage is formed (Ricker).

There is then direct evidence that in at least one pathological condition, epilepsy, vasoconstrictor activity of great degree can occur. Similarly there has been developing an increasing appreciation of the importance of functional circulatory disturbances in organic disease of the central nervous system not directly related to epilepsy. Ricker (1927) pioneered and elaborated the conception of neurovascular tone as being directly related to organic disease. His conception supposes, and is amply supported by experimental facts, that in response to moderate irritants the circulation in the terminal arterioles and in the capillary bed is slowed (peristasis) and leucodiapedesis occurs. More severe irritants lead to an even greater slowing of circulation (prestasis) and a diapedesis of red blood cells occurs. These changes are, according to Ricker, associated with a vasoconstriction of the muscular arteries, and a dilatation of the terminal segments as shown in figure 3 , a diagram taken from a paper by Boumann (1931). If the irritation is of sufficient strength, actual stasis of the blood stream may occur. That extensive tissue necrosis may occur when the circulation is appreciably slowed, as evidenced by the diminution in circulatory rate in the leptomeninges, is shown by unpublished data of McEachern and Evans (1937). That mechanical, electrical and chemical irritation can cause constriction and even obliteration of capillaries given off from arterial branches, was amply demonstrated by Florey (1925), so there is some direct evidence of a mechanism such as that necessary for the support of Ricker's theory.

Chief proponents of the Ricker school on this continent have been Oertel (Scriver and Oertel,1930), Chase (1934 and 1937), and Hiller and Grinker (1930). Of particular importance is the work of Chase on air embolism (1932) in which he has shown that in addition to the mechanical effect of the air embolism in the arteries of the mesentery of the rabbit, there is also a distant effect in the capillary bed consisting mostly of peristasis and prestasis and their related diapedeses. In a fatal human case of cerebral air embolism he was able to find exactly such change in relation to the venous capillary bed and the small veins, there being petechial perivascular cerebral venous hemorrhage with passive hyperemia.

Hiller (1924) described lesions in Ammon's horn in cases of carbon monoxide and looked on them as evidence of a functional vascular change similar to that proposed by Spielmeyer. "Spielmeyer and his co-worker, Neubürger, were able to show that this type of lesion, especially in the grey matter, was identical with that caused by organic vascular occlusions. There is apparently a gradual transition from a reparable disturbance of brain function on a functional circulatory basis (the explanation of certain transient nervous symptoms) to permanent defects. In this large group of circulatory disorders there exist pathologic gradations from slight ganglion-cell reactions corresponding to Spielmeyer's 'Erbleichungen' foci in which only ganglion cells show the results of ischemic degeneration and fade away without reactive glial response, to incomplete and complete softenings and coagulation necrosis".

Hiller and Grinker (1930) emphasize that the functional circulatory disorders described by Spielmeyer cause a pathological picture closely resembling those in case of fat and air emboli described by Neubürger and we have already mentioned that Chase has shown the importance of Ricker's conception in explaining the lesions resulting from air embolus. There is, then, ample evidence of the importance of the circulation in cerebral softening and there is also evidence that softening may occur not only as the result of organic vascular changes but also as the result of functional vascular changes.

It must, however, be noted that there is a difference in the mechanisms visualized by Ricker and Spielmeyer. This was emphasized by Spielmeyer in the course of the discussion of a paper read by him before the New York Neurological Society (1930). Dr. Bernard Sachs had raised the question of the possible importance of venous stasis in explaining the lesions which Professor Spielmeyer had attributed to vasospasm. The latter says, "I agree with Dr. Sachs that one finds stasis. I do not want to discuss this at length, but there is Ricker in Germany who was one of our first pioneers in this study from the anatomic point of view and who denies that any other functional disturbance of the circulation - than stasis or prestasis - is the cause. I do not see that. I think there is a possibility that vasospasm also can produce partial necrobiosis".

But if one considers that Ricker regards peristasis, prestasis and stasis as the result of trauma to the vessels leading to vasodilatation of the venous capillary bed associated, however, with vasoconstriction of the proximal arteries, one

sees that the views of the two investigators are not so divergent as Spielmeyer himself would seem to indicate - both are essentially dependent on disturbance of blood flow.

We have attempted to gather evidence on the question of nervous control of blood vessel tone by observing the vessels over the convexity of the hemisphere at the time of dissecting the central trunk of the middle cerebral artery preparatory to placing a clip upon it. In one instance (P-1443) dissection of the trunk without clipping of the vessel resulted in a loss of the cardiac pulsations in the arteries over the convexity of the hemisphere which were plainly visible before the manipulation was begun. Such a loss of pulsation suggests strongly a reduction in blood flow for it is an invariable accompaniment of any experiment in which the chief vessel supplying an area is occluded. The pulsations did not return in the fifty-minute period of observation during which the cortex remained exposed. Unfortunately microscopic observations of the rate of blood flow were not made in this instance.

On another occasion (P-1440) a twenty-five per cent occlusion of the diameter of the middle cerebral trunk was without either immediate or late effect. However, in a third experiment (P-1433), when a clip was placed not upon the trunk of the middle cerebral artery itself, but upon two of the perforating branches derived from it and entering the anterior perforated space to supply the basal ganglia, there were observed immediately after the clipping a definite pallor and loss of arterial pulsation indicative of a decreased blood

flow over the convexity of the hemisphere and a note was made at the time, "the microscopic observation of the decrease in rate of blood flow following the clipping leaves no doubt as to the relative paucity of blood in the distribution of the middle cerebral artery". It is, of course, to be remembered that these experiments were made under dial anesthesia which probably masked to some extent any neurovascular or purely vascular spasm. It is easy, then, to visualize frequently recurring vascular insults of similar degree (embolism, e.g.) which might cause serious cerebral damage.

In summary, the evidence in favor of the occurrence of vasospasm on a functional basis is weighty. As will be seen free use is made of this conception in the chapters that follow in helping to explain the formation of various types of cerebral cicatrix.

III. CEREBRAL ARTERIAL OCCLUSION. *, **

INTRODUCTION:

Pathologists have, for many decades, interested themselves in the changes following occlusion of cerebral vessels. Hiller's monograph (1936) presents a comprehensive review of the subject, with special emphasis on the excellent descriptive work of the German investigators, including that of Schob (1930) on porencephaly and of Schwartz (1930) on apoplexy. A second valuable monograph with detailed bibliography is that of Ley (1932).

However, there have been only a few attempts made to study the problem of arterial occlusion by the experimental method. Notable for the experimental approach are the contributions of Schaeffer (1910), of Bodechtel and Müller (1930) and of Cone and Barrera (1931).

Schaeffer injected melted paraffin into the carotid artery of dogs. Naturally, the sites of lodgement of the

* Footnote No. 1: This chapter was presented in summary at the meeting of the American Neurological Association on June 4th, 1937 under the title, "The Anatomical End Results of Cerebral Arterial Occlusion: An Experimental and Clinical Correlation", by Joseph P. Evans and J. Norman Petersen. It will be published separately.

** Footnote No. 2: In connection with this chapter the author would like to express his appreciation of the kindness of Professor Otfrid Foerster in extending to him the courtesy of his laboratory and for permission to study the case from his service at the Wenzel-Hancke Krankenhaus. His thanks are also due to Professor O. Gagel for help and advice in preparing the pathological material of the third clinical case cited in the text.

of the emboli, whether central or peripheral, in the cerebral vascular tree, were unpredictable. Schaeffer concluded that there were four stages in the resultant process: 1) of ischemia, lasting up to ten or fifteen hours, 2) of congestion and diapedesis, reaching its maximum in three or four days, 3) of elimination and disintegration signalled by the appearance of granular cells, beginning in three or four days and sometimes lasting several months, 4) of repair and cicatrization, a process in which he felt glia plays the primary role. He includes in his paper a number of clinical cases but unfortunately the histories and pathological notes are very brief and there are few illustrations. L'hermitte and Schaeffer (1910), in a second paper, of clinical interest, regard cerebral softening as purely a mechanical lesion, "une nécrose relevant des perturbations profondes dans la circulation sanguine de l'encéphale".

Cone and Barrera, employing the same experimental method, confirmed and amplified Schaeffer's findings. Their study was limited to animals surviving only seven days and was concerned chiefly with cellular reactions. Likewise, Bodechtel and Müller reported only the changes of the first week. It seemed to us that it would be worthwhile to employ a method of simulating cerebral emoblism in which the degree and the site of the "insult" could be controlled. It was decided to observe at various time intervals the cicatrization resulting from the placing of silver clips at various points on the middle cerebral artery of monkeys.

The anatomical end results have been striking and seem to us to deserve reporting. As a corollary, several clinical cases presenting analogous anatomical defects are included. We believe that it is now possible when presented with a diverse group of pathological specimens, the late results of various cerebral accidents, to pick out a certain group and to say with assurance of this group, "This condition is the result of cerebral arterial occlusion".

Before going on to a detailed account of our findings, it would be well to restate the fact that the placing of a silver clip on the middle cerebral artery of the monkey, either on its main trunk or on its more important branches, does not lead to a cessation of flow in the peripheral segments of that vessel (Evans and McEachern, 1937). Microscopic examination of the blood stream in vivo shows that there is a persistence of flow, maintained through collateral channels, but its rate is appreciably diminished. This slowing beyond the site of occlusion is, no doubt, the essential physiological factor in the chain of events leading to tissue destruction in the peripheral districts. It seems reasonable to assume that a slow occlusion of the middle cerebral artery would permit the establishment of a more efficient collateral circulation. The work of Pfeiffer (1928) and of Cobb and Talbott (1927) leaves no doubt concerning the presence of anastomotic networks in the arterial bed. Observations of our own on vessels injected with bismuth solution amply confirm these facts, and testify to their employment as collateral channels when a main artery of supply is occluded. A further point, one of pathological interest, is that the closure of an artery near its point of origin need not lead to a collapse of the vessels distal to the point of occlusion (unless the

Fig. 4.

P 1526. Shows only local damage to the temporal lobe, the result of deliberately rough retraction of the lobe. 24 hours post-operatively.

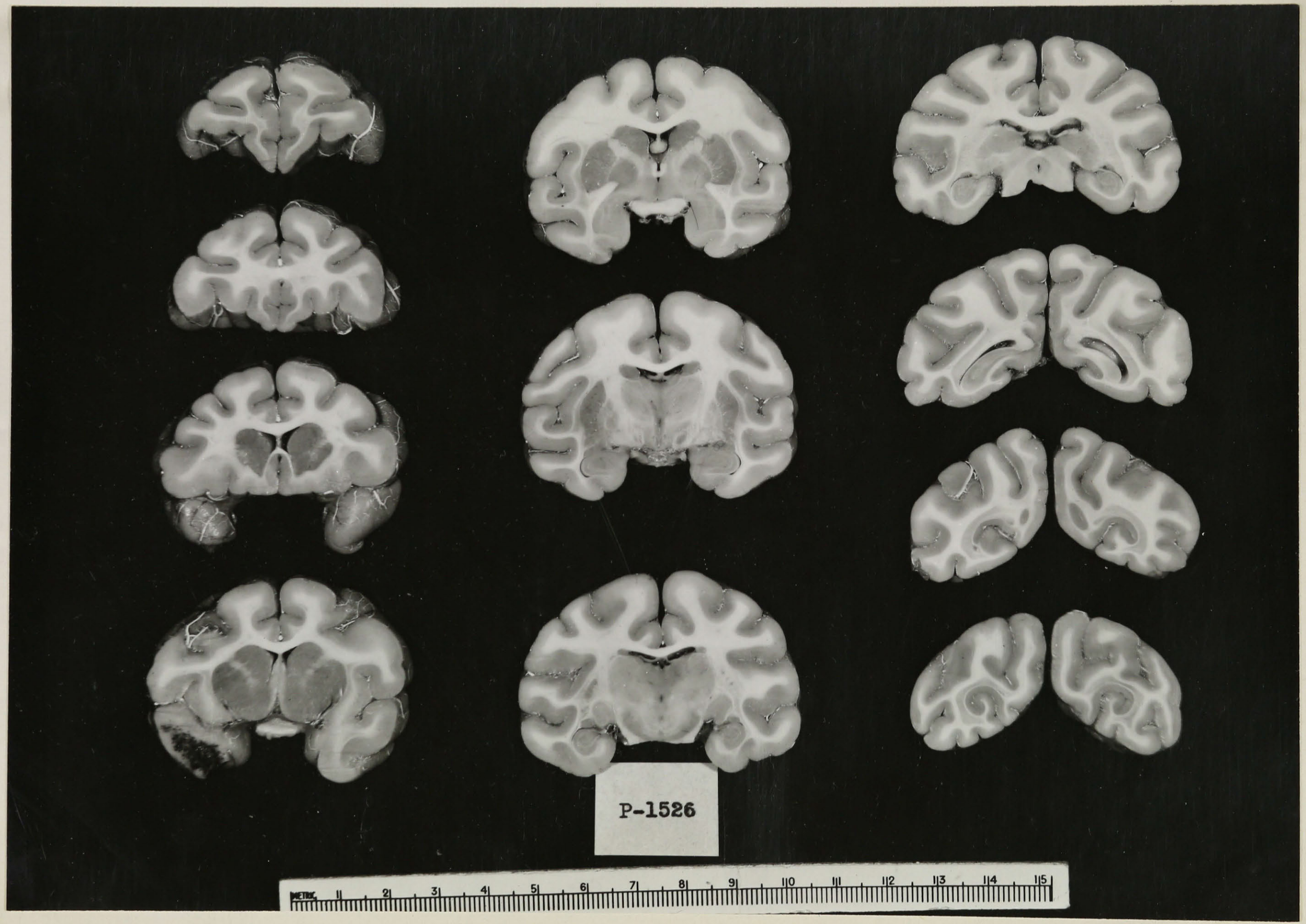


Fig. 4.

occlusive process is of the nature of a progressive arteritis). Hence in the microscopic preparations illustrated below, all vessels in the changed area will be found to be patent.

EXPERIMENTAL:

A. The Method. Macaccus rhesus monkeys were used. Under standard neurosurgical conditions, with dial as the anesthetic agent, a right osteoplastic craniotomy was performed. The temporal lobe was retracted and the middle cerebral identified in the Sylvian fissure. By careful dissection it is not difficult to isolate the artery and to clip it securely. In the fifth monkey cited accidental interruption of the middle cerebral artery occurred during an operative procedure carried out for another purpose.

After appropriate time intervals the animals were sacrificed, the brains washed through, via the carotid artery, with normal saline, following which ten per cent formalin was injected. The brains were then removed for study.

B. The Material.

P-1526. Operation March 2nd, 1937. Sacrificed twenty-four hours after operation. This animal, operated upon as a control experiment, was deliberately subjected to very strong and rough retraction of the temporal lobe. No clip was placed upon the artery, which was merely identified. The monkey was sacrificed twenty-four hours later and serial coronal sections of the brain (Fig. 4) show local damage in the temporal lobe, but no evidence of general disturbance such as would be indicated by brain swelling.

Fig. 5.

The arrows indicated by "2", "3" and "4" point to the placement of the clips in the 2nd., 3rd. and 4th. experiments. (i.e., P 1476, P 1439 and E 107).

Fig. 5.

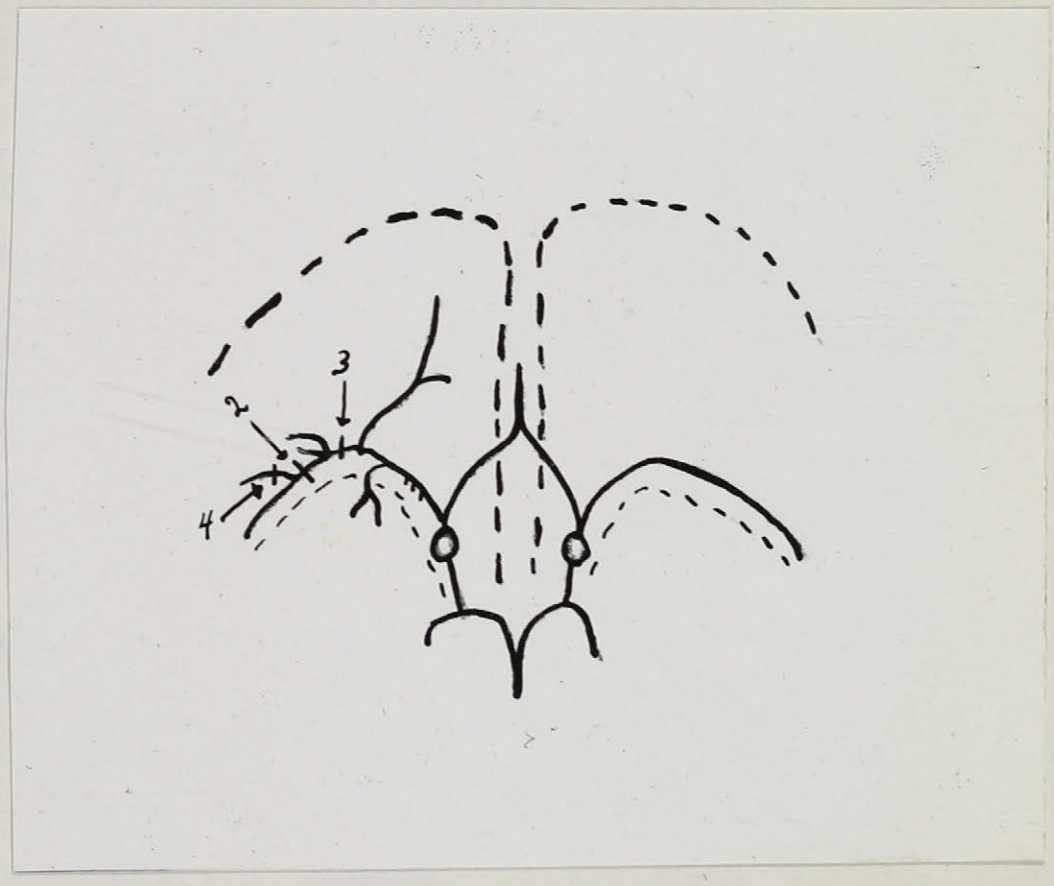


Fig. 6.

P 1476. Coronal sections showing the degree of swelling of the right hemisphere, the displacement of the midline from right to left and of the Sylvian fissure downward. There is evidence of moderate trauma to the temporal lobe. 24 hours post-operatively. The convexity of the right hemisphere, with its dural covering, had been cut away before photographing for a study of meningeal adhesions.

Fig. 6.

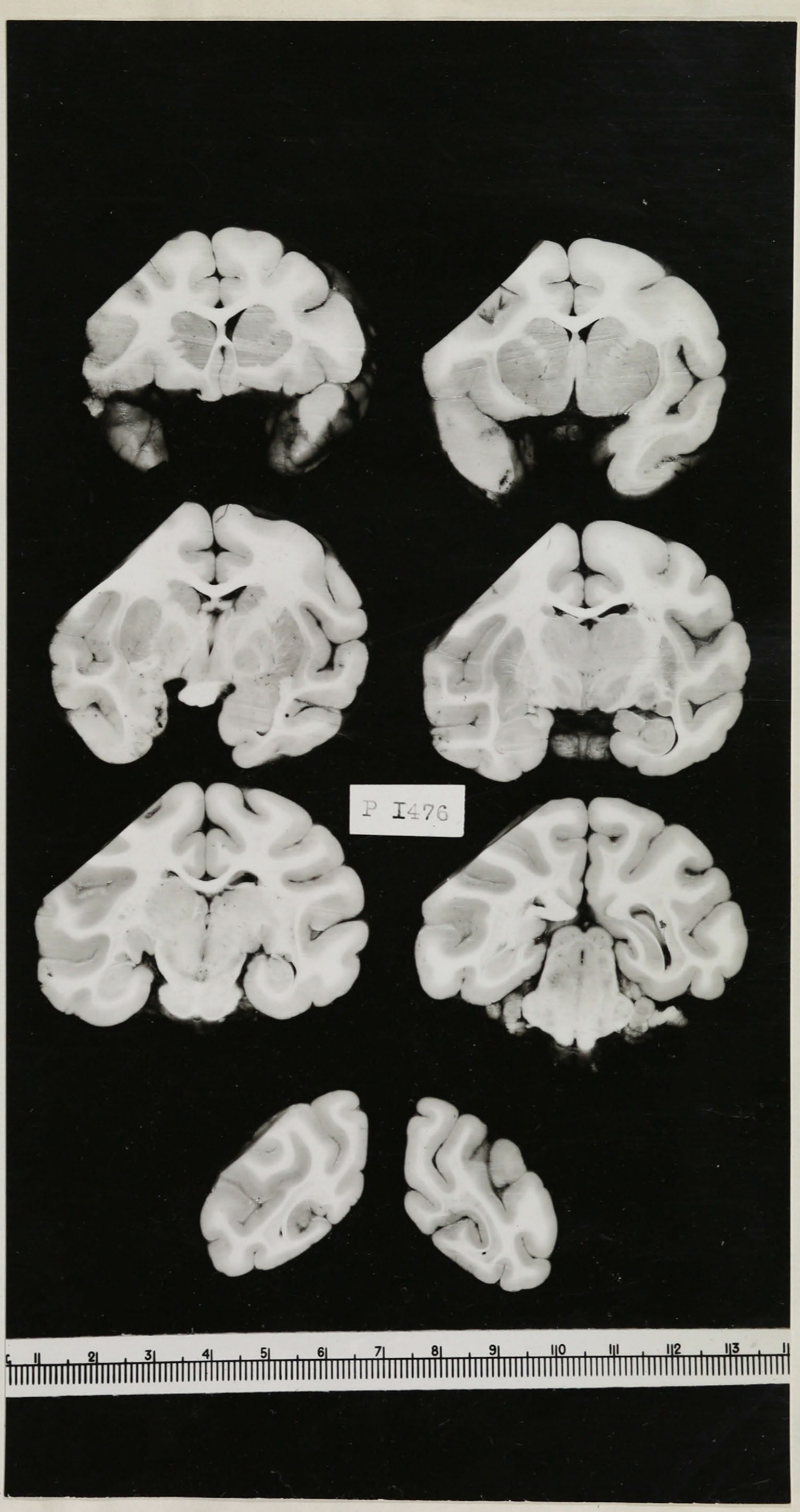


Fig. 7.

P 1439. 70 days post-operatively. Showing the marked atrophy of the right hemisphere and the peri-Sylvian degeneration.

Fig. 7.

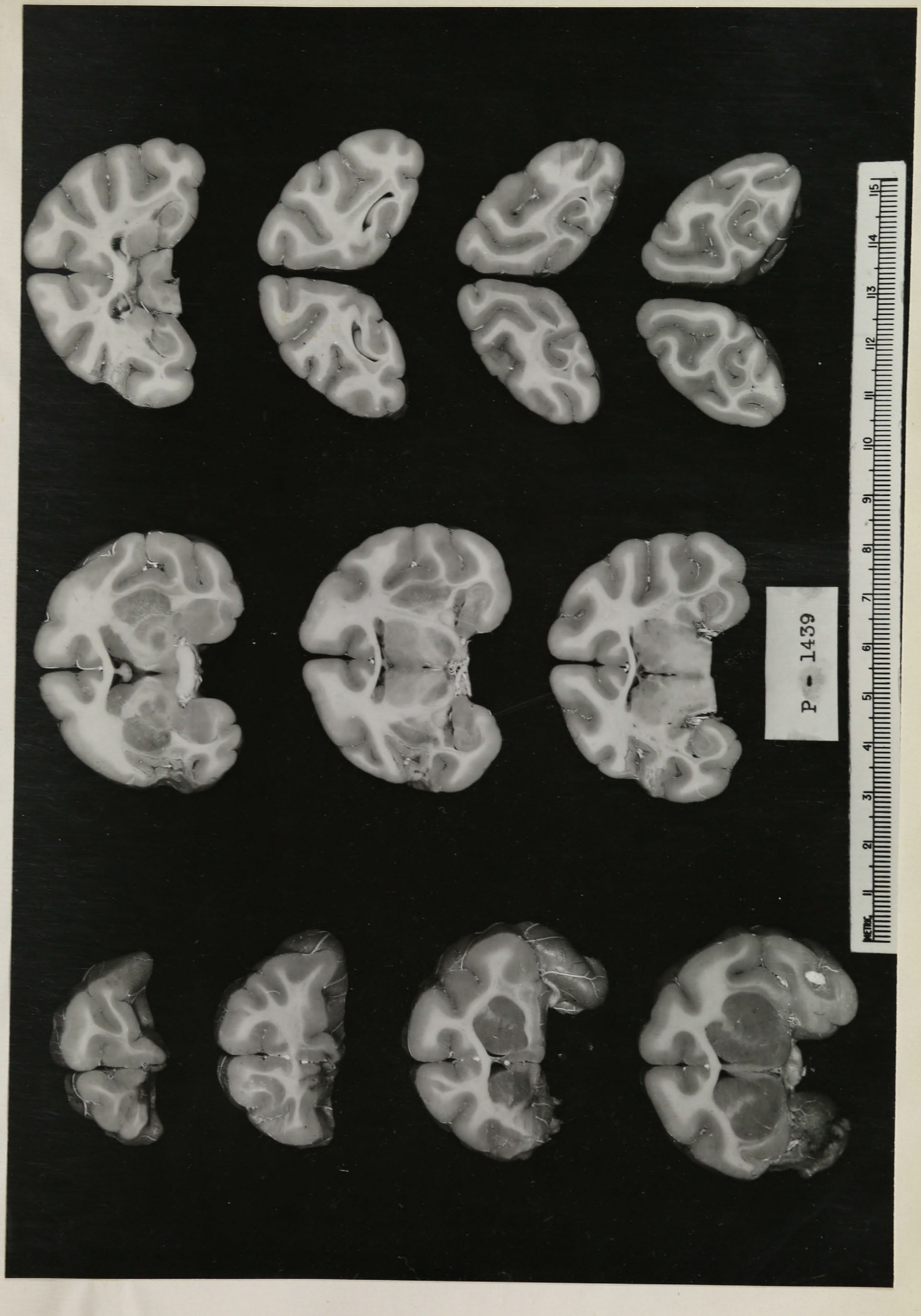
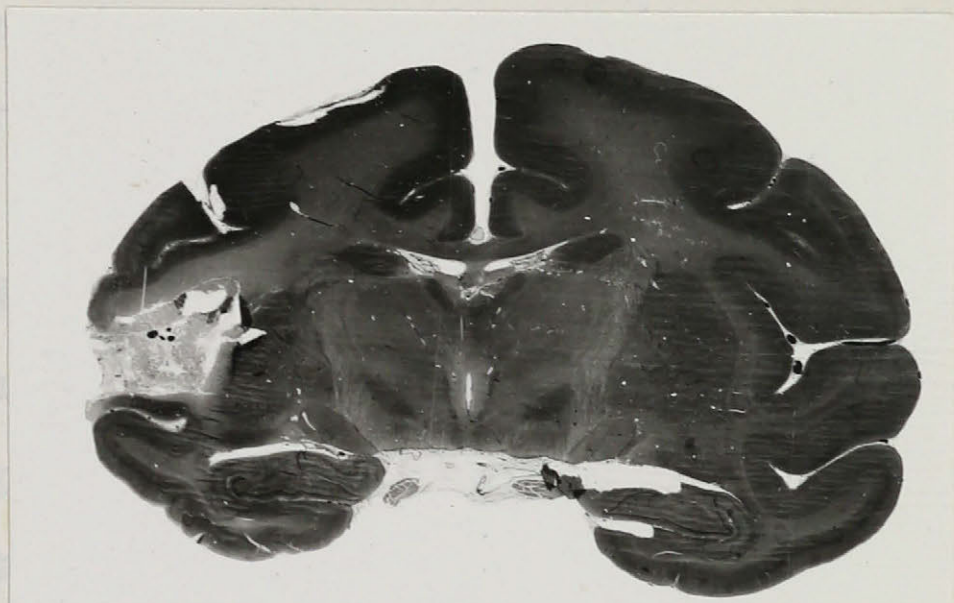


Fig. 8.

P 1439, 70 days post-operatively. Hematoxylin and van Gieson (X 1½). Note the clean cut edges of the lesion.

Fig. 8.



P-1476. Operation December 10th, 1936. Sacrificed twenty-four hours after operation. In this instance the temporal lobe was retracted with maximum care and a clip was placed upon the right middle cerebral artery at a point distal to the branching of the perforating and of the basifrontal arteries (Fig.5). The coronal sections are shown in figure 6 . The convexity of the right hemisphere has been cut away for a study of meningocerebral adhesions but two points are nevertheless clear: 1) There is relatively little gross damage to the temporal lobe in comparison with that seen in monkey P-1526; 2) There is, however, obvious swelling of the hemisphere indicating a definite degree of circulatory disturbance.

P-1439. Operation November 24th, 1936. Sacrificed seventy days after operation. This animal is included to demonstrate an intermediate stage. A clip was placed upon the right middle cerebral artery distal to several important bifurcating vessels, as shown in the orientation sketch (Fig.5).

The coronal sections (Fig.7) show the marked atrophy of the right hemisphere and indicate the general nature of the degenerative process. The hematoxylin and van Gieson preparation (Fig.8) illustrates this in a more detailed manner. Centered about the Sylvian fissure is a zone of tissue which has almost completely lost power to take up the stain. A very striking feature is the presence of normal vessels in the fissureitself, the vessels being filled with bismuth injected at the time of death and therefore appearing in the picture as black dots of varying size. Obviously the blood vessels have remained open and some smaller branches can be traced into the adjacent gyri. These vessels likewise show no degenerative changes.

Fig. 9.

E 107, 118 days post-operatively. Degeneration in the distribution of the middle cerebral artery resulting from its sudden occlusion.

Fig. 9.

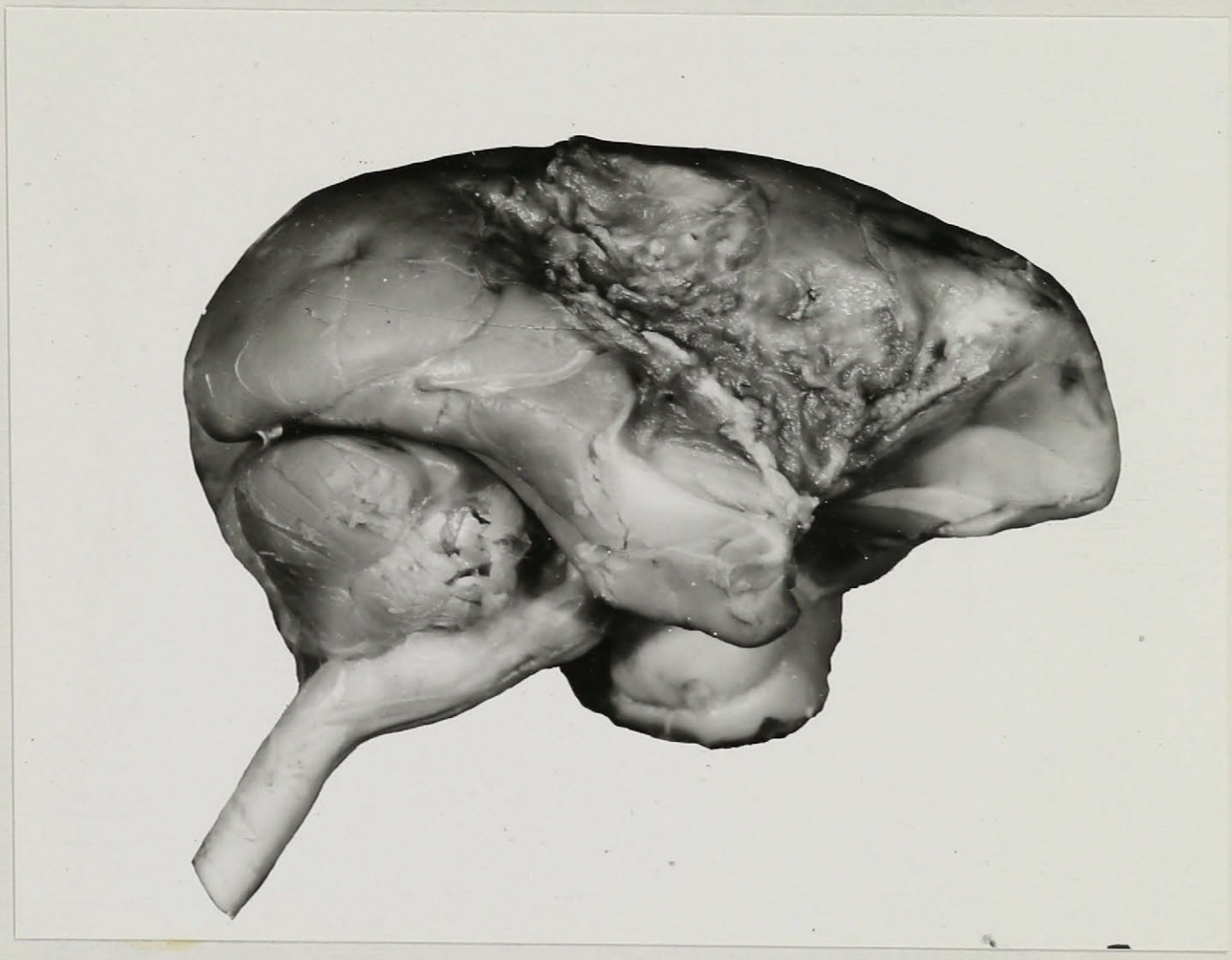
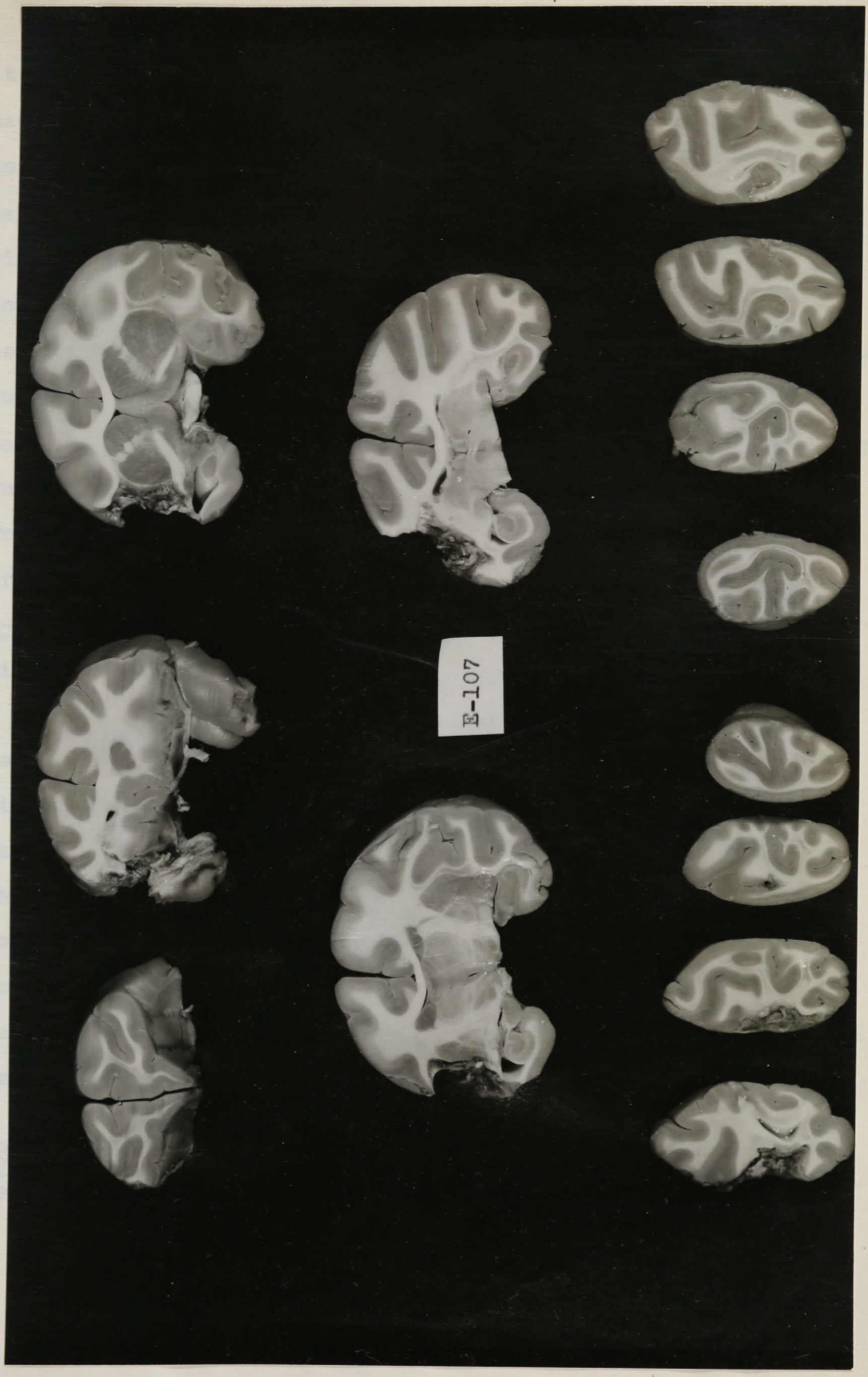


Fig. 10.

E 107, 118 days. Coronal sections. Note loss of substance. No primary degeneration of the basal ganglia because the clip was placed distal to the perforating branches.

Fig. 10.



As one proceeds away from the Sylvian fissure and into the depths of the adjacent gyri one comes upon a zone intermediate between frankly necrotic tissue and tissue that appears normal. In this area is a moderate proliferation of new capillaries which seem to be derived from vessels in the necrotic tissue, though this point is difficult to decide with assurance. However, it is in this zone that active phagocytosis is proceeding. The phagocytes appear to be attacking the necrotic tissue, the normal tissue being walled off by a glial barrier, but here and there the barrier is incomplete and there is some slight invasion of cerebral tissue by new capillaries and by phagocytes. Probably these changes are secondary to the extension of fingers of tissue necrosis into the adjacent normal areas.

* E-107. Operation April 8th, 1936. Sacrificed one hundred and eighteen days after operation.

A clip was placed on the right middle cerebral artery as indicated in the orientation sketch (Fig. 5). A lateral view of the brain (Fig. 9) shows extensive degeneration in a large part of the distribution of the middle cerebral artery. This degenerative zone was definitely cystic, but because of post-operative dural-leptomeningeal adhesions the leptomeningeal covering of the cyst was necessarily torn away in removing the dura. The coronal sections (Fig.10) indicate the extensive degeneration, sparing the basal ganglia because the perforating

* Footnote: Dr. William de G. Mahoney kindly injected the brain of this animal and forwarded it to Montreal after the author's departure from Germany.

Fig. 11.

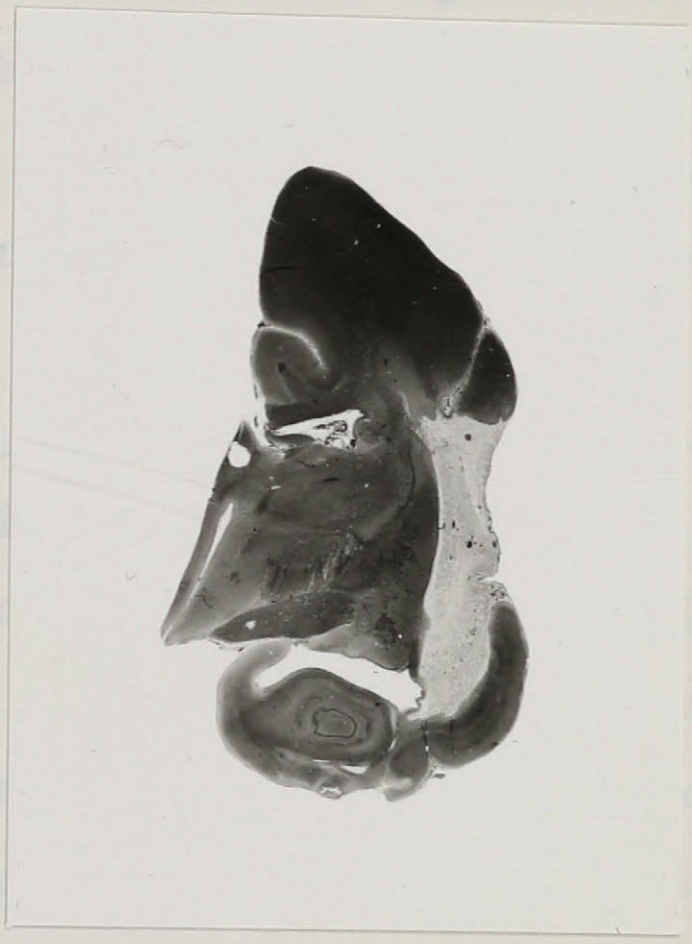
E 107, 118 days. H. and V.G. (X2). Note sharp border of old degenerative process, except infero-mesially where there are islands still undergoing digestion by phagocytes.

Fig. 11.

Fig. 12.

4213, 270 days. H. & V.G. (X2). Note sharp border of degenerative process, shift of the third ventricle, and local dilatation of inferior horn. The lateral ventricle is also dilated.

Fig. 12.



branches of the artery were left intact. The hematoxylin and van Gieson preparation (Fig.11) shows how sharp is the border of the lesion resulting from sudden occlusion of the artery. There is a tangential arrangement of glia which is only moderately hypertrophied in a limited area about the cyst. There is almost no vascular hypertrophy. Degenerating cerebral tissue is present here and there in clumps, and macrophages may be seen about these whorl-like areas which are made up chiefly of glial fibers. Foreign body giant cells are frequent and lymphocytes are abundant throughout the section. It is obvious that an active phagocytic process is going on but that the process is sharply limited at the border offered by the tangential arrangement of glia.

4213. Operation June 6th, 1930. Sacrificed two hundred and seventy days after operation.

During the course of an earlier unrelated investigation this animal was subjected to a right frontal lobe amputation. An attempt was then made through the same limited exposure to amputate the tip of the temporal lobe. When the animal came to autopsy there was found a degeneration similar in its distribution to that described in the animals above and it was quite obvious that the middle cerebral artery had been interrupted in its course. This was a chance finding and suggested the later studies which are reported above. Unfortunately we have only the microscopic preparations for study. The hematoxylin and van Gieson section (Fig.12) shows the general nature of the process which is not unlike that in the protocol cited immediately above. In this instance, however, the process of absorption seems to have gone on more slowly and there is greater thickening of the meninges over the cystic area. The paucity of connective tissue

proliferation and infiltration into the adjacent brain tissue is, however, as striking and as definite as in E-107.

SUMMARY OF THE EXPERIMENTAL FINDINGS:

It seems wholly improbable that retraction of the temporal lobe could give rise to the degenerative picture which has been detailed in the protocols. When, however, the middle cerebral artery is clipped (distal to its perforating branches in the experiments here cited) there results an initial swelling of the hemisphere on the side clipped. On sectioning the brains the swelling is found unaccompanied by gross signs of the so-called red infarction, as described by Schaeffer, and an explanation of this variation will be offered below. The immediate stage is followed by a degenerative process resulting in an extreme loss of bulk on the affected side. There is local destruction and resorption of tissue in the zone deriving its chief source of blood supply from the clipped branch of the middle cerebral artery. Histologically the picture is one of an absorption of devitalized tissue. The end result of sudden occlusion of the middle cerebral artery is the formation of a large cyst which is formed by the absorption and by the carrying away of the necrosed tissue. Externally the cyst is made up of a semi-transparent membrane comprised of the thickened leptomeninges to the undersurface of which may be attached bits of undigested tissue beset with macrophages, foreign body giant cells and lymphocytes. The deeper walls are made up of a relatively benign zone of gliosis which separates any residual digestive process from the adjacent, normal appearing cerebral

Fig. 13.

Illustration from Hiller (1936). Hiller considers the condition to be the end result of a softening in the distribution of the temporal branches of the middle cerebral artery.

Fig. 13.

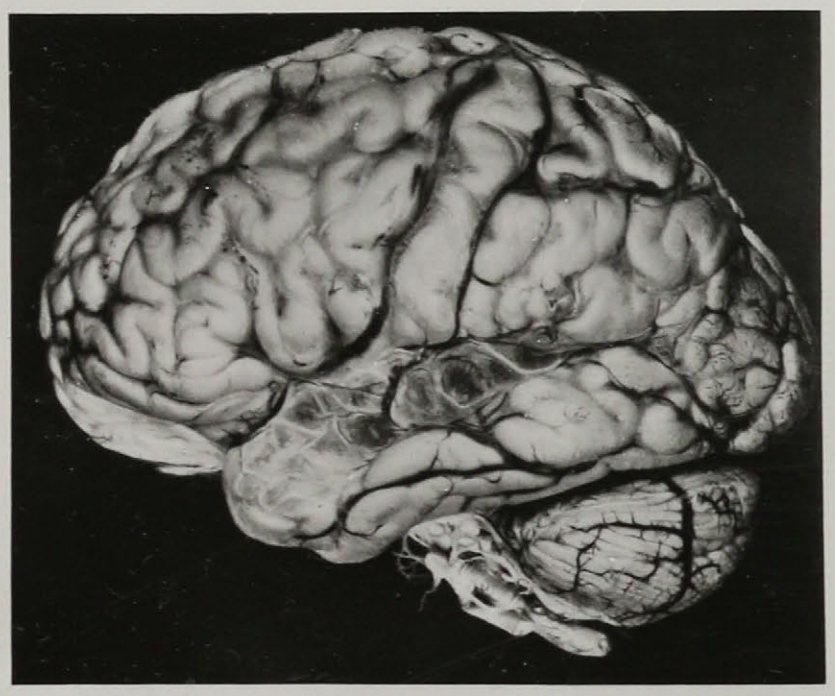


Abb. 54. Cystischer Ausheilungszustand einer Erweichung im Bereich der Temporaläste der A. cerebri media. (Aus dem anatomischen Laboratorium der psychiatrischen Klinik München; Prof. H. SPATZ.)

Fig. 14.

A cyst divided by thick scar tissue septa. Hiller regards this condition as the result of a large, chiefly subcortical encephalomalacia. (From Hiller, 1936).

Fig. 14.

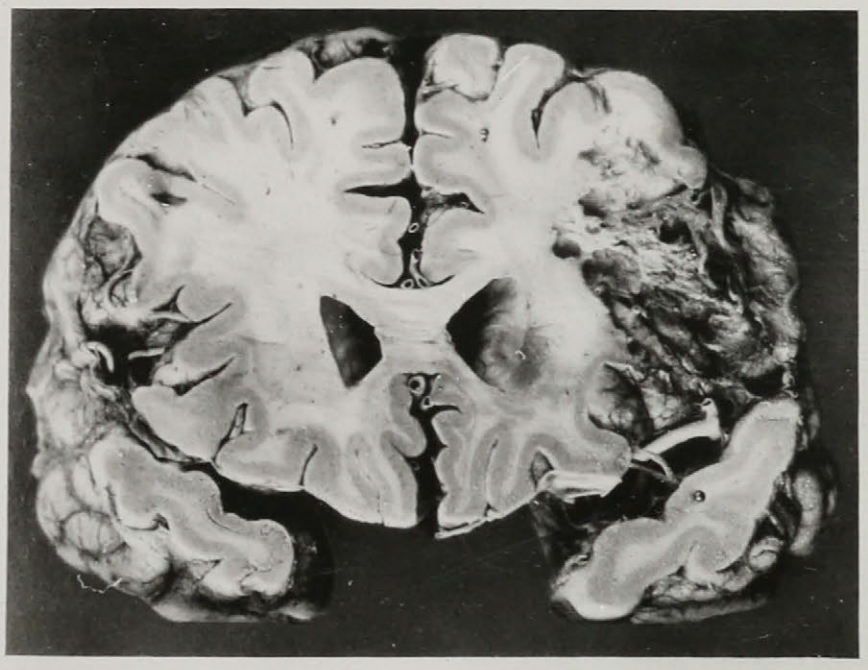
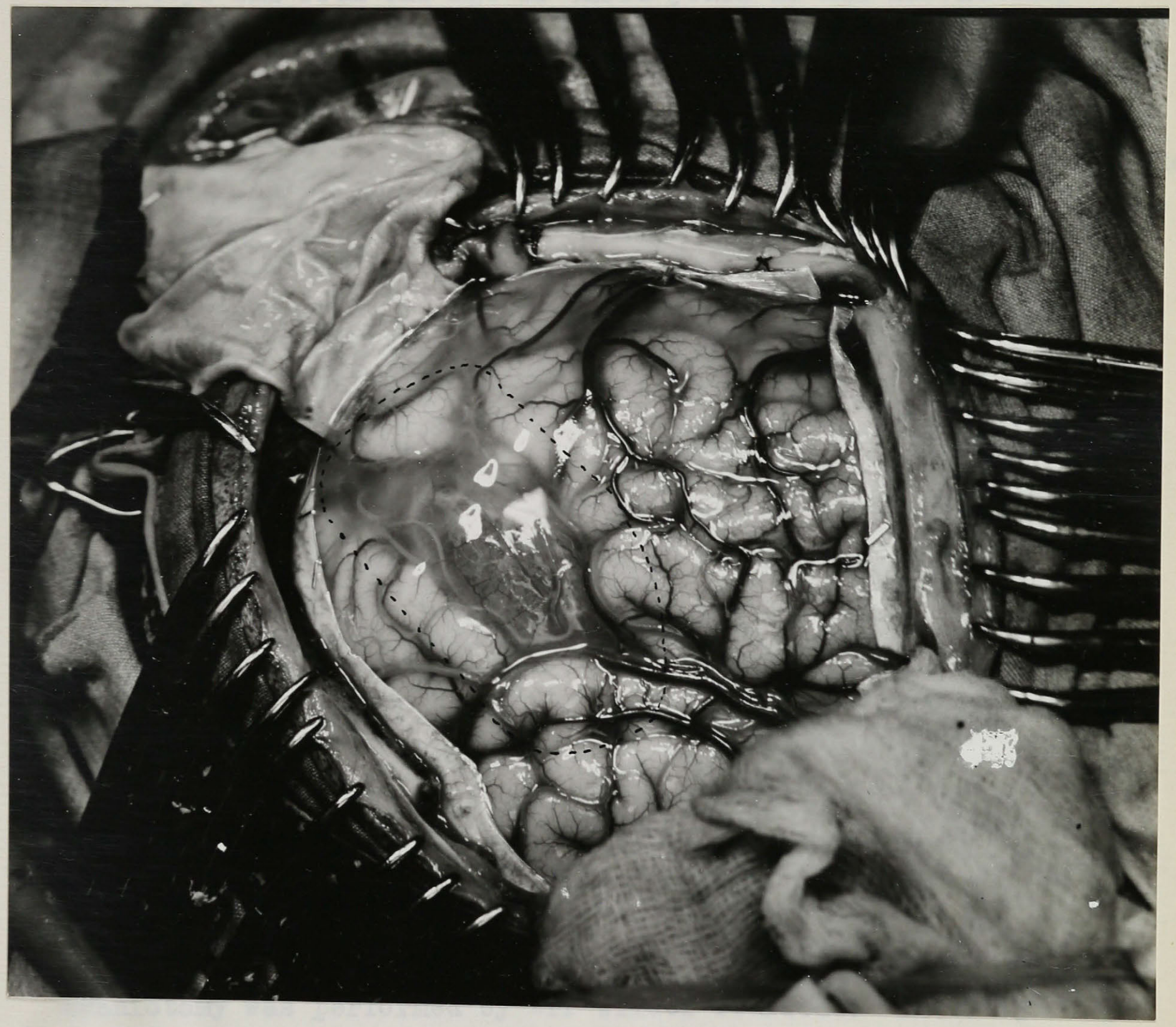


Abb. 56. Von dichtem Narbengewebe durchzogene Cyste als Restzustand einer großen, vorwiegend subcorticalen Encephalomalacie.

Fig. 15.

M.N.I. Case #423. Photograph made at operation of the cyst situated immediately above the fissure of Sylvius and lying in the region of the central fissure. For technical reasons the hemisphere appears to be the right, but in reality is the left. The interrupted line marks the extent of the operative removal.

Fig. 15.



have been some interlocking of the twins but otherwise the birth was normal. The child nursed normally, began to walk at two and one-half years and to talk at three years. At the age of eight months it was noted that he did not use his right hand in playing with toys and from the age of three years he had involuntary clonic movements of the right upper extremity at irregular intervals and convulsions which were more marked on the right side.

On examination there was atrophy of the entire right side of the body, including the face, arm and leg. There was obvious mental retardation. The patient had a hemiplegic gait, right hemiparesis with positive Babinski, astereognosis and diminution of two-point sensibility on the right side. The cerebrospinal fluid Wassermann reaction was negative and the total proteins were 20 mgm. per cent.

Encephalography showed that the left lateral ventricle was larger than the right and there was a large cyst in the left hemisphere measuring 3x5x5 cm. and situated above and lateral to portion 3 of the left lateral ventricle. The septum pellucidum and third ventricle were slightly to the left of the midline and there appeared to be some thickening of the left side of the cranium.

On March 27th, 1935 a left parietal osteoplastic craniotomy was performed by Dr. Wilder Penfield. After opening the dura it was seen that there was a fluid-filled cyst above the fissure of Sylvius and apparently in the former central fissure (Fig.15). It began in the fissure of Sylvius and passed upward and backward, being somewhat larger at the base than it was above. The cyst passed downward to the ventricle and there was a thin transparent membrane between it and the ventricle.

Fig. 16.

M.N.I. Case #423. A cross section cut through the center of the block of tissue excised at operation. Note the thinness of the cyst wall. Rule is in centimeters.

Fig. 16.

Fig. 17.

M.N.I. Case #423. Hematoxylin and van Gieson stain (X2) to show general nature of the process. The sharp black dots of various sizes are blood vessels, quite normal in microscopic appearance, containing bismuth injected at the time of death.

Fig. 17.

This membrane did not seem to be complete but doubtless represented the old ependymal wall of the ventricle. The cyst was covered over with transparent pia-arachnoid. Close to it, in its wall, there was some yellow tissue but there was no gelatine-like tissue, such as is seen in meningocerebral cicatrices, and there were no adhesions between the pia-arachnoid and the dura. Dr. Penfield concluded from this that there had never been a subdural hemorrhage nor any wound passing through the dura and that the cause of the lesion must have been obliteration of the middle cerebral artery or of one of its large branches. The brain around the cyst appeared normal; it was somewhat suffused but the convolutions themselves were of good size and consistency, perhaps they were a little dense, suggesting a small amount of gliosis. The cyst was removed by silk sutures and suction.

Pathological examination showed the inner surface of the cyst (Fig.16) to be smooth, of a light pinkish-purple color and in the wall there were several large vessels. Microscopically (Fig.17) the arachnoid was found to be thickened, slightly so beyond the cyst, and much more so as the cyst was approached. There was much collagen in fine strands, with many spaces in the meshes. There were, in addition, many lymphocytes in the arachnoid. The nerve cells were pyknotic immediately adjacent to the cyst and in a few instances there were more than the normal number of satellites. There seemed to be a small amount of cerebral tissue on the inner surface of the cyst and this was greatly altered, being broken up into numerous small rounded fragments which contained many groups of lymphocytes. In places the blood vessels were greatly increased in number. No cerebral tissue was

found containing fibrous connective tissue and none was definitely invaded by the leptomeningeal proliferative process. There was a striking absence of dense scarring in the leptomeninges and in the cerebral tissue and a surprisingly small degree of reaction in the brain. A large vessel was cut transversely, and in part longitudinally. It may very well have been the middle cerebral artery and it showed no pathological changes.

M.N.I. Case No. 2266:

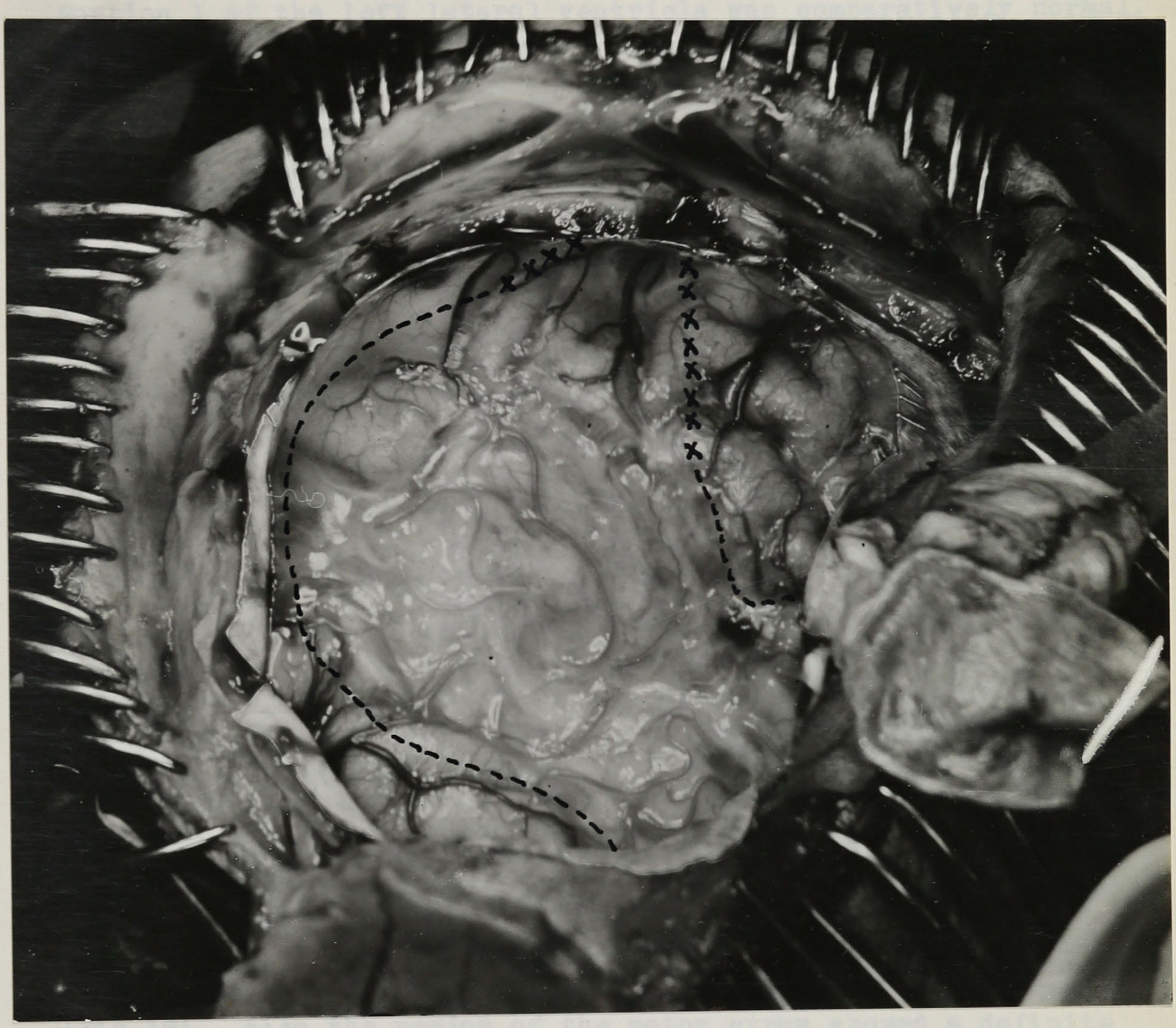
At birth this patient, a woman of twenty-five years, was a transverse presentation but no instruments were used. She was somewhat blue but cried spontaneously. She talked at one year of age but did not walk until three years because of the weakness described below. When the child was one week old the mother noticed that her right side was weak and two weeks later it was observed that the patient's right hand was closed most of the time, that she had little power in grasping things and that the right arm moved very little. At the age of ten years the patient began to have Jacksonian epileptic attacks, manifested by head and eye turning to the right, clonic movements of the right arm and then unconsciousness and generalized clonic movements.

Examination showed that the patient was mentally retarded. Her head was small, somewhat flattened at the vertex and the left side was smaller than the right. The right side of the chest was smaller than the left. There was a high-pitched systolic murmur in the mitral area and the spleen was palpable. There were both motor and sensory deficiencies on the right side which need not be detailed here. The Wassermann reactions in the blood and cerebrospinal fluid were negative and the total proteins in the latter were 18 mgm. per cent.

Fig. 18.

M.N.I. Case #2266. Photograph made at operation of the gutter of altered tissue corresponding to the fissure of Sylvius. For technical reasons the hemisphere appears to be the right, but is in reality the left. The interrupted line indicates the extent of the removal, except mesially where the crosses indicate tissue removed from the central gyri as far as the falx.

Fig. 18.



Encephalography showed that the skull was asymmetrical, the left side being much flatter than the right. The cranial cavity was small in relation to the size of the face and jaws. The right lateral ventricle was displaced to the left but otherwise it had a normal appearance and showed very little dilatation. Portion 1 of the left lateral ventricle was comparatively normal. There was enormous dilatation involving portions 2, 3 and 4 and most of portion 6 on the left side. In one region the width of brain external to the ventricle was only 1.3 cm. The third ventricle was quite large and displaced slightly to the left of the midline. There was, consequently, very marked atrophy involving the left hemisphere, least marked in the anterior portion of the frontal lobe. The subarachnoid space of the right hemisphere was not very unusual except for a few rather broad intergyral sulci. Several widened sulci were present on the left side, particularly in the parietal and occipital regions.

On February 18th, 1937 a left osteoplastic craniotomy was performed by Dr. Wilder Penfield. There were no adhesions, aside from Pacchionian granulations, between the dura and the brain and nothing to suggest previous hemorrhage. The brain itself presented a gutter of altered tissue corresponding to the fissure of Sylvius and extending upward and backward a long way beyond what should have been the fissure of Sylvius (Fig.18). Also the region of the motor gyrus showed a definite decrease in size of the gyri and gliosis extending upward as far as the falx. The other gyri appeared quite normal. Within the scar which was in the fissure of Sylvius there was one cyst which was not very large. The roof of the inferior horn

Fig. 19.

M.N.I. Case #2266. Cross sections through the block of tissue excised at operation. Note the gliosis, meningeal thickening, and the patent vessels in the meninges. Rule is in centimeters.

Fig. 19.

S-241-37

Fig. 20.

M.N.I. Case #2266. Hematoxylin and van Gieson (X2). Note the numerous cysts surrounded by proliferated connective tissue encompassing islands of glia. Many patent vessels filled with bismuth may be seen.

Fig. 20.

of the ventricle was quite thin. When the scar was extirpated there was no vessel found which could be identified as the middle cerebral artery, although the scar itself pulsated quite actively and seemed to have an increased amount of blood supply and an increased number of large vessels. The scar was removed entirely with deep brain sutures and blunt dissection and the excision was carried upward so as to include the convolution on either side of the fissure of Rolando as far as the falx itself. The general nature of the excised scar can be judged from the picture of the gross specimen (Fig.19). The thickened meninges are clearly shown and at least three large patent vessels may be seen superficially. The multilocular cysts are obviously lined by heavy gliosed bands of degenerative and of proliferative tissue. The adjacent gyri, though less affected, are obviously abnormal. These points are demonstrated in more detail in the hematoxylin and van Gieson preparation (Fig.20) which shows islands of glial tissue, devoid of nerve cells and surrounded by bands of proliferated connective tissue, heavily laden with collagen. Scattered clusters of phagocytes are still to be found in isolated areas. The blood vessels filled with bismuth, and therefore appearing as black dots, are normal.

Case Ger. Kas. of the Wenzel-Hancke Krankenhaus (Breslau). Service of Professor Otfrid Foerster.

This patient, a boy of thirteen years, was born of a mother who had had three miscarriages. The child's birth and early development were normal up to the age of six months when he developed "a paralysis, especially marked on the right side". Further details of this illness are lacking. For approximately two years before admission he had been having occasional

Fig. 21.

Ger. Kas. Note particularly the gutter of altered tissue in the distribution of the middle cerebral artery.

Fig. 21.

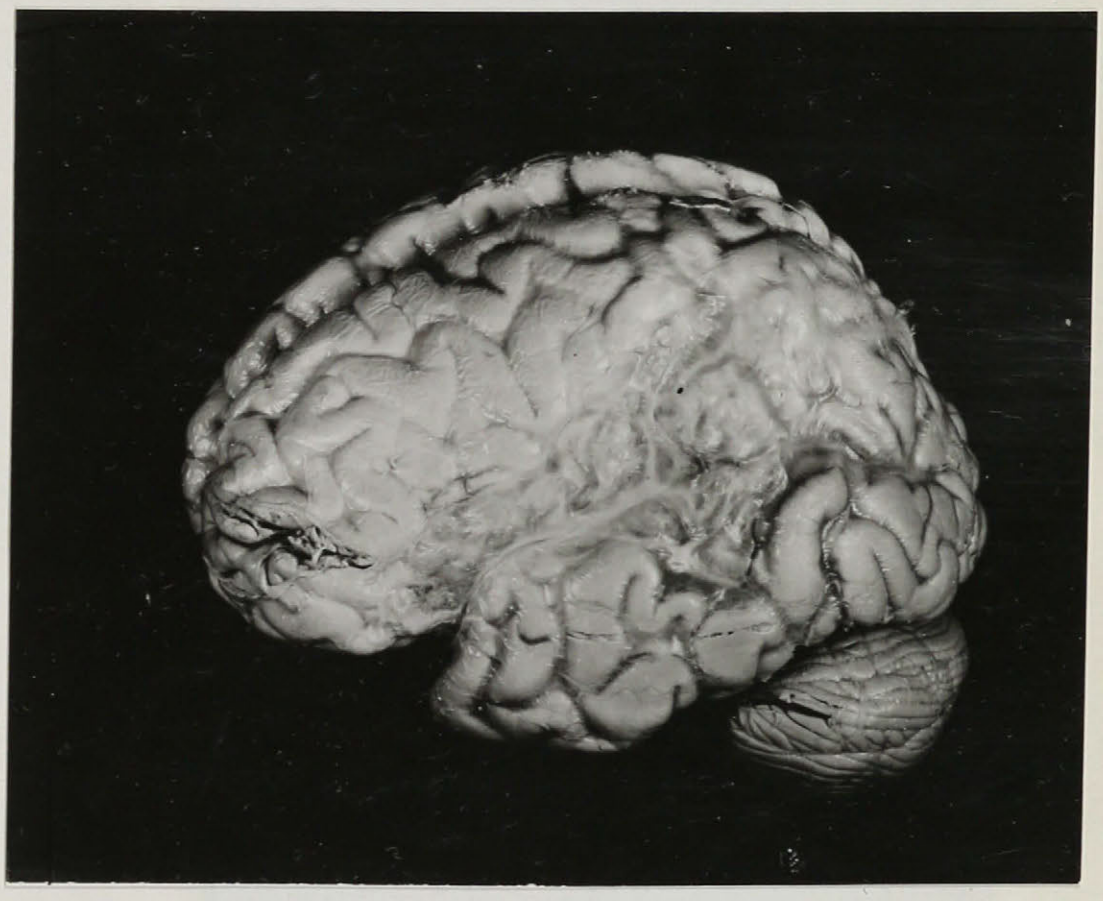
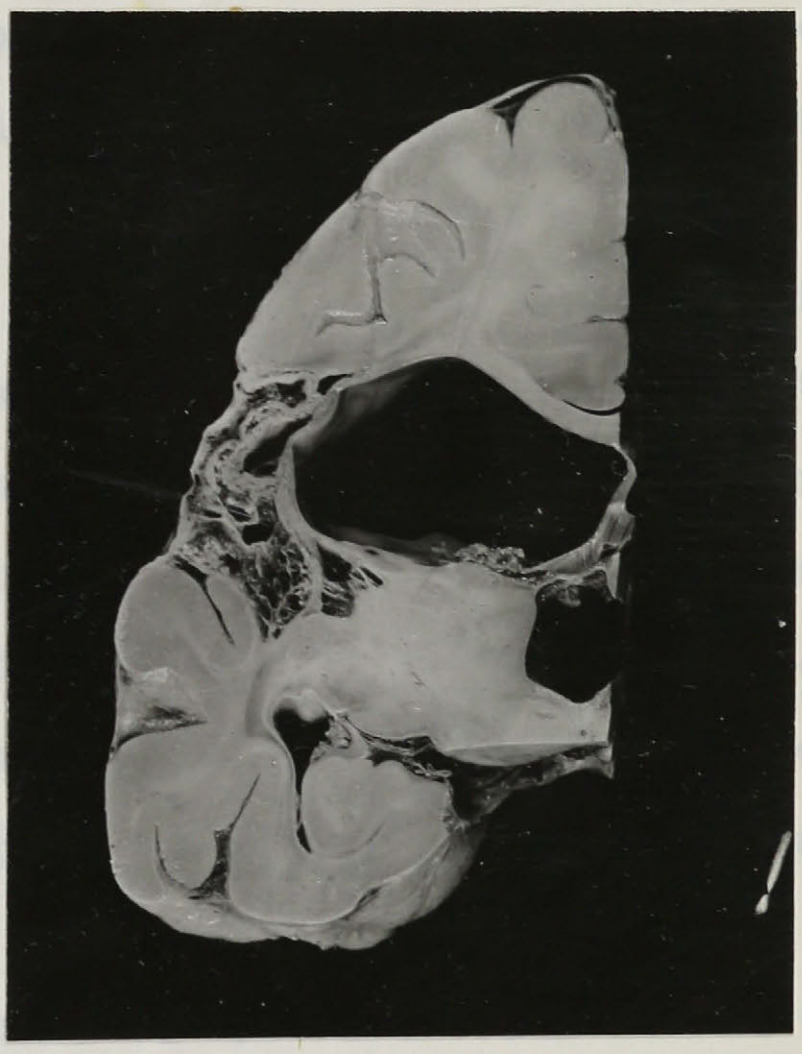


Fig. 22.

Ger. Kas. See Text.

Fig. 22.



epileptic seizures, usually beginning in the left leg but sometimes in the right. The seizures became widespread, were accompanied by loss of consciousness and sometimes by loss of speech. These had increased in frequency and he was admitted to the hospital in status epilepticus.

Physical examination showed that the left side of the skull was somewhat flattened, especially anteriorly. He presented signs of motor and sensory disturbance in the right side which are irrelevant to the present investigation. There were no cells in the cerebrospinal fluid and the Wassermann reaction, mastic and gold-sol curve were all negative.

Encephalography showed a marked degree of brain atrophy on the left side. There was marked widening of the left lateral ventricle which reached to the surface of the brain where there was also a large collection of air. It seemed as if the left lateral ventricle was subdivided into a number of cysts. The whole ventricular system was drawn to the left as the result of atrophy of the left hemisphere. There was widening also of the third ventricle.

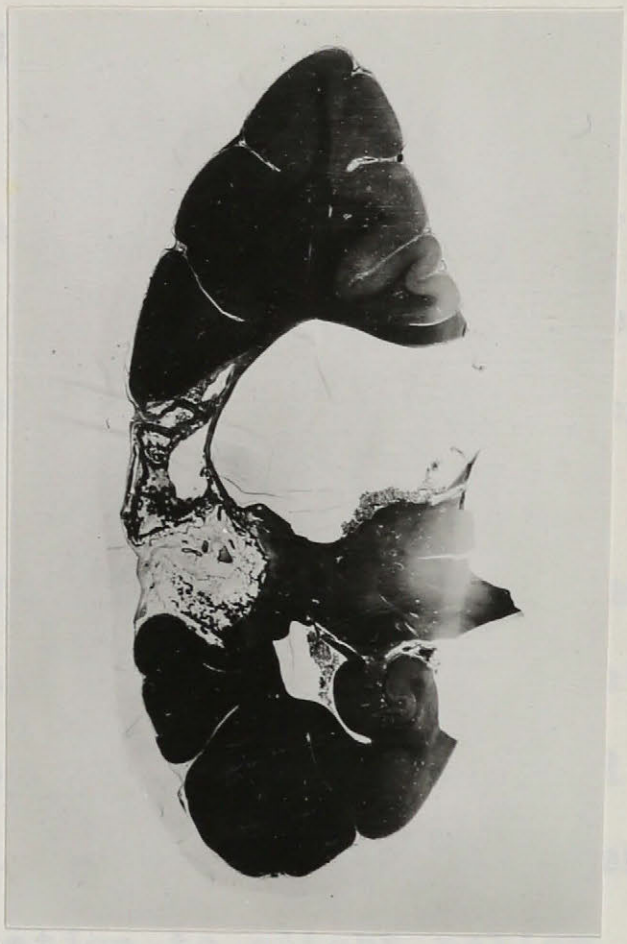
An exploratory craniotomy was carried out on this patient but circulatory collapse and death occurred two hours post-operatively.

Autopsy revealed that in addition to the pathological condition in the nervous system, there was status thymo-lymphaticus. There was hemiatrophy of the left cerebral hemisphere (Fig. 21) and right cerebellar hemisphere. Massive degeneration and absorption of cerebral tissue were to be seen in the left cerebral hemisphere, with enlargement of the left lateral ventricle and of the left half of the third ventricle (Fig. 22).

Fig. 23.

Ger. Kas. Hematoxylin and van Gieson. Note particularly the islets of glial tissue and the multilocular nature of the cyst.

Fig. 23.



The area of degeneration, cyst formation, honeycombing and loss of substance (Fig.23) involved the foot of the precentral and postcentral gyri, the inferior margin of the surface of the marginal gyrus, the whole of the angular gyrus, the superior temporal convolution and the upper half of the middle temporal convolution. The pia-arachnoid over this involved area was thickened and gray and there was a distinct depression in the zone overlying the degenerated material. The cyst formation was lined externally by the inner face of the pia-arachnoid which was studded with pinpoint bits of cerebral tissue.

The thalamus was reduced to about half its normal size, the internal capsule was very small and the sclerotic edge of the huge cyst extended to the lateral regions of the basal ganglia.

Microscopically the corpus callosum showed no definite changes other than a reduction in bulk and the stratum griseum appeared normal. The cingulate, postcentral and superior parietal gyri showed diffuse loss of cells due to ischemic changes which ranged from obliteration to slight pallor. In the lower half of the superior parietal gyrus the indiscriminate loss of cells became more marked and when the cystic areas were reached only very small islands of cells remained and these were so pale as to be almost indistinguishable as neurones. In the paracentral gyrus the cells were better preserved and only a few showed chronic ischemic changes.

In the area of degeneration there were small islets of degenerating astrocytes which had formed abundant fibers and these islets were loosely embedded in connective tissue.

The middle temporal convolution rapidly approached normality away from the cystic area. In the immediate neighborhood of the cyst there was a general paucity and pallor of cells. Occasional pyknotic, shrunken cells with shrivelled processes were to be seen. The third temporal convolution showed similar cellular changes of a lesser degree. In the hippocampal gyrus there were some areas of focal cell loss and some cells showing chronic changes. In the thalamus the small cells showed no definite changes but scattered large cells showed chronic changes of anemic type, pyknosis, shrunken, displaced nuclei and glassy cytoplasm. This was particularly true of the dorso-lateral cell group. In the caudate nucleus occasional cells could be found showing chronic changes but in the claustrum, putamen, globus pallidus and lateral geniculate bodies no cellular changes were found.

Fiber tract degeneration could be followed through the pons and into the brain stem. There was almost complete loss of the pyramid on the left side at the level of the inferior olive and the opposite pyramid appeared to be actually hypertrophied.

The dilated left lateral ventricle was irregularly lined with ependyma which laterally was often defective and replaced by thickened astrocytes. The lining of the third ventricle was normal.

There was dense chronic thickening of the pia-arachnoid without cellular infiltration, except at the base, but with abundant collagen formation over the intact gyri and the intervening sulci. In the region of the cystic degeneration

there was arachnoidal and connective-tissue infiltration as deep as the ependyma. In the cellular interstices there were scattered numerous heavily laden phagocytes. The connective-tissue infiltration was not altogether made up of a loose meshwork, but in places of a heavy collagenous feltwork.

In those parts of the brain and meninges not directly involved in the cystic changes the blood vessels presented as their only abnormality a perivascular cuffing of lymphocytes that undoubtedly was due to the fatal post-operative hemorrhage. In the cystic area there was vascular proliferation that took an active part in the process of scarring. There was also a gliosis of small-cell type, with abundant fiber formation. Within the area of cyst formation the presence of fat could be shown in macrophages, indicating an active phagocytosis fourteen years after the ictus.

COMMENT:

The anatomical distribution of the lesions in the three clinical cases leaves little room to doubt that the pathological process has centered about the middle cerebral artery as a whole, or about one or more of its branches. The resemblance of the clinical cases to the experimental lesions is striking. However, the degree of gliosis and connective-tissue proliferation in the second and third clinical cases is deserving of attention and should be compared with the histological picture seen in the first case. We shall return presently to a consideration of this question.

At this point it would be well to emphasize that the histories are not of positive value in determining the nature of the pathological processes responsible for the lesions.

Birth injury seems to be ruled out in all. It is possible that in the second case the neurological disability developed in utero and was not recognized until the end of the first week of life. In the third case the history of "Kinderlähmung" is vague and is not supported by details. We are, therefore, unable to define the nature of the process to which we would attribute the arterial occlusion in these cases, but we would emphasize our belief that it is arterial in distribution. It is true that we have not proven experimentally that venous occlusions will not produce similar changes. Watts (1934) has shown that the unilateral clipping of four or five of the chief tributaries of the median longitudinal sinus of the monkey produces no gross cerebral lesion. It would seem very likely that an extensive obliterative process in the venous circulation would be necessary to produce focal lesions, and our clinical cases showed no evidence of such a process. Therefore, we believe that venous occlusion is not responsible for the clinical results we have cited, and we think it unlikely, though not irrefutably proven, that obstruction of the venous circulation could produce lesions similar to those we have here demonstrated.

Furthermore, we believe that intracerebral hemorrhage can be ruled out in these cases for three reasons: 1) the extent and distribution of the lesions, 2) the absence of late tell-tale signs of hemorrhage, e.g., bile staining and the presence of hemosiderin crystals, and 3) the absence of adhesions between the pachy- and the leptomeninges in the first two cases, and their probable absence as judged from observation of the pathological specimen in the third case.

Fig. 24.

Same specimen as fig. 16. Note the sharp border of the cyst, and the preservation at the cyst's periphery of gross anatomical configuration.

Fig.24.

We have already drawn attention to the similarity in anatomical distribution and the disparity in the pathological appearance of cases two and three as compared to case one and the experimental lesions. An explanation of the disparity is called for and we believe that the greater gliosis and connective-tissue proliferation in the last two clinical cases is the result of the establishment of collateral circulation in the periphery of these two lesions. Unfortunately we know as yet of no way of producing a slower occlusion of an artery than the sudden interruption produced by the placing of a silver clip, so that experimental proof of our contention is lacking. However, as has been demonstrated above, sudden occlusion of a large artery produced experimentally leads to the formation of a relatively benign cyst. The condition in the first clinical case is very similar in nature to that of the experimental cases, though of lesser extent (presumably the condition resulted from sudden occlusion of the vessels of supply to the Rolandic region, the other branches of the middle cerebral artery not being directly involved in the process). Figure 24 demonstrates clearly the sharp border of the cyst and the preservation at the cyst's periphery of gyri which have retained their gross anatomical configuration, though microscopic study shows many cellular changes indicating a disturbance of circulation of lesser degree in these gyri.

It appears then that sudden ischemia of a large portion of brain tissue leads to a central necrosis and the eventual absorption of the central core of tissue. At the periphery, however, one finds a slight to a moderate degree

of gliosis and connective-tissue hypertrophy with few or no nerve cells present. This is not a surprising finding , for it is a well known fact that a relative anemia leads to neuronal loss with the development in the involved area of glial and connective-tissue hypertrophy, providing the anemia is not severe enough to lead to the death of glia and connective tissue.

It, therefore, seems reasonable to believe that the relatively benign appearance of the experimental cysts is due to the fact that clipping being sudden, there is relatively little opportunity for collateral circulation to become established about the periphery of the anemic zone. Hence the area of central necrosis is great, the zone of glial and connective-tissue hypertrophy is narrow. If, on the other hand, the occlusion is relatively slow - perhaps in terms of hours, perhaps in terms of days: the evidence is insufficient to decide - there is a consequent broadening of the zone of hypertrophy about the cyst, with the result that the cyst's periphery becomes surrounded by an outer covering of tough glial tissue, heavily infiltrated with new vessel growth. Hence one finds the histological appearance to be seen in the second and third clinical cases.

Specific note has not been made, except in the third clinical case, of the microscopic changes underlying the general atrophy of the affected hemisphere observed in the clinical and experimental cases alike, but attention should be drawn to the fact that atrophy of cells at a distance has been observed, affecting even the contralateral hemisphere. Such atrophy, which we have not studied in detail, is apparently secondary to degeneration in association and commissural fibers.

Some comment upon the question of red infarction must be made. As has been stated, the cut section of the brains of the experimental animals, sacrificed at all periods - from one to one hundred and eighteen days after operation - failed to show evidence of red infarction. The most satisfactory explanation of this finding, surprising in view of clinical experience, is that the peristent, though much reduced, circulation in the leptomeninges (and presumably therefore) in the cerebral substance, is adequate to preserve the integrity of the vessel walls, so that diapedesis does not occur. If this be the correct interpretation it but serves to emphasize the far greater dependence of neurones, than of connective-tissue elements, on normal blood supply, and it is of significance that the structures that tend to remain after complete sudden occlusion of a vessel are those making up the vascular tree, and to a very much lesser extent the interstitial cells, whereas neurones suffer to the greatest extent. Furthermore, the occurrence of massive destruction of cerebral tissue such as has been described, unaccompanied by red infarction or other evidence of severe vessel damage, is strong presumptive evidence against the clinical conclusion of Globus and Strauss (1927) that local cerebral destruction is an essential precursor of cerebral hemorrhage.

Finally, it seems legitimate to conclude that the probable reason red infarction is seen frequently in clinical cases is that the cerebral vessels in these cares are often so diseased that after occlusion centrally (e.g. by embolism), blood flow is reduced so low - because of diseased peripheral vessels with diminished caliber - that even the vessels, most resistant to oxygen lack of all structure concerned, are

unable to receive sufficient nourishment. Hence diapedesis and hemorrhage occur. The late histological result would in such a case be different from that to be expected in a similar occlusion in a brain with healthy vessels, for in the former case the outpouring of blood either in the form of multiple petechial hemorrhages, or as a single massive hemorrhage, would stimulate scar tissue formation (see chapter on intracerebral hemorrhage). On the contrary, as has been demonstrated, when the vessels are healthy, sudden complete occlusion results in cystic degeneration in the peripheral distribution of the occluded vessel.

In conclusion, the need of clarification of the changes underlying the "fixed lesions of the brain" (Crothers, Vogt, and Eley, 1930) is evident and we believe that the facts and the interpretations presented above may be of value in this regard.

SUMMARY:

1. Various stages in the development of the late anatomical changes resulting from experimental occlusion of the main branches of the middle cerebral artery are described.
2. Three clinical cases are presented for comparison with the experimental material.
3. It is suggested that the anatomical end result of occlusion of the middle cerebral artery or its branches gives a definite anatomical picture.
4. It seems possible that the gradations in the histological picture found in such cases may be due to the relative rate of occlusion of the middle cerebral artery, i.e., that sudden occlusion with massive softening leads to cyst

formation, that slow occlusion provides opportunity for the establishment of collateral circulation in the periphery of the softened area and therby allows proliferative glial and connective-tissue changes to take place. As a result, greater cicatrization is found in such cases.

5. Sudden complete occlusion of the middle cerebral artery in monkeys possessed of a normal vascular tree is unaccompanied by red infarction. It is suggested that the diminished circulation persisting after the occlusion, though insufficient to support the life of the parenchymal tissue, is adequate to preserve the vessel walls and to prevent diapedesis. It follows as a probable corollary that "red infarction" occurs clinically when the vessel walls are so diseased that the impaired circulation following sudden occlusion is still further impaired by pre-existing vascular disease with the result that the vessel walls are so poorly nourished that diapedesis occurs through them.

IV. INTRACEREBRAL HEMORRHAGE.

In the preceding chapter we have discussed the morbific physiology of one form of apoplexy, that of cerebral embolism, and we have attempted to show the relation of the disturbed physiology to the production of cerebral scarring. We now propose to discuss another of the large sub-groups of apoplexy, that of hemorrhage, again from the standpoint of its morbific physiology and the disturbances which result in scar tissue formation.

As the result of much intensive research, particularly on the part of the German investigators, notably Ph. Schwartz (1930), a much clearer conception of the mechanism of cerebral hemorrhage is now had. The early views of Conheim on diapedesis from plugged terminal arteries have now been abandoned.

Similarly, the miliary aneurysms described by Charcot and Bouchard, and regarded by them as the sites of origin of cerebral hemorrhage, have become subject to reinterpretation. Modern views on hemorrhage associated with arterial hypertension are best set forth in English in the recent work of Chase (1937). Inasmuch as we are here directly concerned with the etiology of hemorrhage only insofar as it helps to explain the later cicatricial changes, we shall only cite briefly the conclusion which Chase draws from a study of eighteen cases of hypertension and brain hemorrhage, without associated arteriosclerosis. He accepts Ricker's conception of neurovascular tonus and argues that in

hypertension there is a condition of vascular hyperinstability and increased neurovascular tone - reflected anatomically by hypertrophy of muscular arteries. In transient hypertension he has not infrequently observed petechial hemorrhages from the capillary bed. In long-continued hypertension even large hemorrhages may occur from the capillary bed and from the vasa-vasorum of hypertrophied paretic muscular arteries, leading eventually to massive bleeding. The histological picture of these pericapillary hemorrhages he has found to be similar to the picture of small vessel hemorrhage seen in the living rabbits' mesentery following the application of irritants.

Accepting this modern interpretation of the mechanism of intracerebral hemorrhage one is struck by the obvious implication - that a variable degree of circulatory insufficiency is present. Whether, then, the bleeding be from the peri-vascular hemorrhages of hypertension or whether it be due to the frank rupture of an aneurysm, the effect of the poured-out blood is to destroy by direct extension - and probably by fermentative action - the tissue immediately adjacent. Contiguous tissue must also be destroyed by partial mechanical occlusion of its blood supply - which mechanical occlusion is further heightened by the edema which we have, in the preceding chapter, clearly shown to be associated with inadequate circulation. Degenerative ganglioncell changes in the peripheral zone of perivascular hemorrhage about a large intracerebral hemorrhage is further presumptive proof of such inadequate circulation (vide Fig. 242 Grinker, 1934).

Fig. 25.

a.) "Punctate extravasation of blood cells extending out from a terminal segment in brain of case of transient hypertension. The blood cells in the vessel at either end of the hemorrhage are conglutinated. This indicates that blood movement continued after the hemorrhage occurred. X 200" (Chase, 1937).

b.) "Focal hemorrhage probably from terminal districts adjacent to the intact small artery in prolonged hypertension. The distal half of this vessel is thrombosed, while the cells in the proximal half are still conglutinated. X 90". (Chase, 1937).

Fig. 25a.

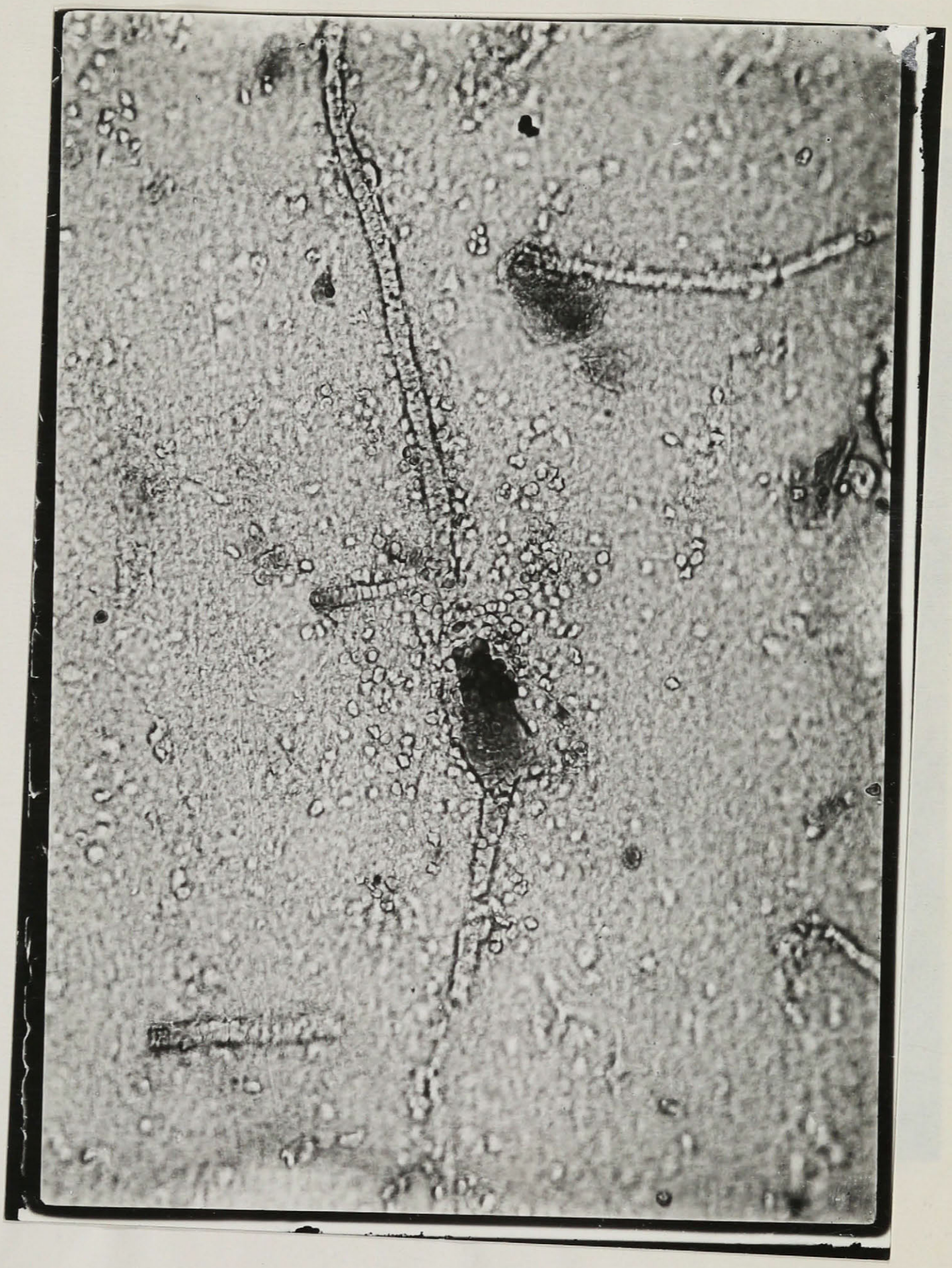


Fig. 25b.

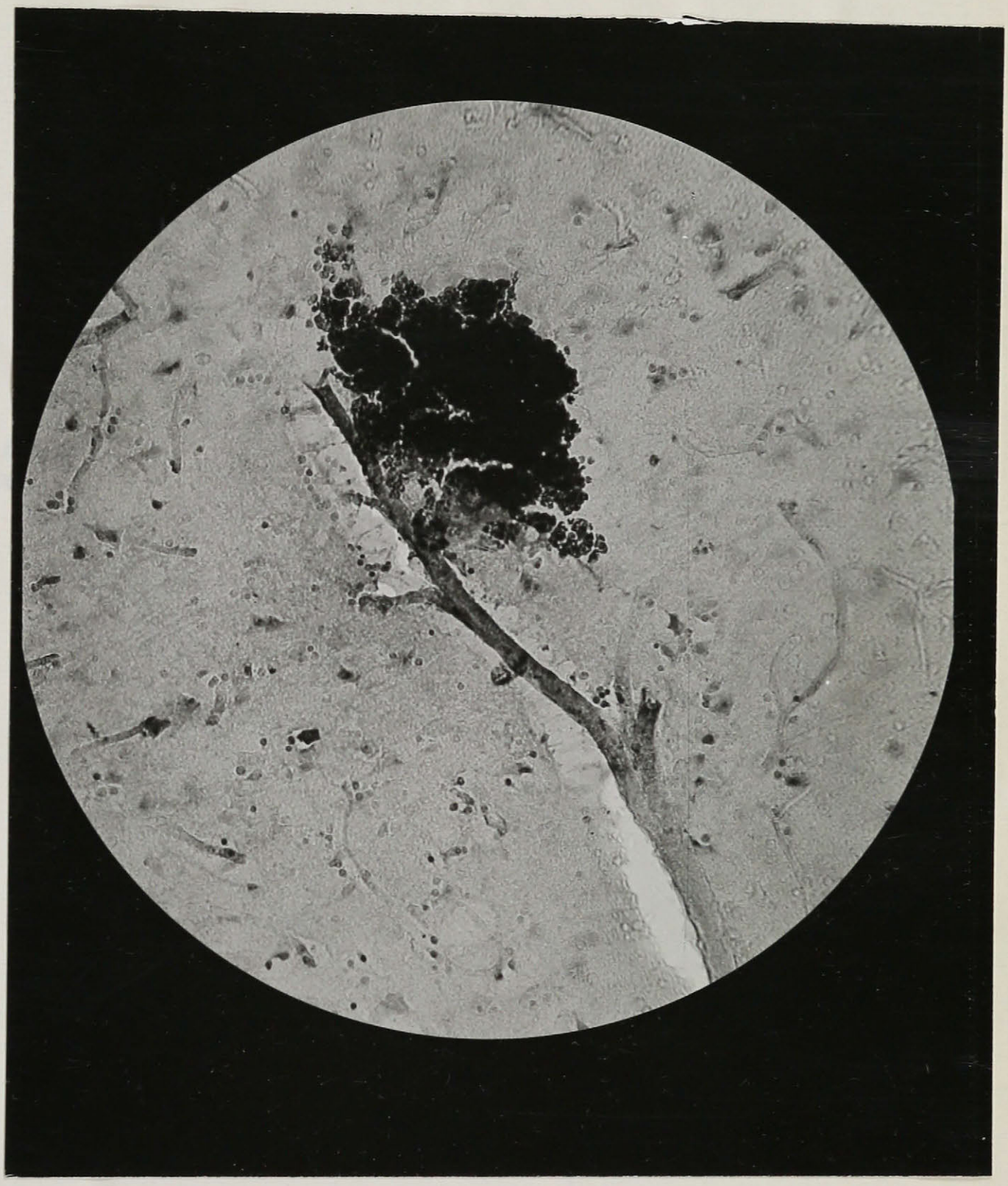


Fig. 26.

Fig. 82 from Schwartz, 1930. Late apoplectic damage, whose origin Schwartz regarded as uncertain. We regard it as the end result of hemorrhage.

Fig. 26.

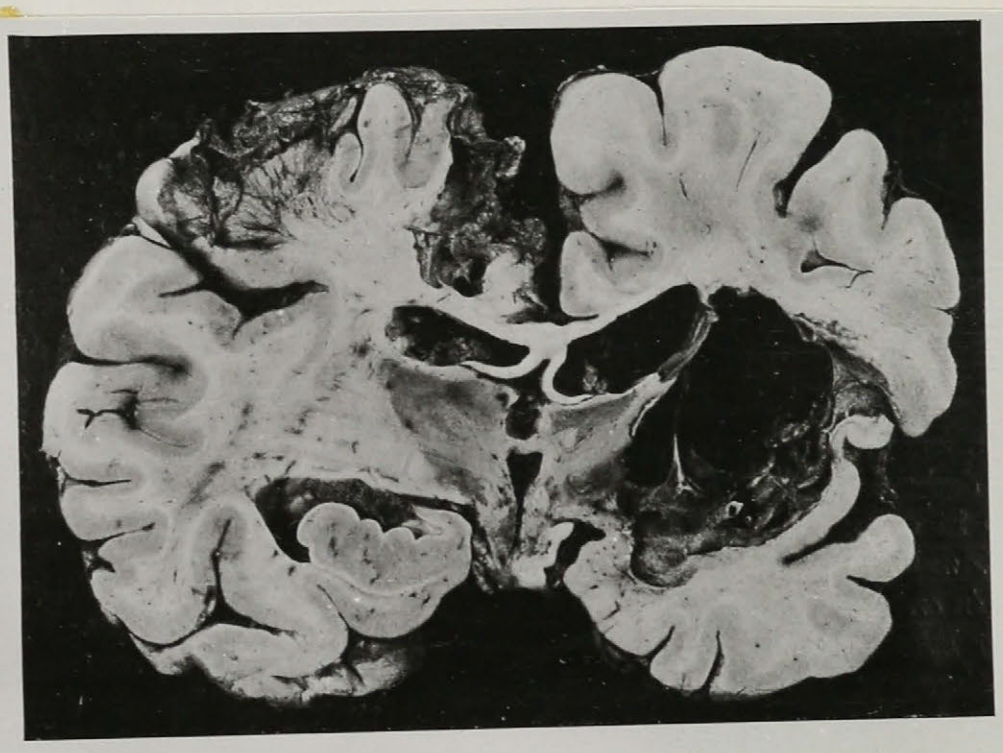


Abb. 82. Große alte Erweichungshöhle nach apoplektischer Schädigung. Nähere Genese unklar.

The early stages of cerebral hemorrhage (in hypertension) are well illustrated by Chase, from whose article the accompanying illustrations are taken (Fig.25). An excellent illustration of a late stage of cerebral hemorrhage is shown in figure 26 from Ph. Schwartz's monograph (1930, Fig. 82). The late cystic changes in the left hemisphere we, in agreement with Hiller, regard as the end result of hemorrhage, though Schwartz himself regarded its etiology as not clear.

It is not difficult to visualize on theoretical grounds the changes which may be expected to occur in the later stages on the basis of what has already been said of the development of collateral circulation. Complete destruction of the central core may reasonably be expected to result in an eventual absorption and digestion of the necrosed tissue. As one proceeds peripherally from the center of the lesion there will be successive changes in tissue until normal brain parenchyma is reached. These changes will occur in zones from within, outward - first a zone about the core where proliferated connective tissue and glial elements alone will persist. Because of irregularities in degree of blood supply there will be much irregularity in the structures in this zone, and multilocular chambers made up of varying degrees of proliferated glial and connective-tissue elements may be found. Proceeding further outward these elements will more and more approach their normal structure, but meantime occasional shadows of neurones will make their appearance - lagging behind the more nearly normal connective tissue and glial structures because of the greater sensitivity of nerve cells to oxygen lack. Eventually toward the periphery, neurones which have

Fig. 27.

Fig. 74 from Hiller, 1936. "Angionecrosis" and diapedetic hemorrhage in the region of "artificial hemorrhage". Five hours after the injection of blood.

Fig. 27.

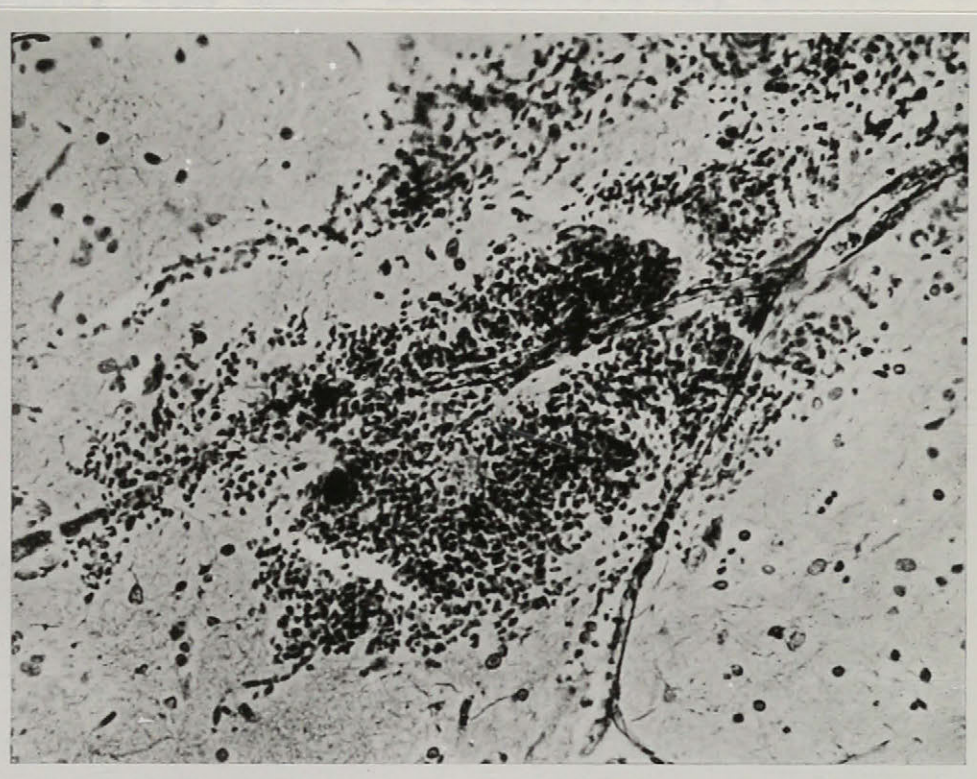


Abb. 74. „Angionekrose“ und diapedetische Blutungen aus kleinen Gefäßen und Capillaren in beginnend nekrotischem Hirngewebe (vorwiegend Ödem) im Randbereich einer artefiziellen Blutung; 5 Stunden nach Injektion des Blutes.

suffered only partial damage will appear, and finally brain normal in all respe cts may be encountered if the insult has not been too severe.

Detailed histological considerations and the support for the contentions cited above will be found in the section on experimental cerebral hemorrhage which follows.

EXPERIMENTAL INTRACEREBRAL HEMORRHAGE:

Until satisfactory methods are developed for producing hypertension and hypertensive intracerebral hemorrhage in experimental animals, one must be satisfied, so far as histology is concerned, with a study of the changes following the injection of blood directly into the cerebral substance. Indeed, according to Hiller, the intracerebral injection of blood mimics in its effects very closely those of massive bleeding in humans. In his 1936 monograph he reviews his earlier work on the histological changes that occur in the first two or three weeks following the injection of blood into the cerebri of dogs. In the course of a few hours he found focal changes resembling in all respects apoplectic bleeding: a more or less complete structural necrosis, with countless hemorrhages out of and around damaged blood vessels. Figure 27 shows an early typical form of perivascular hemorrhage (Hiller, fig. 74). There could be found in the necrotic tissue vessels with obliterated lumina and necrosed walls. He concludes that as the result of intracerebral hemorrhage there occurs a secondary stasis, due to functional disturbances in the circulation. This stasis, and ferments derived from the extravasated blood, add their effects to the primary damage caused by the initial outpouring of blood.

On the basis of Hiller's findings it seems legitimate to assume that the late histological changes following the injection of blood may be regarded as reproducing fairly faithfully those following intracerebral hemorrhage in the human.

The most succinct description of the cellular changes following the injection of whole blood into the brain substance is that of Carmichael (1929) who injected into the brain of rabbits .5 cc. of blood drawn from an ear vein. He studied animals killed at various intervals up to twenty-two days. He found that in twenty-four hours the microglia were increased in number and had begun to undergo characteristic swelling of the cell bodies and retraction of their processes. At the end of four days "nerve cells" that appeared to be "large macrophage cells, closely resembling those derived from the reticulo-endothelial system" made their appearance, cells that since the work of D. Russell (1929) must be regarded as phagocytic microglia. The maximum change in microglia was observed at seven days and by twenty-two days there were only a few cells remaining in the region of the wound, and the cells around the wound now appeared as normal microglia.

Carmichael found that the astrocytes underwent early regressive changes, first evident at twenty-four hours. But by seven days there were many swollen astrocytes in the wound region proper and outside the normal area there were cells dividing by amitotic division. In other words, a proliferative reaction was under way at this stage. By the twelfth day the wound area was found walled off by large astrocytes with a fair amount of perinuclear cytoplasm, and with thick processes. At twenty-two days "the most striking feature of the picture

was the excess of fibrillary astrocytes walling off the wound from the surrounding structures".

Meantime there had become evident at twelve days a new blood-vessel formation which by fifteen days was quite definite. No note is made of the blood vessels at twenty-two days and his figure 6, a silver stain to show the fibrillary astrocytes, is not well enough reproduced to permit one to form an opinion as to blood-vessel formation at the twenty-two-day stage. The injected red blood cells were found to have begun to disappear in five days and by twelve days none were to be found, though many phagocytes could be seen laden with fine, high refractile yellowish crystals.

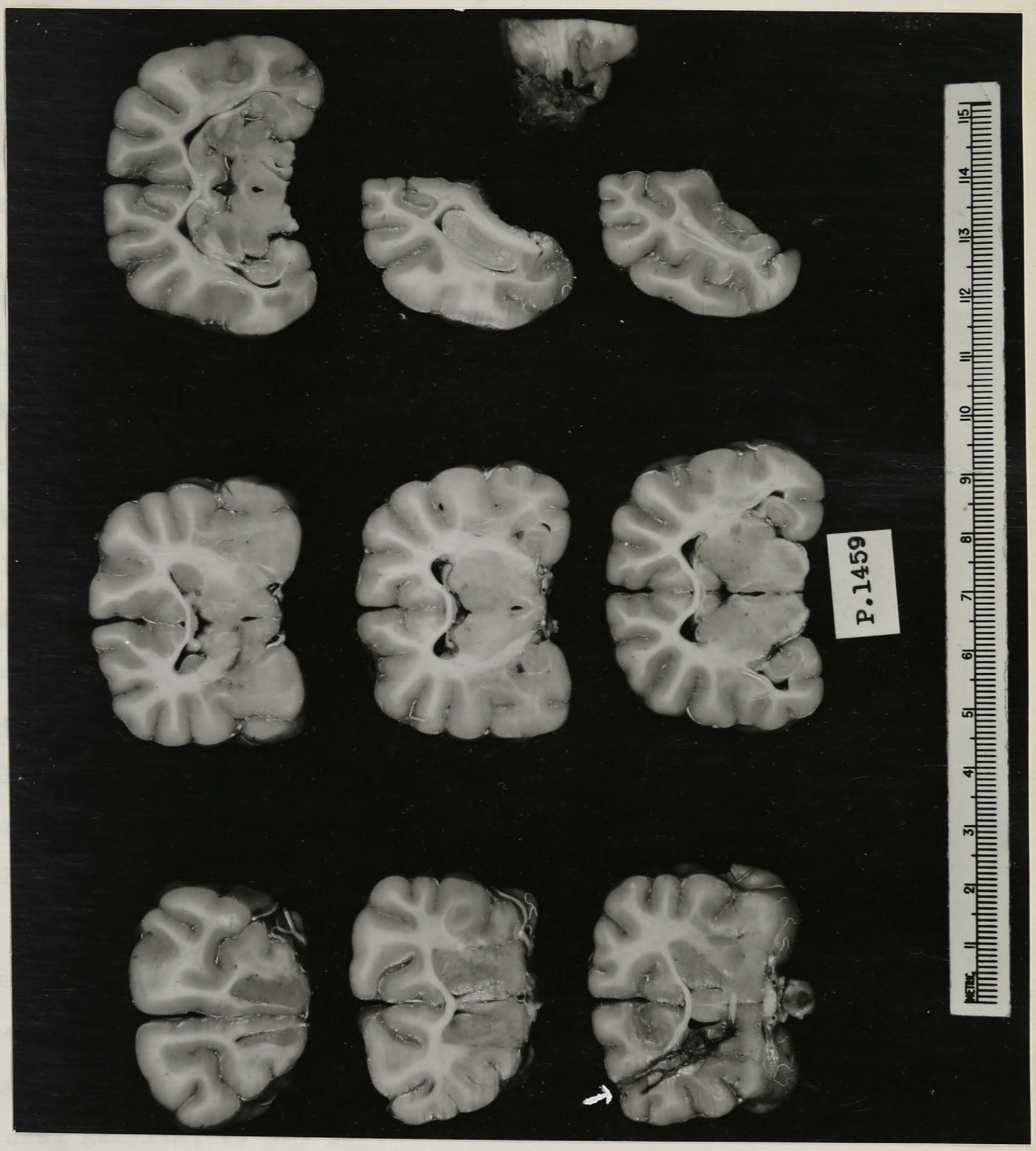
The experiments of Hiller in which he injected blood into the cerebri of dogs and studied the changes for about the same period of time as did Carmichael, add one point of great importance for, as already indicated, he showed the blood-vessel changes and diapedetic hemorrhages about the periphery of his lesions and he correlated his findings with the earlier work of Ricker on the changes in the vascular bed which follow trauma. Confirmatory of his experimental findings is the clinical work of Chase, already cited (1937) on cerebral hemorrhage in arterial hypertension in which he has shown multiple foci of perivascular hemorrhage.

So far as we have been able to find no one has studied the <u>late</u> histological changes resulting from experimental injection of blood into the cerebral hemisphere. Cajal (1928, pp. 730 et seq.) though describing the reactions about hemorrhagic foci resulting from cerebral laceration, is no doubt dealing with essentially the same histological

Fig. 28.

Injection of 2 ccs of whole blood made into the right parietal region of a dog two months before death. The arrow indicates the site of injection. (The change in the occipital pole, to the right of the picture, is irrelevant).

Fig. 28.



problem. He describes in detail the occurrence of fluid-filled cysts surrounded by new blood vessel formation, which are in turn surrounded by a zone of hypertrophied astrocytes.

To study the late changes of uncomplicated experimental hemorrhage we have made injections into the hemispheres of dogs and of monkeys. The animals were sacrificed at periods of two to three months after the "ictus" and their brains studied.

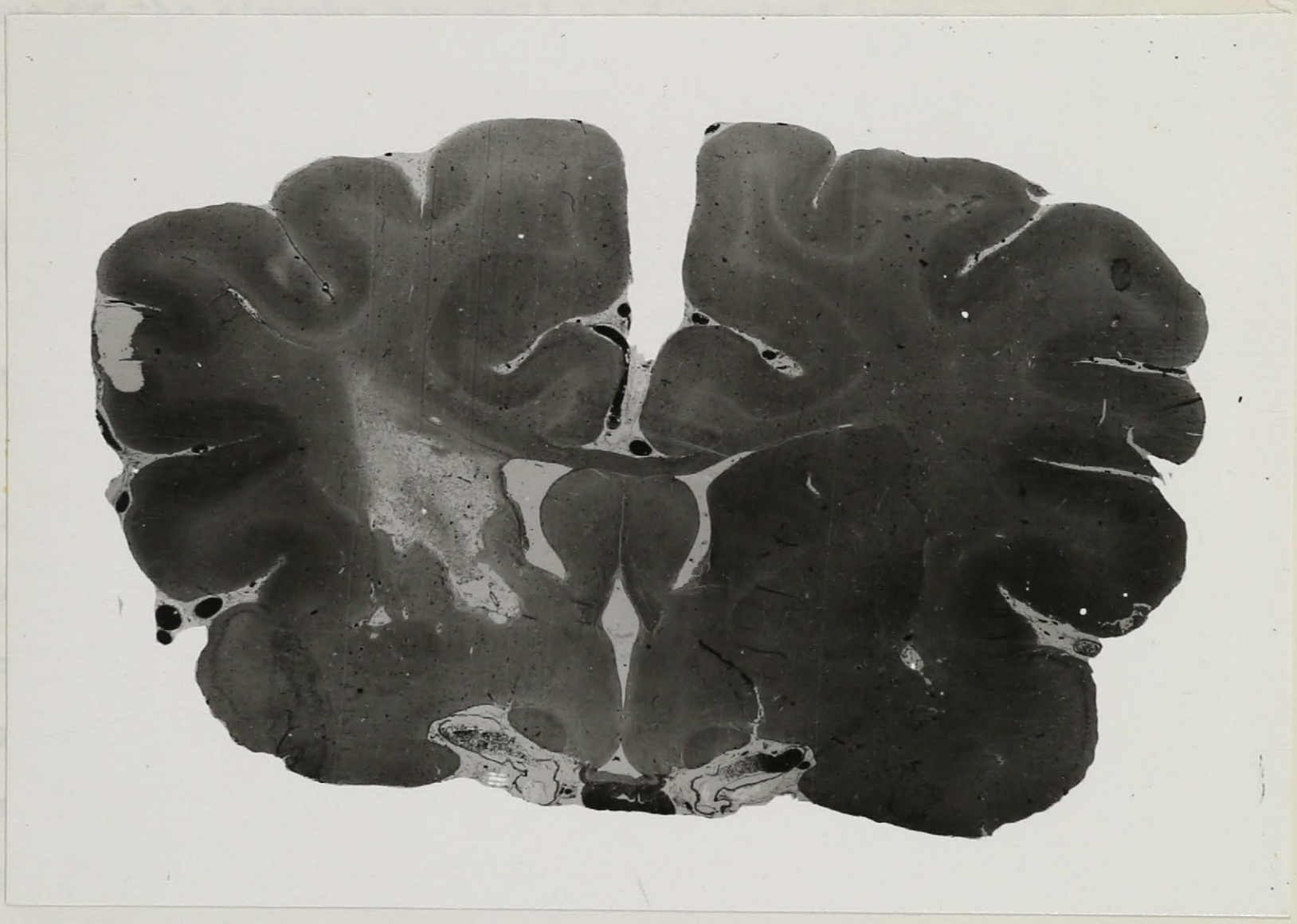
Dog P-1459 was operated upon twice before death. At the first operation two brain wounds were made, one in the right frontal region, the other in the left occipital region. These wounds need not concern us. Suffice it to say that the left occipital region wound bore some resemblance to the area about to be described, the site of the injection of whole blood. This procedure was carried out two months before the dog was sacrificed and a small unguarded drill was used for making the trephine opening. It broke through the internal table of the skull and plunged through the brain almost to the base. The animal gasped but after a moment continued breathing, and thereafter two cc. of blood were injected into the wound track.

When sacrificed at the end of two months the brain showed the changes depicted in the photograph (Fig.28). To be noted particularly are, 1) the loss of bulk in the right hemisphere, 2) the massive degeneration in the region of the basal ganglia, 3) the proliferated tissue in the region of degeneration, 4) the staining and blood pigment in the involved area, 5) the local dilatation of the ipsolateral ventricle in the region of the loss of substance, 6) the shift of the

Fig. 29.

Hematoxylin and van Gieson preparation of a part of the area shown in fig. 28.
See text for description.

Fig. 29.



ventricular system toward the side of atrophy, 7) the loss of bulk in the peduncle on the right side.

The findings indicate clearly that there was an extensive loss of substance on the side of the hemorrhage. Such a loss of substance might be due only to local tissue destruction caused by the presence of the injected blood, but evidence has already been presented to suggest that there occur about such lesions profound vascular disturbances, so that some of the atrophy may well be dependent upon anemia secondary to functional vascular changes in the area surrounding that of the primary insult.

Microscopically this brain failed to show, as is to be expected at such a late stage, any direct evidence of functional vascular disturbance. There were found a large area of cystic degeneration (Fig.29) traversed by loosely fenestrated glial strands, an adjacent zone of active degeneration, and surprisingly little connective-tissue reaction, new-vessel formation, or infiltration by fibrous elements of contiguous normal tissue. Scattered traces of bismuth were found in the center of the cystic area providing evidence that there were present some large patent vessels. Along the tracks of the needle was found very slight glial fenestration, with slight interlacement of collagen. In its essentials the reactive process was a cystic degeneration surrounded by almost no connective-tissue proliferation and by only slight glial hypertrophy.

Scarring of greater degree was found in a second animal, a monkey (P-1571), that underwent three injections at intervals of seventy-four, sixty-seven and ten days before

Fig. 30.

The brain of a monkey 67 days after injection of 3 ccs. of whole blood into the right parietal region. The arrows indicate the extent of the lesion.

Fig. 30.

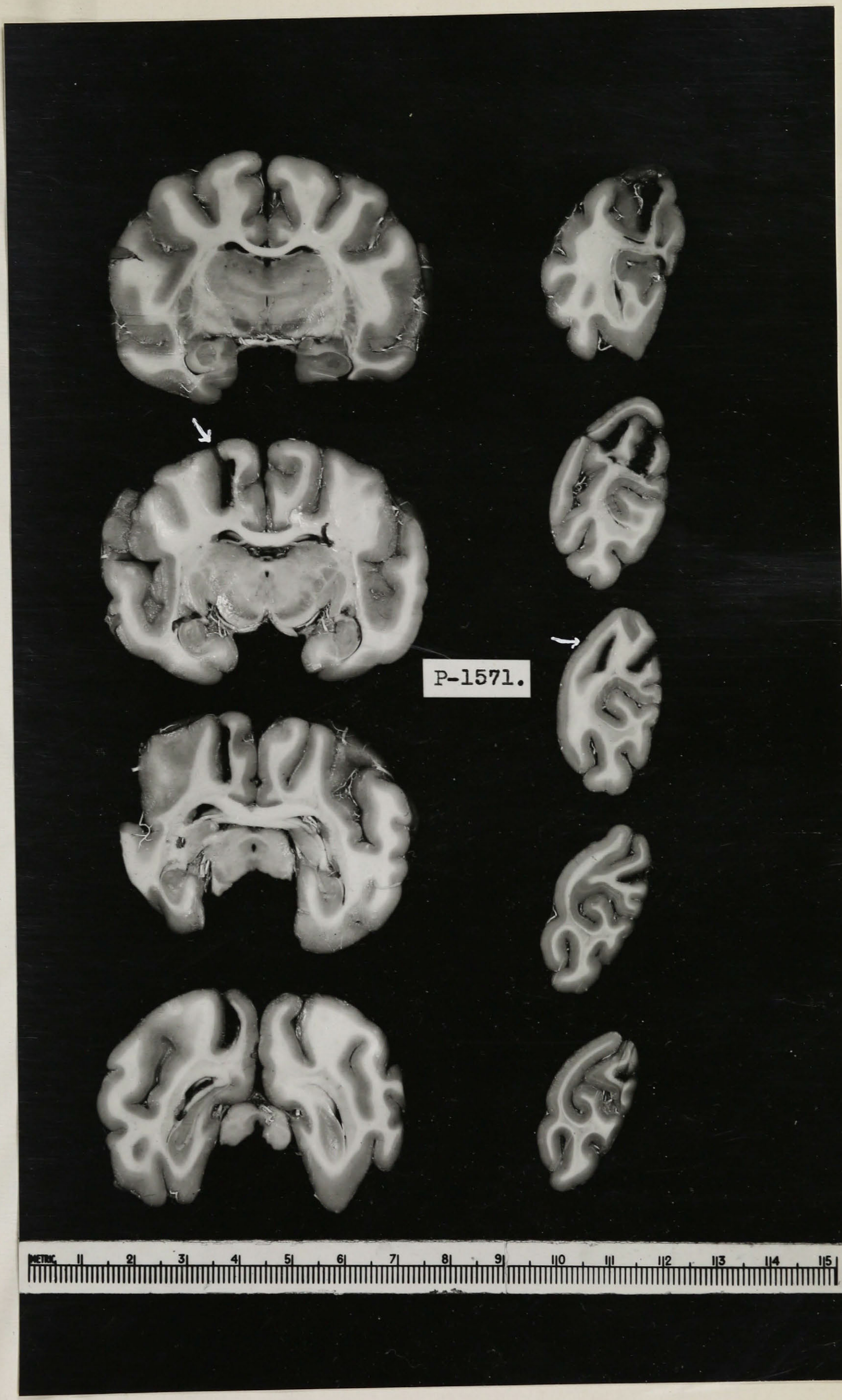
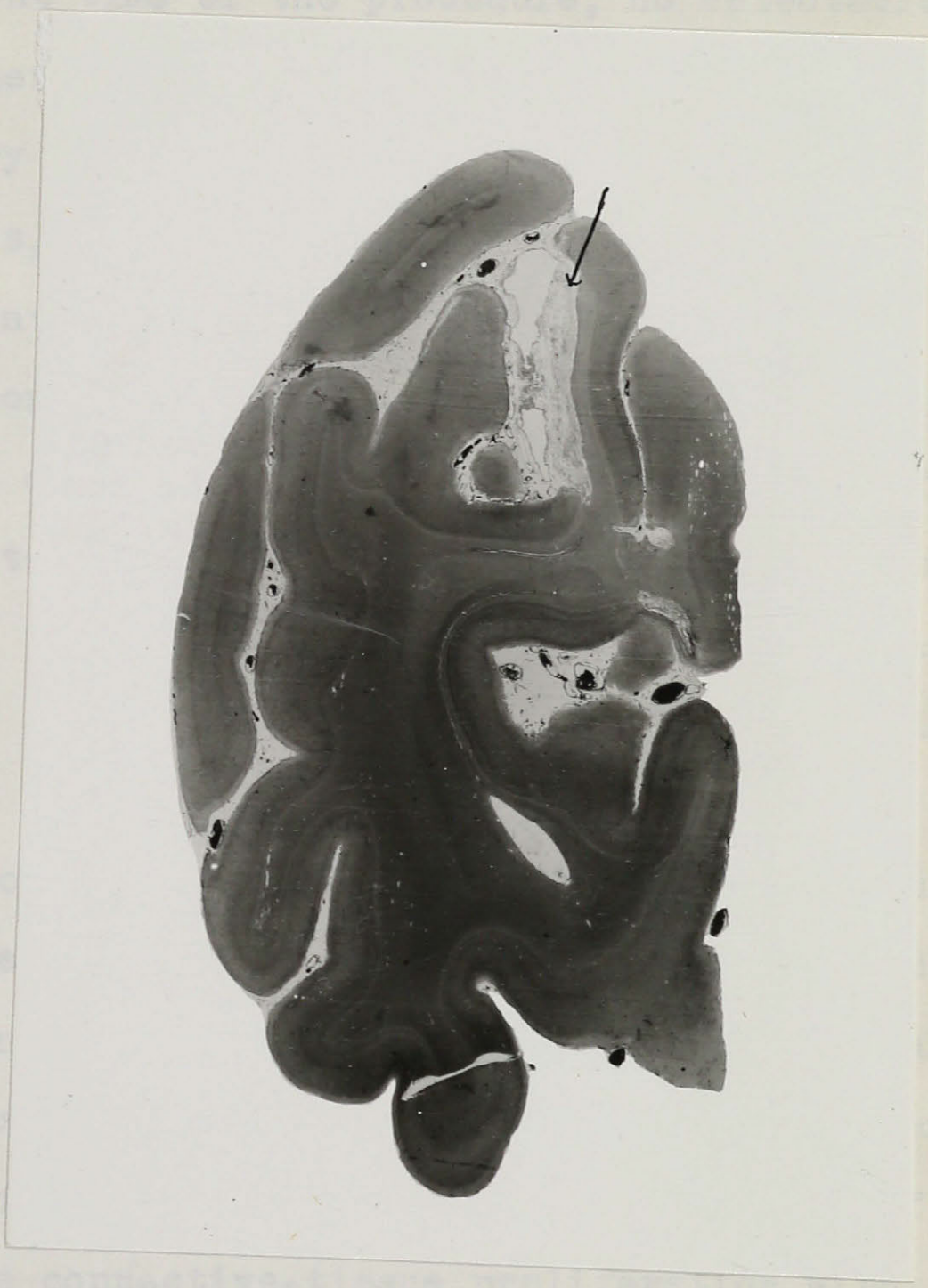


Fig. 31.

Hematoxylin and van Gieson preparation of the zone of damage seen in fig. 30.

Fig. 31.



death. In the first procedure 2 cc. of blood were injected into the left parietal region while the surface of the brain was observed microscopically through a brain window. The experiment was done for two purposes: 1) to see whether, in association with the "hemorrhage", any obvious vasomotor disturbances would occur; 2) to produce a late lesion of "hemorrhage". There occurred, at the time of the procedure, no detectable vascular changes other than, a) an increased pulsation of the arteries, and b) very doubtful perivascular hemorrhages about the meningeal vessels, which probably represented escape of the injected blood into the subarachnoid space.

In the second procedure - with which we are particularly concerned - 3 cc. of the animal's blood were withdrawn from a leg vein and injected through a small drill opening in the skull into the right posterior parietal region. Finally, in the third procedure, 4 cc. of normal saline were injected into the frontal region.

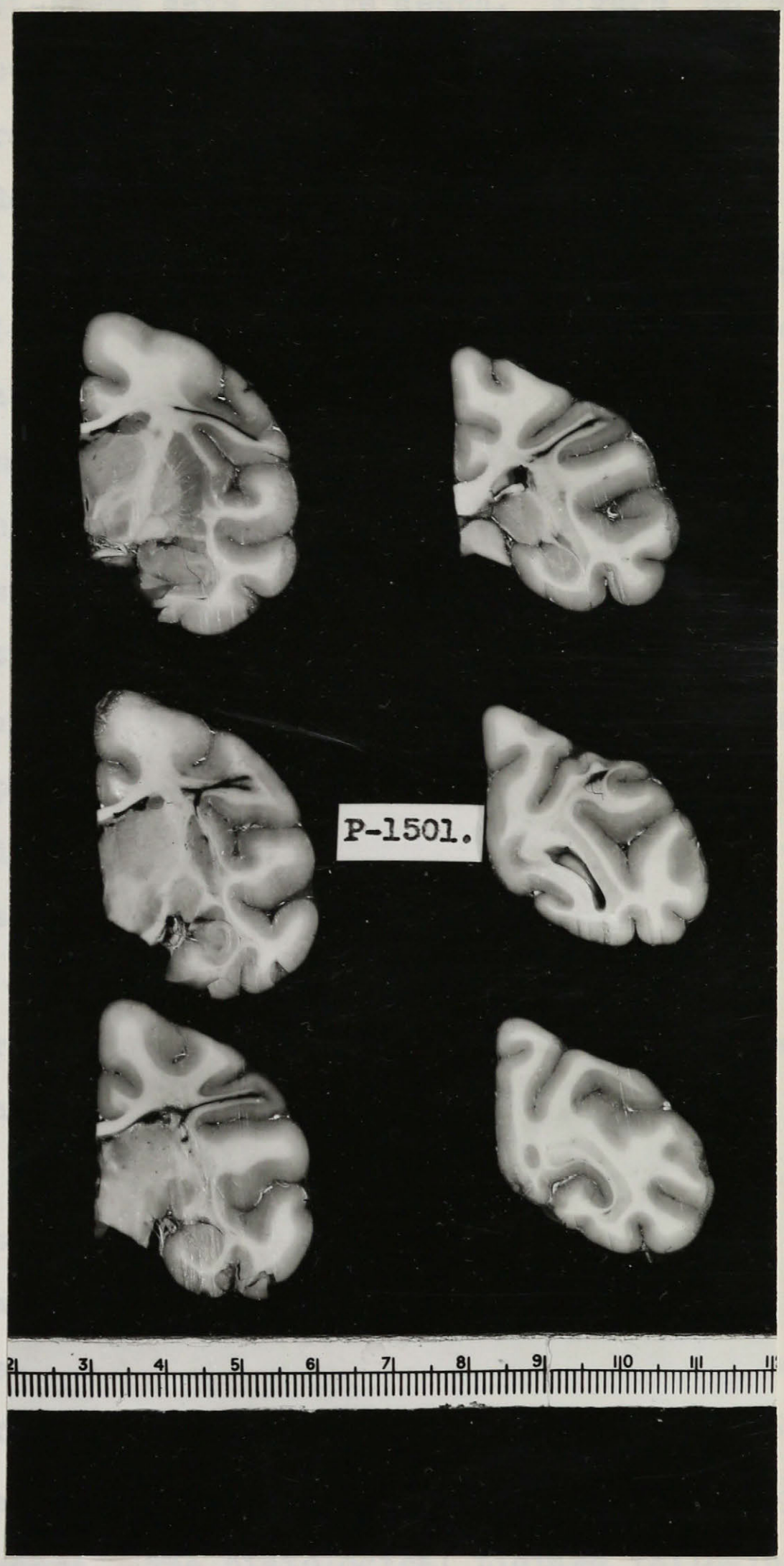
We shall concern ourselves with the second lesion, one of sixty-seven days' duration. Figure 30 shows, in cross section, the appearance of the involved area. Microscopically there was found an extensive separation of tissue by a degenerative zone heavily infiltrated with phagocytes. Portions of the area are invaded by a connective-tissue proliferation with, in some zones, the formation of heavy collagenous tissue. Figure 31 shows the general nature of this process.

In another monkey (P-1501) three procedures were carried out: 1) amputation of the right frontal pole one hundred and forty-three days before death, 2) injection of 2 cc.

Fig. 32.

The brain of a monkey eighty-seven days after the injection of 2 ccs of blood into the left parietal region.

Fig. 32.



of blood into the left parietal region eighty-seven days before death, and 3) injection of 4 cc. of blood into the right occipital region fifty-seven days before death. Figure 32 shows the gross appearance at post-mortem of the left parietal region (second operation) in cross section. Microscopically this eighty-seven-day-old lesion showed the needle track to be heavily laden with a collagen core extending almost to the depth of the ventricle. At the end of the needle track there was found a bifurcating area of tissue destruction - which must have been formed by the injected blood - into which the collagen sprayed indiscriminately. The area of degeneration was made up of tissue which was loosely fenestrated by a new blood-vessel formation and heavily laden with phagocytes containing fragments of red blood cells. There were thick bands of collagen and hypertrophied glial fibers interlacing indiscriminately, and connective-tissue invasion of the adjacent cerebral tissue was extensive. There were no perivascular hemorrhages.

To summarize briefly the late histological changes following the intracerebral injection of blood, it may be said that there is a tendency toward degeneration and absorption of the most affected or central area so that a cyst may be found at the center of the lesion. Toward the periphery there are found varying degrees of connective-tissue and of glial proliferation which may be assumed, we believe, to be due to the relative degree of impairment of blood supply in the peripheral zones. The histological picture following

Fig. 33.

Fig. 82 from Schwartz's monograph, reproduced by Hiller as a lesion representing the late result of intracerebral hemorrhage. Schwartz was uncertain as to its etiology.

Fig. 33.

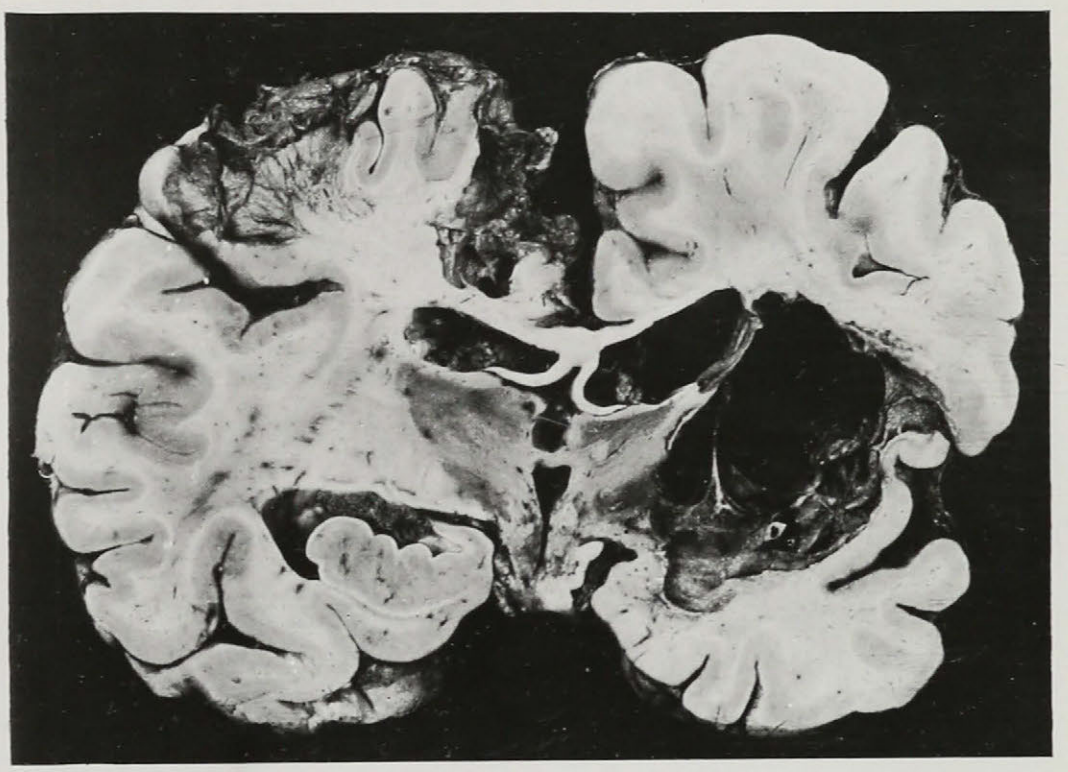


Abb. 86. Postapoplektische Cyste, wie sie SCHWARTZ abbildet (Abb. 82, S. 129 seiner Monographie), deren Genese nach Ansicht des Autors unklar ist. — Nach den Ausführungen im Text ist mit Sicherheit anzunehmen, daß es sich hier um das Residuum einer Massenblutung (Putamenclaustrum-Apoplexie) handelt.

the injection of blood is in essential agreement with that of Cajal, referred to above, on the changes about large areas of hemorrhage caused by cerebral laceration.

These findings may be translated directly to the field of human pathology and thus we are in accord with Hiller in attributing lesions such as he depicts in his figure 86 to intracerebral hemorrhage (Fig.33).

It is relevant to recall at this point the absence of red infarction, as described in the preceding chapter, in the brains of monkeys in which the middle cerebral artery was occluded. The absence of red infarction can be directly correlated with the minimum amount of scar tissue found about the large cysts following vascular occlusion - for as has been demonstrated in this chapter, extravasated blood serves as a potent stimulus to cicatrix formation,1) because of its local mechanical effect on both tissue and blood supply, 2) probably because of a fermentative action, and 3) probably because of associated functional vascular disturbances.

One must not, moreover, loose sight of another vascular factor active in scarring, the evidence for which - as presented in the preceding chapter - is indirect, and yet fairly conclusive. This factor is the tendency for inadequate oxygenation resulting from reduced blood flow - oftentimes severe enough to lead to extensive loss of neurones - to cause in the interstitial and vascular tissues a chronic hypertrophy resulting in gliosis and fibrosis. *

* Footnote: Dr. Stanley Cobb in a personal communication has suggested that the study of the brains of animals kept in a chamber for a prolonged period of time under reduced oxygen content, would be of considerable interest and might give more direct evidence on the point in question than is as yet available.

SUMMARY:

Some of the earlier views on the mechanisms involved in the production of intracerebral hemorrhage are briefly cited. Reference has then been made to the work of Chase on intracerebral hemorrhage occurring in hypertension. His interpretation of hemorrhage as being due to circulatory insufficiency is accepted as a working basis.

The work of Carmichael and of Hiller on the early histological changes following the experimental injection of blood into the hemisphere is then reviewed and findings of our own on the late histological changes are cited. These latter findings have been found to be in essential agreement with those of Cajal on the changes occurring about large hemorrhagic areas resulting from cerebral laceration.

Finally these changes are related to the mechanical and functional vascular disturbances that we believe occur in association with hemorrhage.

V. CEREBRAL CONCUSSION AND CONTUSION.

A sharp differentiation between the terms concussion and contusion which holds for both clinical and pathological findings is difficult to discover in the literature. Very early writers (Galen, Hippocrates, and later Paré) used the term concussion to apply to all forms of commotio cerebri. Later there developed a tendency for concussion to be considered as associated with scattered petechial hemorrhages. Miller (1927) in an excellent review of the historical development of the subject, treats the literature quite adequately. He concluded that, "Concussion appears to be due to direct mechanical action on the cells which causes a temporary disturbance of cell equilibrium and temporary loss of function". Miller regards this phenomenon as a reversible one, and he goes on to say that, "the term concussion should be used to denote the generalized, paralytic effects of an impact on the cortex and the medulla, and should be distinguished from the term contusion, whether a gross or microscopic contusion is meant, and also from the term hemorrhage, whether reference is made to diffuse or petechial hemorrhage". He denies to cerebral anemia a role in the causation of concussion. He points out that when cerebral anemia is produced experimentally there occur an initial rise in blood pressure and a temporary increase of respiratory activity. On the other hand, his tracings, from his own experimental work, show that with severe sudden trauma to the head there occur instantaneous interruption of respiration and a prompt drop in blood pressure due to vagal arrest of the heart. These changes are so prompt that

cerebral anemia - which requires from seven to fifteen seconds for its full development - cannot be held responsible.

Miller's definition of concussion is in essential agreement with the well known clinical definition advanced by Trotter (1924), "I may say at once that I use the term concussion, as I think it should only be used in the strict clinical sense, to indicate an essentially traumatic state due to head injury which is of instantaneous onset, manifests widespread symptoms of a purely paralytic kind, does not as such comprise any evidence of structural cerebral injury and is always followed by amnesia for the actual moment of the accident".

Experimental demonstration of the electrical activity which must be associated with such a profound physiological disturbance is as yet lacking, but it seems wholly reasonable to believe that as a result of the injury there must occur a diffuse discharge of electrical potentials, whose utter confusion might well be regarded as the cause of the disruption of the normal physiological state until a better explanation is advanced.

What then of contusion? Most authors agree that it represents a state of injury, either microscopic or macroscopic, in which organic alterations in the brain can be objectively demonstrated. For the purpose of the discussion presented in this chapter obvious cerebral lacerations and frank hemorrhagic lesions will be set aside to be considered in a later section, and we may concern ourselves with cellular changes, both neuronal and parenchymal and with circulatory disturbances.

At this point may be introduced a classical description of a case of head injury followed from the outset by a trained observer. The description is quoted by Miller from Archibald's article in American Practice of Surgery.

"Gussenbauer and a friend, while on a tour through the Alps, suffered a fall down the Eiger. The friend was rendered unconscious. Gussenbauer fortunately came to no harm. On rising, he found his friend completely unconscious; the pupils were wide; the corneal and other reflexes were abolished; all the muscles were flaccid; the face was deathly pale; and a chance wound was not bleeding. He was not breathing and looked quite lifeless. Evidently, there were both cardiac and respiratory standstill. After a short while there returned spontaneously signs of life; first the pulse, very weak and slow; then the respiration, shallow and slow; then bleeding from the wound. Later, the reflexes appeared; the man gradually began to hear; half opened his eyes; and returned to a condition of semi-consciousness. A week later, all concussion symptoms had disappeared, save that he had lost all memory of the events immediately preceding the accident".

From the evidence given in this description one would of course make a diagnosis of cerebral concussion. One wonders, however, whether had Gussenbauer made examinations of the reflexes at frequent intervals he might not have found evidence of cerebral contusion. In fact must not the twenty-four hour sleep be regarded as evidence of contusion? The point is worth laboring for the evidence of a profound circulatory disturbance in this case is so definite.

If then one recalls the evidence presented in the chapter on cerebral circulation concerning the nature of the histological changes which follow varying degrees of reduction in rate of blood flow: neuronal and interstitial cell changes, and, if stasis supervenes, perivascular hemorrhages, one can realize the importance of such general circulatory changes as described by Gussenbauer. Moreover, there is abundant experimental evidence that local vascular disturbance may occur as the result of trauma directly applied to the meningeal vessels (Florey 1925) and it is not inconceivable that in clinical cases of head injury local cerebral areas might therefore suffer in varying degree. Such considerations need not negate possible direct cellular commotion which may well be associated with sudden dislocation of the brain in its case, but they serve to emphasize the possible importance of circulatory changes, both general and local, and suggest that experimental observations on the cerebral circulation following head injury would be of great academic and practical significance, possibly offering new therapeutic leads in the treatment of cases of head injury. Such circulatory changes might well be localized to the site of the injury or to the site of the contre-coup effect, or might be more diffuse. That complete cessation of flow, and consequent thrombosis, is not essential to tissue destruction has been demonstrated in the chapter on arterial occlusion. With sufficient slowing of the circulation there would result local or diffuse perivascular hemorrhage, depending on the portion of the vascular tree affected, which in turn would result in local or in general cerebral atrophy.

Such functional circulatory disturbances may well be an alternative explanation of perivascular hemorrhage to the mechanical one advanced by Cassasa (1924) and supported by Martland and Beling (1929). Cassasa studied five cases of head injury in which there was at the time of injury momentary unconsciousness. After a lucid interval of from three to twenty-four hours these patients became irritable, developed hyperactive reflexes, became comatose and died. On microscopic examination of the brain of these cases the only lesions found were perivascular hemorrhages in the brain substance, and occasional minor hemorrhages in the pia. The theoretical explanation advanced by Cassasa for these findings was the following: "Sudden overfilling of the perivascular lymph space with cerebrospinal fluid conceivably could produce laceration of a vessel by tearing of its wall in the neighborhood of such a fibrillar attachment (He refers to the fibrillary bands crossing the Virchow-Robin space and attaching to the sheath of the vessel). Otherwise, without such an attachment, the laceration of a vessel surrounded by fluid could not be produced by any pressure exerted through that fluid which would only tend to compress the vessel but not lacerate it. Such an increase of cerebrospinal fluid in one perivascular space would be caused by the cerebrospinal fluid from the surface of the brain being drawn into it by pressure exerted by the change of shape in the skull - the result of a blow or fall. This change of shape under an area of violence is in the direction of flattening and diminution of space for the cerebrospinal fluid in that area. This fluid must find its way out of that area through the various sulci of the brain and in connection therewith; such fluid as cannot find its

way through these channels, must find a way into the perivascular lymph spaces in the reverse direction of the normal flow in these channels".

Martland and Beling conclude, "The mechanical theory of concussion advanced by Cassasa appears to be the best explanation of the causation of these hemorrhages", but they specifically draw attention to the occurrence of a similar appearing lesion in fat embolism. Hence, because of the demonstrated relationship of venous stasis to perivascular hemorrhages in this type of lesion (Chase, 1934) one must consider the possibility that vasomotor disturbances, the result of trauma, may be effective in producing the perivascular hemorrhages in cases of head injury. It is now well known that vessels react to mechanical stimulation and it seems eminently reasonable that a hydraulic trauma as described by Cassasa as responsible for vessel rupture might, in lesser degree, not cause actual rupture of a specific vessel but would serve as a traumatic stimulus adequate to upset normal vasomotor control. As a result of this upset there might occur the perivascular hemorrhage typically seen in severe head injuries. One would then place actual vessel rupture in the group of cerebral lacerations.

Viewed in this way concussion would be defined as the physiological state of shock (which might be due in part, but not an essential part, to a mechanical disruption of nerve cells), contusion as the stage of vasomotor paresis associated with perivascular hemorrhages; and laceration, as the name implies, associated with arterial tearing and rupture of continuity of cerebral structures. This last condition,

laceration, will be discussed in the next chapter.

Some additional support for the conception of vasomotor disturbance as playing a role in head injuries is the case described by Osnato and Giliberti (1927). A young man in the early thirties was injured in a motorcycle accident. Thrown to the pavement, he was immediately rendered unconscious. He soon regained consciousness but later in the day a diagnosis of middle meningeal hemorrhage was made and trepanation was done; the meninges were not opened. Respiratory and cardiac disturbance developed on the operating table, the operation was suspended and the patient died within thirty-six hours of the accident. Examination of the sectioned brain showed small petechial hemorrhages scattered throughout the centrum ovale, corpus callosum and pons. A striking finding was the presence of fibrin thrombi in the vessels of the meninges, choroid plexuses, and cortical vessels. Doctor L. H. Cornwall, who made the pathological examination in this case commented, "Agonal thrombi, however, do not completely fill the lumina of the vessels in which they are situated. In this case the thrombi completely filled many of the vessels and were intimately attached to the intima". He notes further that many fat emboli were encountered in the small capillaries of the brain. For this reason the obvious slowing of circulation must not be too readily attributed to the head injury itself, for it is conceivable that the stasis, and thrombus formation, was dependent on the fat emboli.

A more convincing case of this type, uncomplicated by the presence of fat emboli, is the following:

B.C.L. M.N.I. Case 1655:

A man, 35 years of age, was thrown from his automobile and landed on his right shoulder and the right side of his face. On admission to the hospital he was unconscious and was suffering from multiple body injuries including fractured clavicles, mandible, and ribs, and rupture of the cardiac end of the stomach. Neurological examination showed spasticity of the legs with exaggerated deep reflexes, absent superficial reflexes, and ankle clonus. There were twelve hundred red blood cells in the spinal fluid. The patient failed to regain consciousness and died the third day after the accident.

Relevant to the present discussion is the description by Dr. W. L. Reid of a section through the left frontal pole. He says, "The main feature in this section is the hemorrhage which extends into the grey matter. There is a fairly clear-cut cavity in which the hemorrhage is contained. This cavity appears to be, partly at least, a small sulcus. In the brain tissue immediately surrounding the larger hemorrhage there are numerous petechial hemorrhages with discoloration of the brain tissue. Most of the petechial hemorrhages are visibly associated with small blood vessels and in many instances red cells are clustered around vessel walls. There are, however, numerous red blood cells scattered throughout the tissue. An occasional small thrombosed vessel can be seen. The brain tissue away from the hemorrhage appears fairly healthy but immediately adjoining the area of hemorrhage it has lost largely its normal architecture and those cells present appear degenerate, diminished in size and misshapen....". No histological

evidence suggestive of fat or air embolism was found in either the general or neurological examinations made after death.

Inasmuch as the patient's systolic blood pressure, taken every fifteen minutes during his hospital stay, ranged between one hundred and thirty and one hundred and forty, and inasmuch as the spinal fluid pressure, determined by puncture made thirty-four hours after the injury, was one hundred and thirty, it seems reasonable to conclude that the thromboses described by Dr. Reid were due to slowing of the blood stream locally. Since there is no definite evidence of increased intracranial pressure (lumbar puncture readings may, of course, give false information), the slowing of circulation may have resulted from local dilatation of the vascular bed, produced by vasoparesis of traumatic origin.

So far as we are aware, Martland and Beling (1929) were the first to point out, in a series of cases, the similarity of the perivascular hemorrhages in head injury to those in fat emboli, whether fat embolus was or was not associated with the particular case under study. From these observations it is but a step to the related observations of Chase on air embolism (1934) and the etiology of hypertensive intracerebral hemorrhage (1937) - views based on the original work of Ricker (1927) who, as already pointed out, postulated a neurovascular tonus, disturbances of which by various traumatic agents, result in perivascular hemorrhage.

Bodechtel (1936) offers further support in favor of the occurrence of vascular pareses in cases of head trauma. He reviewed seven cases of brain injury and laid special

emphasis on those in which death occurred in the characteristic form of "spätapoplexie". These showed no gross focal lesions, no organic bleeding, but there were found diffuse cell changes well removed from the site of the trauma. Characteristic early histological changes were the development of "brushwork" glia, particularly in the cerebellum, changes which Ricker, Neubürger and others consider to be associated with vasomotor disturbances. The scattered zones of damage in such cases argue against any "toxic" effect, and likewise against a special areal susceptibility of cells to noxious agents.

Jacob, in his beautifully illustrated monograph (1913) reviewed the previous description of ganglion cell changes in "concussion", including experimental work. Following detailed protocols of his own researches with minute description of his pathological material he concluded that the ganglion cell changes which he described were the result of direct trauma. He was well aware of the views of some earlier investigators (Friedmann, Windscheid)postulating the occurrence of vasomotor phenomena in head injuries and attributing the late changes in part at least to vascular disturbances. These views he was unable to accept. One cannot help but wonder whether in the light of the work of the past twenty-five years he might not, in reviewing the evidence, attribute more importance to vascular disturbances.

One must next ask whether or not the histological pictures seen in cases of cerebral contusion are consistent with the mechanism proposed above. Differentiation between cerebral destruction due to direct local trauma and that due to disturbances in circulation is difficult to make. But let us first

ask, "What is the mechanism involved in destruction due to direct or contrecoup trauma?" Does agitation of the cell lead to its breakdown and the extrusion of some fermentative substance that stimulates the characteristic secondary changes? Admittedly, frank rupture of blood vessels may sometimes occur, but in these cases is it merely the added element of the outpoured blood that leads to greater destruction and subsequent scarring?

It seems to us that it is more reasonable to admit that such direct changes do occur, and that they may be of decided import, but it also seems to us important to emphasize the role played by the circulation, a role whose importance at once becomes obvious when one grants the possibility of areas of the vascular tree reacting locally to injury. Here one has a ready mechanism, for obviously vessels surrounded by perivascular hemorrhage are not normal vessels and where perivascular hemorrhage is present it serves as an index of abnormal circulation. In other words, perivascular hemorrhage probably occurs only under two conditions: 1) vessel rupture, 2) as a concomitant of a circulation so slow as to permit diapedesis of red blood cells. In the case of arterial vessel rupture it seems likely that the circulation in that portion of the vessel would be abnormal and probably would be slowed by direct mechanical action if for no other reason. Hence one has some reason for looking on the contused area as being possessed of an abnormally slow circulation, without doubt often due to a general lowering of blood pressure, but at other times, as we have attempted to show above, due to local vascular

paresis. The slow circulation must be a very important contributory, if not a primary, cause of the subsequent changes which are observed in cerebral contusion.

Are the late histological changes found in cerebral contusion consistent with such a mechanism? Let us consider a clinical case:

K.W., M.N.I. Case 2479, age 27:

Eight years before her last admission to the Hospital she suffered a severe head injury.

Since the time of her injury she had had headache and dizzy spells, and six years ago she began to have seizures. The significant objective findings on admission were: Diminution of vision, more marked on the left; slight emotional weakness of the left side of the face; increase in left biceps and triceps jerks; absent abdominal reflexes; and drooping of the right eyelid.

At operation a block of scarred cerebral tissue 3x2 centimeters in size was removed from the left occipital region. It varied from .5 to 1.0 centimeters in thickness.

Microscopic study of the excised block showed a very much thickened arachnoid, heavily laden with collagen. The vessels in the arachnoid were thickened and here and there occasional occluded vessels were to be found - in one instance showing recanalization. Underlying one of the areas of greatest arachnoidal thickening was a zone of cortical degeneration. In the center of the zone which involved only cortical layers, was loss of tissue. There was found penetration of loosely arranged chronic hypertrophic astrocytes, and immediately subadjacent to the pia was a zone of heavy gliosis.

There was an extensive proliferation of connective tissue within the degenerative area, and in the proliferation was a striking presence of very thick-walled capillaries, forming a vascular network of unusual type. There was no real intermingling of blood vessels and astrocytes as is so often seen in cicatrix.

Thionin sections showed extensive loss of neurones, and in other areas swollen cells with eccentric nuclei and yellow cytoplasm. In a neighboring area were found many chronically shrunken cells in all layers - small cell bodies, pyknotic nuclei, dark-staining cytoplasm, and shrivelled processes.

These changes are not unlike those observed in experiments in which the pia arachnoid was stripped from over the gyri of the brains of cats. The changes were followed up to eighty days. The effect of the pia-arachnoidal stripping was wholly vascular and was unaccompanied by severe diffuse injury, yet the resultant histological picture was not greatly unlike that described in the clinical case noted above.

Hence, though the evidence is not yet conclusive, there is considerable support for the conception that the most important element in cerebral contusion is impairment of the cerebral circulation.

Interesting in this connection is a consideration of the following case:*

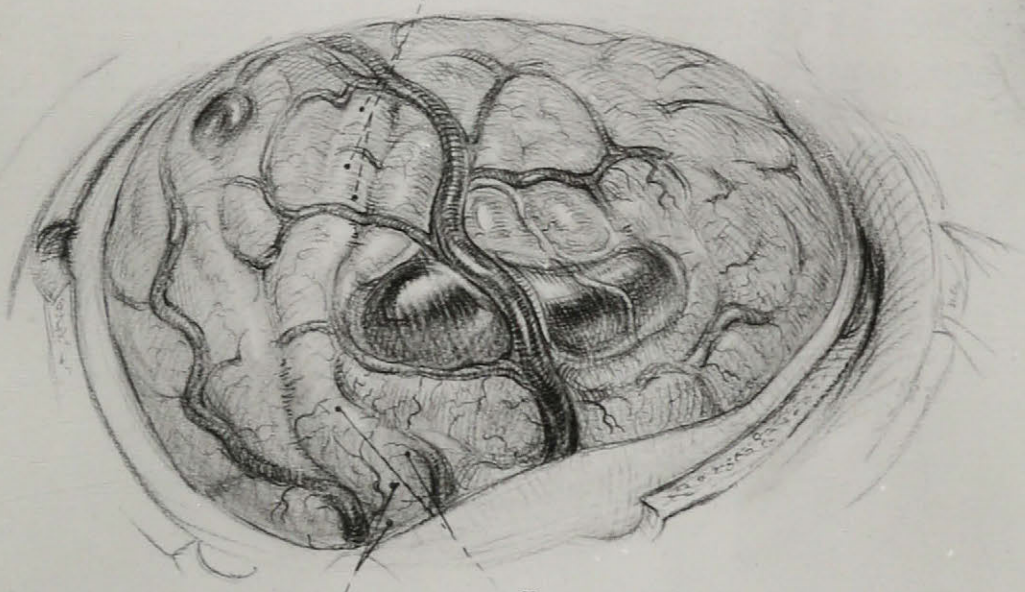
* Footnote: This case has been previously reported. Vide: Slight, D.S. and Cone, W.V. (1937).

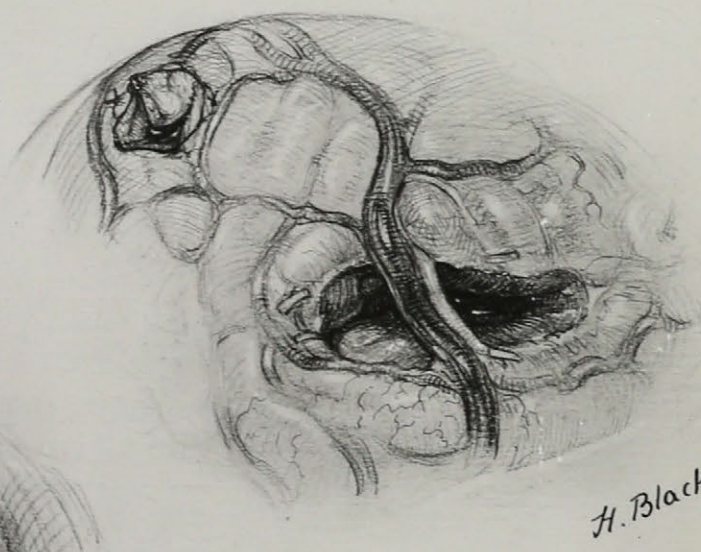
Fig. 34.

The artist's drawing of the cysts as exposed at operation, and of excision sites.

Fig. 34.

Right Cerebral Hemisphere.





H. Blackstock

Removal of Cicatrices.

W. Stelling Case No. 72465

Op. 7:3.30. R.V.H. Dr Cone.

W.S. R.V.H. Case 72465, age 21:

Seven and one-half years before admission to the hospital, this young man, while descending a set of basement stairs, struck his head lightly on an overhead beam. He was rendered unconscious for a brief period. Four weeks after the injury he noticed twitching of the left side of the mouth and a year after the injury he began to have attacks of unconsciousness.

A right osteoplastic craniotomy was performed by Doctor William Cone and two cicatrices were found, one four centimeters anterior to the motor area for the face, the other just posterior to the postcentral convolution. The artist's drawing shows the general appearance of these cysts (Fig. 34). Dr. Cone's operative note reads, ".....The dura was adherent to the arachnoid over the two scarred areas. Many fine vessels, small arteries and veins ran from the brain to the dura so that the dura was separated with difficulty. When the dura was pulled back, the brain did not sink in. These two scarred areas were cystic and had a yellowish cast before the arachnoid was opened. The cysts were apparently covered by arachnoid, pia, and a thin layer of brain. When they were unroofed, the cyst lining was found smooth and glistening and the underlying nervous tissue was very firm. The cyst in the right lower frontal region measured about one centimeter in depth and in diameter, that in the parietal region was irregular in outline and measured, with the scarred brain, about three and one-half centimeters in length and two and one-half centimeters in depth. A very large vein crossed the parietal scar just back of the postcentral convolution....."

Microscopic study of the excised cysts showed their walls to be made up of a heavily gliosed cerebral tissue in which hypertrophied astrocytes intermingled with connective-tissue elements to form a typical cerebral cicatrix. The walls of the blood vessels showed chronic thickening but no thrombosis.

The most likely mechanism to explain the anatomical changes seems to us the following: That at the time of the injury local central contusion, with local vasoparesis, occurred. Then followed dilatation of the vascular bed which resulted in multiple perivascular hemorrhages. These coalesced to form a hemorrhagic area. About this area were zones of perivascular hemorrhage of lessening severity.

In the course of time absorption of the central core took place and a cyst was formed. Meantime, at the periphery of the lesion, because of impaired oxygenation and because of blood extravasated from the vessels, glial and connective-tissue proliferation had occurred which resulted in the formatic of the cicatricial lining of the cyst which has been described above.

Admittedly this interpretation of the sequence of events is not susceptible of direct proof, yet it fits well with the experimental facts cited in the preceding chapters.

In summary, there has been made in this section, an effort to emphasize the differentiation between concussion and contusion. We believe concussion to be a state of disorganized neuronal activity, precipitated by a massive, diffuse stimulus.

It, of itself, has no demonstrable anatomical substratum. Cerebral contusion, on the other hand, is a recognizable anatomical state, one which may or may not give functional signs, depending on the location and the severity of the lesion. The anatomical substratum is perivascular hemorrhage and the cause of perivascular hemorrhage is slowing of the blood stream. Slowing of the blood stream may be due to a general systemic lowering of the blood pressure of such a degree that the cerebral vascular mechanisms are unable to compensate for it. However, evidence has been presented to show that slowing of the blood stream may also occur locally, or in scattered zones, because of local vasodilatation resulting from injury to the local vascular bed. A vasoparesis is thus established which results in local vasodilation and in diapedesis.

Cerebral concussion and contusion usually accompany one another. In fact cerebral concussion may, by disorganizing the vasomotor and cardiac centers and thus disturbing the general circulation, be a direct cause of slowed cerebral circulation sufficient to cause perivascular hemorrhages, the telltale sign of contusion.

It must be conceded that perivascular hemorrhage may also occur as the result of laceration of cerebral vessels - this condition then merges into cerebral laceration. Similarly, the coalescence of perivascular hemorrhages into a massive hemorrhagic area may occur, and might be regarded as cerebral laceration. For the sake of clarity of exposition we have made an arbitrary differentiation between contusion and laceration and hence it should be borne in mind that though there occurs at this point a chapter ending, the problem under discussion in reality passes over insensibly into the next chapter.

VI. CEREBRAL LACERATION AND POST-TRAUMATIC CICATRIX

Lesions in which there is actual rupture of cerebral tissue fall into two classes, those in which cerebral laceration occurs without involvement of the meninges, and those in which cerebrum and meninges are both involved. The latter group can, in turn, be subdivided into two groups depending on whether or not the dura is penetrated. In general, wounds which penetrate the dura tend to be more extensive because of the nature of the causative agent. But it must be emphasized here that cicatrices of great extent and characterized by tremendous proliferation of connective tissue may occur in lesions originating wholly within the brain proper and not involving the dura in any respect.* (Vide: clinical cases 2 and 3, Chapter III,

* Footnote: This point is of great importance in considering the question of epilepsy subsequent to cerebral injury, a matter not immediately germane to the problem at hand. There has been a definite tendency to regard penetration of the dura as an unexplained factor responsible for the high incidence of post-traumatic epilepsy in these cases, and there has been a tendency to regard cases of so-called "post-traumatic epilepsy" as being especially suitable for operative treatment. This, on theoretical grounds, seems to us a misconception. It is obvious that the requisite factors for the occurrence of seizures are to be found in cases of "birth injury" (a term which in the past has often concealed instances of asphyxia) and likewise in cases of intracerebral hemorrhage, inasmuch as these cases also are subject to epilepsy. But, it will be answered, the incidence of epilepsy is so much higher in penetrating wounds of the brain; for example, in war wounds. This is true, but so far as we are aware, the statistics on the occurrence of seizures in such cases have never been critically analyzed. Furthermore, we are not cognizant of any accurate figures on the relationship of various types of cerebral insult in children to the occurrence of epilepsy which can be compared with, let us say, the war-wound statistics. Ford's (1927) analysis of birth injuries is too limited, and indeed the cerebral insults of infancy and childhood are too little understood for a statistical study of value.

There are complicating factors entering into the formation of the cicatrices of wartime. Men with cerebral injuries often lie in the fields for hours or days in varying states of shock. Enough has already been said of the influence of cerebral circulation on scar formation to suggest that

and the case of "birth injury" (case 5) reported by Foerster and Penfield, 1930).

Rand and Courville (1932 and 1936) have described the architectural disruption that occurs in clinical cases of cerebral laceration: irregular wound outlines, frequent extensive hemorrhage because of the rupture of large vessels, sometimes scattered islands of isolated neurones - morphologically sound but functionally useless - undermining of adjacent normal tissue by hemorrhage, zones of destruction in the most severely affected parts, surrounded by proliferated reacting astrocytes and finally by tissue approaching normal structure. They do not devote attention to the histological or physiological reactions in the vascular bed.

The severe gunshot wounds of the World War provided Foerster and Penfield (1930) with material for a detailed

Footnote continued from preceding page:
the slowing of cerebral circulation attendant on such states of shock must exert an important influence on the resultant cicatrices. Furthermore, many of these cases must have been subject, if not to fulminating infection, at least to low-grade and often unrecognized pyogenic action, with its resultant intensification of scar formation.

So far as operative treatment is concerned, the point we wish to emphasize is that all cases of epilepsy due to cerebral scarring are intimately related in their pathological nature. There is thus reason for looking on all as belonging to the group of "post-traumatic epilepsy", and for considering properly chosen cases of all groups as amenable to surgical therapy. The figures of Penfield, on the therapeutic results of the excision of areas of focal atrophy and focal cerebral cicatrix compare very well with his results in cases of meningocerebral cicatrix, and lend support to this contention. (Penfield 1936).

A consideration of whether or not the invasion of a cerebral scar by vascular and nervous elements derived from the external carotid circulation, as occurs in penetrating wounds of the dura, need not detain us here since it is a special problem related to the mechanism of the epileptic seizure.

histological study of well-aged meningocerebral cicatrices. Their conclusions are reported in English by Penfield (1930). Histological examination of the human material showed abundant "fibrous tissue, and adhesion to the meninges. Thus connective tissue and an astonishingly rich plexus of vessels were invariably present in the scars, intermingled with fibrous astrocytes whose fibers were in general arranged in parallel and extended.....upward toward the cicatrix. Deeper down in the brain the astrocytes and blood vessels still continue to form the only framework capable of withstanding tension, the vaso-astral framework .

"In the areas of gliosis nerve fibers are rare and the 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 the blood vessels which have been shut off and they seem to indicate that the process of 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 in epilepsy of a different type".

These findings are quite similar to those described by Cajal (1928) as the late result of cerebral laceration.

Penfield, in seeking a mechanism to explain the late onset of epilepsy in such cases, emphasized the presence of abundant connective tissue which he postulated could, as in scar tissue elsewhere, contract. As 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 noticed as soon as the bone was removed and the edges of the adherent dura incised. The center of the scar thus drew itself together, sucking the attached dura inward as much as one and one-half centimeters as soon as it was freed from the attachment to the overlying skull". He regarded the contractile power of the scar tissue, "probably associated with the atrophy which takes place in the brain about the cicatrix" as responsible for the "ventricular wandering" in cases of gunshot wound of the brain previously described by Foerster (1925). Yet in the same article Penfield cast doubt on the importance of atrophy in the production of ventricular wandering for he said, "That the local atrophy is not the cause of the deflection of the ventricles toward 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 this ventricular displacement and many cases with little or no enlargement of the lateral ventricle may show marked ventricular displacement. Instead of wandering of the ventricles the process is really brain-pull or ventricle-pull".

He made the further statement, "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".

Penfield's clinical views represent the logical outcome of a protracted study of experimental brain wounds carried out with a number of collaborators. Hortega and Penfield (1927) traced the result of stab wounds from the earliest stages when transitional forms of microglia appeared preparatory to beginning their phagocytic activity, through the stages of clasmatodendrosis and later astrocytic hypertrophy, to the final formation of the brain scar - composed of a connective-tissue core in the center and radially arranged astrocytes about the periphery. Wilson (1926) described essentially similar lesions in human cases following ventricular puncture.

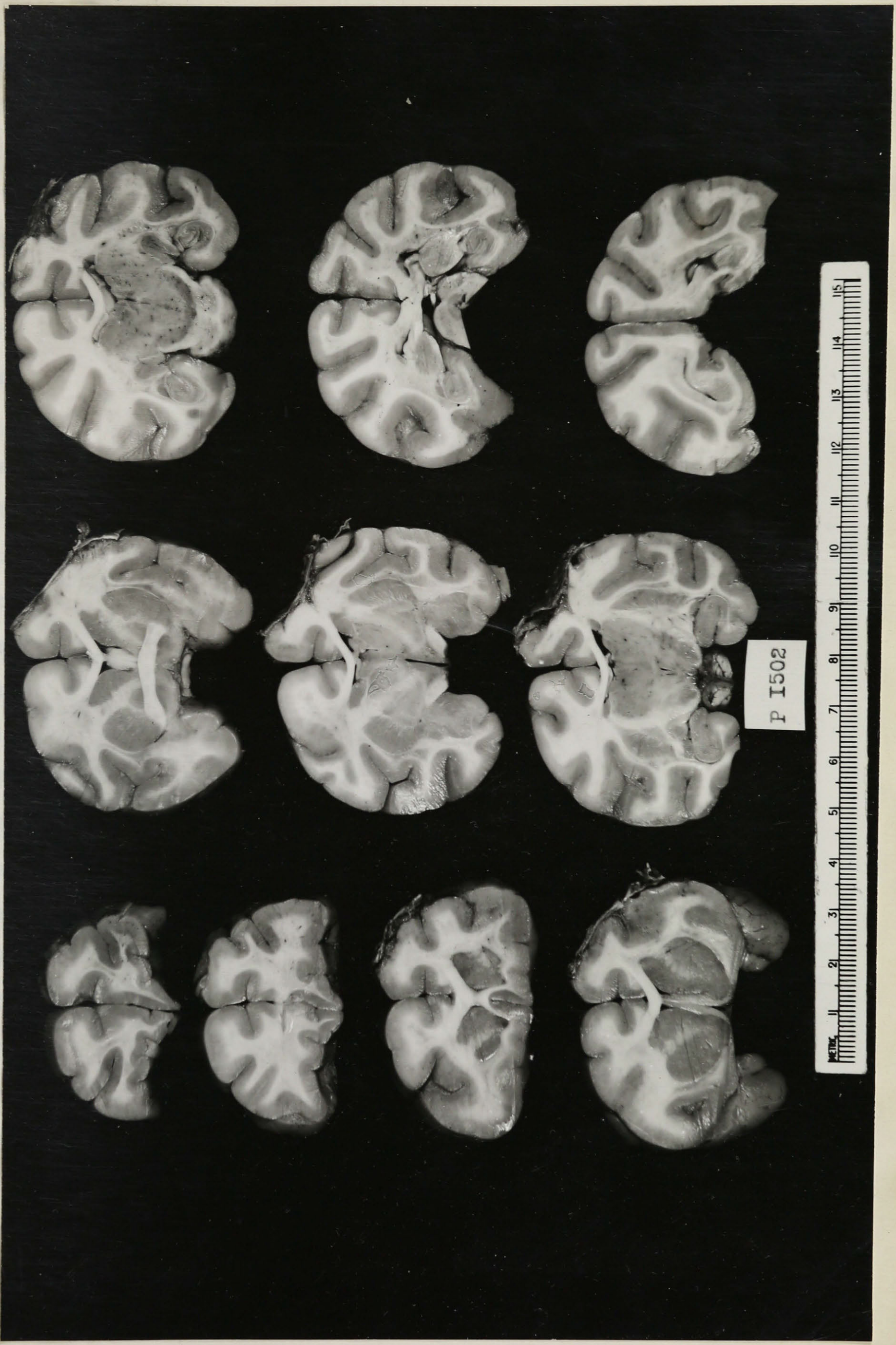
Later Penfield and Buckley (1928) studied stab wounds made with open cannulae and contrasted the two types of stab wounds (blunt and hollow needle) as follows: "About the closed tracks, the astrocytes send in their large expansions concentrically; about the open tracks, these expansions are tangential to the canal. Compound granular corpuscles are more numerous about the closed than about the open tracks. Apparently, both needles cause the same amount of hemorrhage. There is, in general, greater formation of adhesions, greater distortion and greater destruction of the brain about the tracks made by a closed needle than about the tracks made by an open needle of the same size".

Penfield and Buckley go on to a conclusion which, in the light of later evidence, is, in our opinion, untenable. "As a general principle, it follows that if destroyed tissue is left in a wound in the brain, a cicatrix results containing connective tissue which contracts and causes distortion of the brain; a greater resultant gliosis also occurs".

Fig. 35.

The brain of a monkey three months after the infliction of a severe wound in the left parietal region. Note the extensive loss of traumatized brain substance, and the shift of the midline toward the wound site.

Fig. 35.



It now seems clear that devitalized cerebral tissue of itself is not a cause of cerebral cicatrization. That this is so is clearly shown by the facts reported in the section on the experimental production of sudden arterial occlusion. Extensive necrosis occurs in these animals in the central portion of the area supplied by the middle cerebral artery. Nevertheless, the ultimate picture of repair presented by these brains, from the standpoint of minimal resultant scar, is one that the surgeon would wish to duplicate.

Secondly, extensive areas of cerebral trauma are often absorbed almost completely, leaving only a minimum of scar tissue, and if the initial lesion be relatively small almost the only trace of it in gross may be the adhesions between dura and cerebralsurface. This has been a frequently repeated experimental observation. Illustrative of the general principle that extensive absorption of an area of cerebral trauma can occur is the following: A monkey, P-1502, was operated upon on February 26th, 1937 by a fellow worker in the laboratory, Dr. K. v. Santha. A bony decompression was made and fully the mesial half of the pre- and postcentral gyri were vigorously and deliberately traumatized with a blunt instrument to a depth sufficient to involve the white matter; a large dural flap was turned into the wound, and the traumatized brain was left to unite with the overlying loose areolar tissue of the scalp. Figure 35 shows the brain of this animal three months later. Had this zone of lacerated tissue been removed immediately by the surgeon and had the adhesion between scalp and brain been prevented by replacing the bone or by inserting a cellophane transplant, would the resultant scar

have been less? An attempt to answer this question will be made in the next chapter.

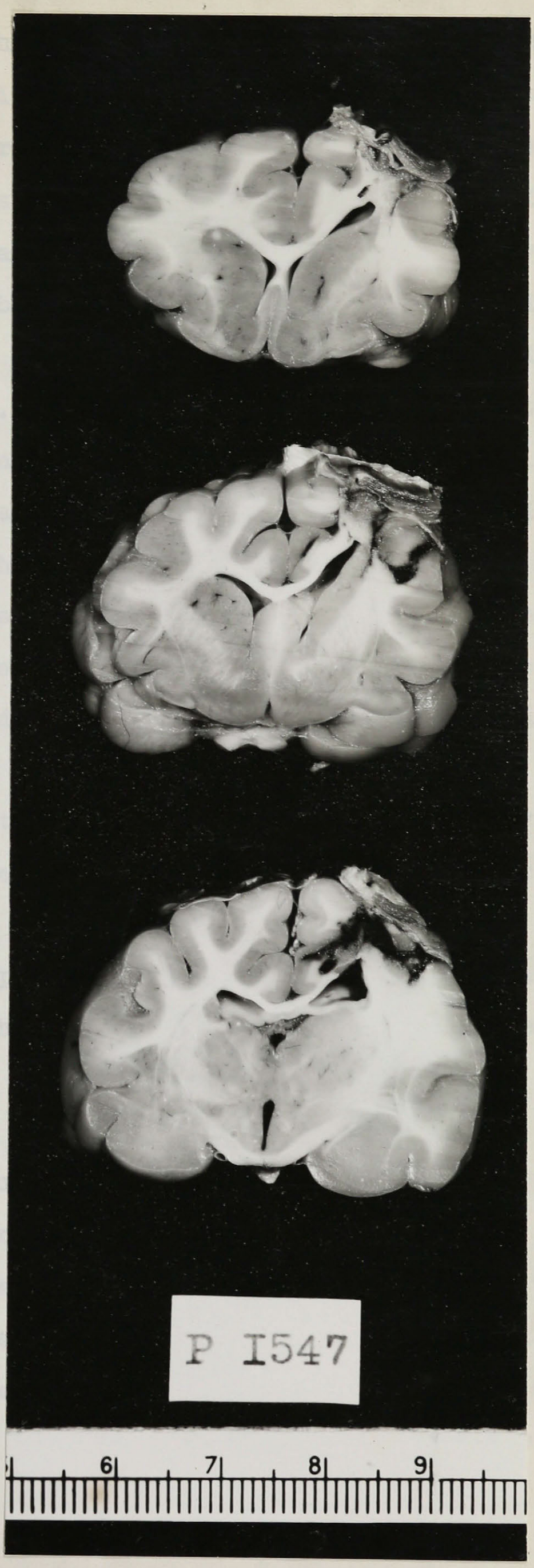
A third point is brought out by this same experiment. Penfield, as quoted above, expresses the conviction that the ventricular wandering seen in cases of post-traumatic epilepsy is due to pull exerted by contractile elements in the scar, "That the local atrophy is not the cause of the deflection of the ventricles toward the side 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". However, it is conceivable some other factor, such as the rigidity of the falx, prevents greater ventricular displacement than is seen in cases of both atrophy and of scar. In any event, in this particular animal gross scarring is relatively slight but the ventricles show distinct displacement. We believe that the displacement is not here due primarily to pull in the injured area but rather is due to a shift of the entire brain toward the site of the injury at which site has occurred considerable cerebral atrophy. This point was first called to our attention and strongly emphasized by the shift of the entire brain, seen following occlusion of the middle cerebral artery, to encompass, as it were, the degenerative area.

Even more convincing proof of the importance of atrophy in the occurrence of ventricular dilatation and ventricular shift is provided by the following evidence: Cat, P-1547, was operated upon on March 17th, 1937 by Dr. K. v. Santha. A craniotomy was done and a very extensive wound was made in the left parietal region, but no cerebral tissue was removed. The animal was sacrificed three weeks

Fig. 36.

The brain of a cat three weeks after extensive wounding of the left parietal region. Note ventricular wandering and ventricular shift toward the area of loss of substance, before the cicatrix has organized sufficiently to exert much pull.

Fig. 36.



later. The photographs (Fig.36) demonstrate clearly ventricular dilatation and shift toward the wounded area. Histological examination showed very extensive degeneration. Islands of cerebral tissue were surrounded by new blood vessels and there were extensive areas of hemorrhage, one of which was partially walled off by collagen on one side and was being actively phagocytosed on the other. Degeneration extended down to the ventricle. Sufficient scar tissue organization at this three-week stage was not found to account for either the ventricular dilatation or the ventricular shift, and it seems quite evident that in this instance cerebral atrophy must be held wholly responsible. This conclusion does not, of course, deny the contributory effect that scar tissue contraction may provide in long-standing, well organized cicatrices.

It is well to emphasize that atrophy alone may cause a shift of the ventricular system when little or no scar tissue is present. This is certainly true in monkeys (see Chapter III.) and is probably also true in children. Whether it be true in adults has been questioned. In this connection the following case is of interest:

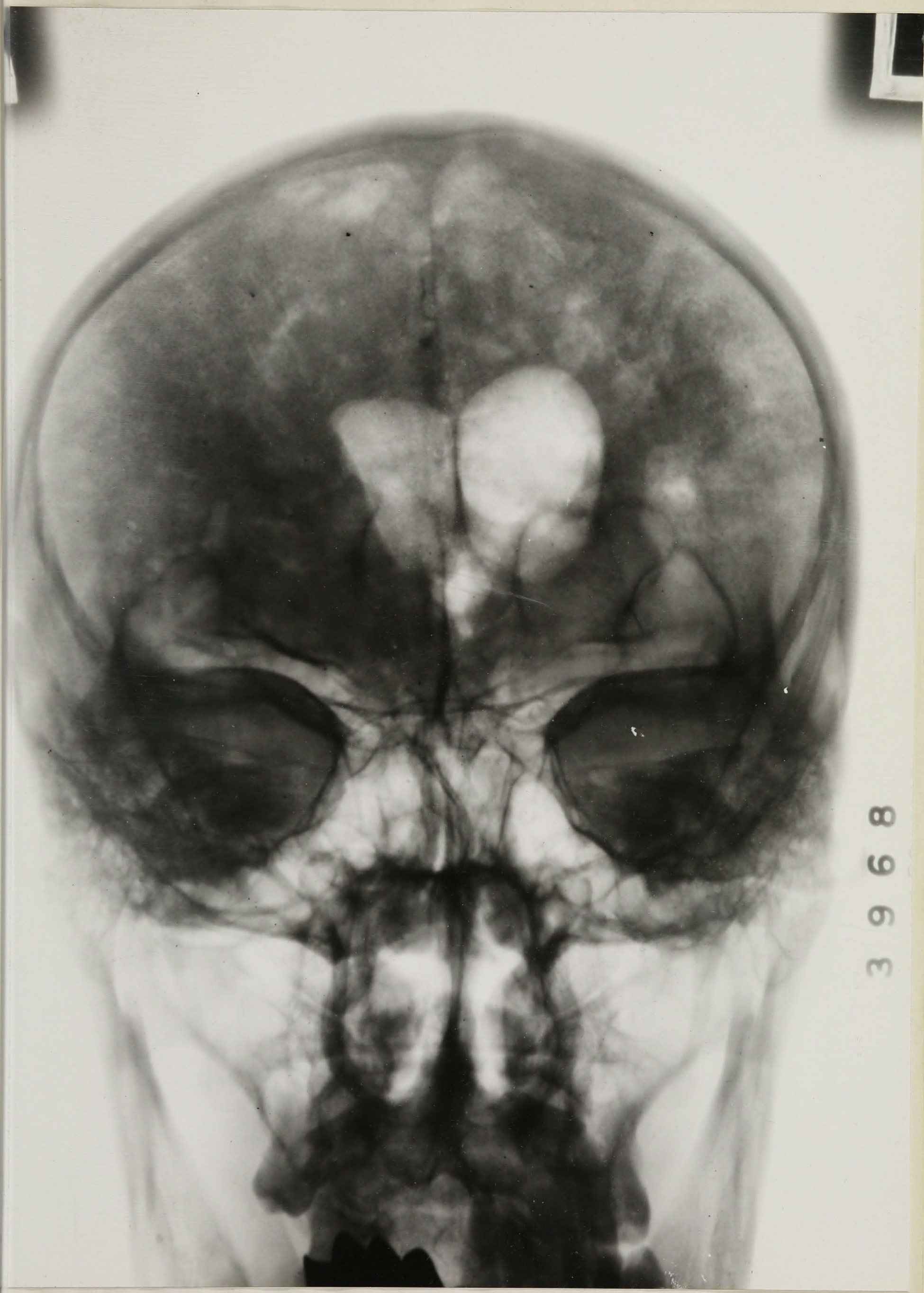
R.B.-M.N.I. 2686:

This man, forty years of age, was admitted to the hospital with the story that he had been well until the age of twenty, when he suddenly had a "stroke" while at work which left him temporarily paralyzed in the right arm, leg, and face. He recovered almost completely in the course of ten days. At the age of twenty-three he had a similar episode

Fig. 37.

Encephalogram, antero-posterior view. Case R.B. Shows ventricular shift in arterial occlusion occurring in an adult.

Fig. 37.



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but the paralysis cleared in the course of an hour. A third mild attack at the age of thirty interfered with speech and with face movements for a half-hour period. At the age of thirty-five he suffered his most severe attack which left him aphasic for three weeks and left him with a residual palsy of the right arm, leg, and face, and a definite speech defect.

Four days following the last stroke he suffered his first convulsive seizure - consisting of sudden, severe headache, the onset of spasticity in the right side, and unconsciousness. Other attacks of the same nature have recurred once or twice a month since then.

Laboratory tests were negative. It is interesting that at the age of thirty-three he developed a primary luetic chancre, which fact probably rules out syphilis as playing any part at the onset of the disease at the age of twenty.

Encephalography was done (Fig.37). The left lateral ventricle was found dilated in portions one, two, three and four. The septum pellucidum was drawn to the left of the mid-line, and the subarachnoid space was dilated over the left hemisphere. Arteriograms were made by Dr. A. R. Elvidge which showed normal filling of the cerebral vessels of the right side. On the left, however, the internal carotid artery apparently terminated at the entrance of the vessel into the skull. The occlusion appeared complete.

In this case, then, one has convincing proof of occlusion of the left internal carotid artery before its entry into the skull, though the etiology of the condition remains obscure. There is, furthermore, evidence of extensive

atrophy of the left hemisphere. The subarachnoid space was dilated on this side, rather than being obliterated, suggesting strongly that there were no dural-arachnoidal adhesions, which are probably the invariable result of hemorrhagic extravasation into the meninges. Hence it seems likely - though without operation the point cannot be settled beyond doubt - that in this adult atrophy is responsible for shift of the ventricular system, as well as for ipsolateral ventricular dilatation.

A final word should be said concerning the statement (Penfield, 1930) that there is, over a period of years following the infliction of a wound, a progressive increase in the vascular elements of the scar. We have no evidence on this point from scars of anything like the duration of those studied by Penfield. However, our impression is rather to the contrary, for we have found in our experimental material that over periods of time up to a year, there seems to be a decrease in vascular elements, certainly of the capillaries. We were first awakened to this possibility by observations of Alexander (1937) who described the falling-out of small vessels in areas of cerebral scarring. Moreover, scars elsewhere - in the skin for example - tend to contract and blanch over a period of years. It is perhaps of significance that the material studied by Penfield was drawn from epileptics, suffering from recurring seizures. It may well be that fresh degeneration and fresh scar-tissue formation were going on in these cases as a reflection of vasomotor disturbances accompanying the epileptic seizures. Such an interpretation is, in fact, exactly that suggested by Penfield in a later paper (1934).

In summary, there has been described in this chapter, very briefly, the early disruption of tissue which occurs in extensive cerebral laceration. There have then been described in more detail the late changes found in cerebral cicatrix, clinical and experimental. These descriptions have been concerned chiefly with the static picture presented by the brain changes at any given time - they have been detailed and have covered the histological aspects of the problem very completely.

In the second half of the chapter we have attempted to present the problem from a dynamic point of view, and to the reader who has followed the argument developed in earlier chapters, it must be evident that interference in the adequate blood supply plays a role of the greatest importance in cerebral cicatrix, for because of oxygen lack can occur not only impairment and loss of neurones, but also, if the anoxemia is not so great as to cause an actual loss of glia and vascular elements, these structures hypertrophy and cause scar formation. Furthermore, sufficient slowing of circulation leads to diapedesis of blood elements and to resultant greater scarring.

Two further points have been discussed. It has been suggested that cerebral atrophy plays an important role in ventricular wandering, and evidence has been presented in support of this view. The importance of cicatricial contraction in well organized scars of long standing has not, however, been denied. Finally, it has been proposed that the areas of degeneration observed in the brains of epileptics many years after the original injury, is not

a sign of progressive degeneration due to continued contractile activity on the part of the scar, but rather that it may be interpreted as an indication of repeated vascular insults occurring because of vasomotor changes associated with recurring seizures.

VII. MEDICAL AND SURGICAL CONSIDERATIONS.

Outline of Presentation:

1. The Importance of Adequate Circulation.

   A. Effects of Anoxemia.

      (1) Destructive.
      (2) Proliferative.

   B. Effect of Diapedesis.

   C. Factors Producing Inadequate Circulation.

      (1) Arterial obstruction.
      (2) Interruption of arterial continuity by trauma.
      (3) Mechanical compression.
      (4) Local neurovascular disturbances.
      (5) Systemic lowering of the general blood pressure.
      (6) Venous obstruction.

II. Means of Preserving or Improving Cerebral Circulation.

   A. "Medical".

      (1) Speeding of blood flow.
         (a) Reduction of mechanical compression.
         (b) Combatting of vascular paresis.
         (c) Improvement in systemic circulation.
         (d) Increase in availability of oxygen supply.
            i. increase in oxygen content of the blood.
            ii. increase in rate of oxygen dissociation.
            iii. opening of collateral pathways.

   B. "Surgical".

      (1) Subtemporal decompression.
      (2) Evacuation of clot.
      (3) Debridement.
      (4) Sympathectomy.

III. The Question of Radical Debridement of Cerebral Wounds.

IV. The Clinical Importance of Cerebral Cicatrix.

   A. The Question of Progressive Destruction of Cerebral Tissue.
   B. "Post-traumatic epilepsy".

Outline of Presentation (continued)

V. The Technique of Cerebral Scar Excision.

A. Bone Flap.

B. Meningeal Adhesions.

C. Excision of Scar.

(1) Sharp dissection.
(2) Suture method.
(3) Electro-surgical unit.

D. Establishment of Ventricular Communication.

E. Question of Drainage.

F. Dural Closure.

G. Replacement of Bone Flap.

(1) Bone decompression.

VI. Summary.

VII. MEDICAL AND SURGICAL CONSIDERATIONS.

In the preceding chapters the argument has been developed that cerebral cicatrix in its manifold forms (exclusive of developmental, degenerative and infectious conditions) depends essentially upon disturbances in blood flow. The scarring is the result of either anoxemia or diapedesis, or may depend upon a combination of the two. Anoxemia of severe degree leads to a necrosis of the affected area and to its dissolution and absorption. If, however, the circulatory disturbance is of a lesser degree so that the anoxemia is not so severe, or if the physiological state of the brain is such that collateral circulation of an inadequate degree only is established, there occurs proliferation of glial and connective tissue, and extensive scarring may result. The exact degree of circulatory slowing necessary for such a reaction cannot be stated at this time.

If the circulatory slowing is of such a degree that prestasis and stasis occur, and the resultant zone of damage is not so extensive as to lead to massive necrosis, the resultant diapedesis of red blood cells leads to extensive perivascular hemorrhage and severe scarring may ultimately ensue. If the hemorrhagic area is very extensive central necrosis and liquefaction occur and there will be found about the periphery of the lesion a cicatricial reaction.

There are, then, two important results of reduction in blood flow so far as scarring is concerned: the first an anoxemia which, if not so severe as to lead to complete destruction of glial and connective-tissue elements, causes its

proliferation; the second, the occurrence when prestasis and stasis occur, of perivascular hemorrhages which stimulate cicatricial formation.

Slowing of circulation may occur due to any one of the following circumstances, or to a combination of them: a) arterial obstruction, b) interruption of arterial continuity by trauma, c) mechanical compression by hemorrhage, edema, etc., d) local vascular disturbances, e.g. dilatation of the peripheral bed in response to trauma, e) systemic lowering of the general blood pressure, e.g., in surgical shock or cardiac failure, and finally, f) as the result of venous obstruction. This last factor, as pointed out earlier, has not been touched on by us experimentally and will be left out of this discussion.

As a general principle in considering the therapeutic problems involved, it should be stated at the outset that the physician's efforts should be directed toward the restoration of a normal circulation, or of a circulation as nearly normal as possible.

Such efforts may be arbitrarily divided into two groups, medical and surgical.

The medical aspects of this problem will be covered in detail in another communication by Dr. Donald McEachern. In general, they are concerned with the speeding of blood flow itself, or of providing for the tissues a more readily available supply of oxygen.

Much exploration remains to be done in this therapeutic field. The reduction of mechanical compression by the use of salt and glucose solution and perhaps by lyophile sera, must be considered. Facilitation of venous return by proper

posture may also play a role of importance, and the necessity of ensuring as nearly a normal systemic circulation as possible is obvious.

The tone of vessels dilated by anoxemia or by vasoparetic agents, must be improved, either by improving the circulation itself or conceivably by vasoconstrictor drugs acting on the paretic vessels without causing too much constriction of the normal vessels.

Finally, means of increasing the availability of the oxygen supply must be considered: a) by heightening the oxygen content of the blood, b) by increasing the rate of oxygen dissociation, or c) by opening up more rapidly and perhaps to a greater degree, the available collateral channels.

These are all hypothetical problems of great complexity, some of the phases of which have already been attacked and on which a later report will be made by Dr. McEachern. The handling of the period immediately subsequent to the ictus - whether it be in the nature of occlusion, hemorrhage, or trauma - is obviously of great importance as far as scar formation is concerned.

The same emphasis may be placed on the essential unity of this trinity of conditions in considering what surgical means are available for treatment. Subtemporal decompression may be considered as a method conceivably applicable to any one of the three conditions, the reason for its application being its ability to reduce, in varying degrees, intracranial pressure. Its use would depend on special clinical circumstances.

The logic of evacuation of a large intracerebral clot, as has been done by Penfield (1933) and others* becomes quite evident, and for the same reason radical debridement of badly lacerated cerebral substance seems a wholly rational procedure under certain circumstances.

A question as to the value of sympathectomy as a prophylactic measure may well be raised at this point. If one grants the reality of severe vasospasm in pathological conditions, and regards it as of nervous origin, consideration of sympathectomy in well chosen cases of either embolism or hemorrhage becomes reasonable. The whole problem remains to be worked out, but a word of caution is perhaps in order. As White (1935) has clearly shown, vessels whose post-ganglionic fibers have been sectioned become unduly sensitive to hormonal activity. Hence the site of election for section of the sympathetic fibers supplying the cerebral circulation would probably be the trunk immediately below the inferior cervical ganglion - which operative site also offers the opportunity of sectioning the vertebral chain as well, below the vertebral ganglion. The possibility of circulating toxins or hormones acting directly on the vessel walls in such cases must also be considered, so that nerve section may be pre-doomed to failure no matter how excellent the surgical technique employed may be.

Footnote: White (1937) reports that a census of the experience of the members of the Harvey Cushing Society reveals that thirty-seven cases of intracerebral hemorrhage had been so treated by various members of the Society.

We may now proceed to more practical consideration, and discuss in some detail the rationale of radical debridement of cerebral tissue in cases of head injury.

There are three obvious reasons for recommending such a procedure: 1) To reduce the amount of early cellular loss resulting from relative anoxemia during the acute stage of brain swelling following the injury; 2) To reduce the extent of progressive cerebral degeneration associated with cerebral cicatrix, if such progressive cerebral degeneration does actually occur as a process separate from the epileptic seizures; and 3) To reduce the likelihood of the later occurrence of seizures precipitated by the formation of scar tissue. A fourth consideration may also be proposed: that the debridement of the cerebral wound reduces the degree and extent of possible meningeal complications of head injury, in which group of complications probably belongs post-traumatic headache.

It is obvious that the removal of badly damaged cerebral tissue, swollen and edematous, will tend to relieve the mechanical compression of the circulation which follows all head injuries in varying degrees. This point does not need laboring as such, though the evaluation of its importance in any individual case requires a high degree of clinical insight.

We have discussed, in the preceding chapter, the question of progressive cerebral degeneration. We do not deny the theoretical possibility that contracting bands of scar tissue may reduce blood supply and cause tissue necrosis in the normal, or nearly normal, cerebral tissue as well as in the scar itself. However, as Penfield (1930) suggests in his

study of war wound cases, "These areas of degeneration recall the perivascular destruction described by Spielmeyer in epilepsy of a different type". Obviously he is referring to Spielmeyer's description of the changes in Ammon's horn which were regarded as resulting from vasospasm. We should incline to the view that the progressive degeneration seen in cerebral scars is associated with vasomotor changes which accompany the epileptic seizure. The cases in which Penfield described these changes were all epileptics, and in our own experience with one exception, we have observed such changes only in the brains of epileptic patients. In the exception the evidence for degeneration was slight. This entire question should, however, probably be explored further.

The third, and probably much the most important consideration, deals with the likelihood of post-traumatic epilepsy resulting from the injury. Figures on the incidence of post-traumatic epilepsy vary from the .5% in civil practice reported by Muskens (1928) to the war figures of Steinhal and Nagel (see Steinhal, 1929) who found the incidence of seizures to be 28.9% among six hundred and thirty-nine surviving cases of gunshot wound of the head. These latter figures are such as to suggest to us that in severe injuries to the head occurring in civil practice, debridement is justifiable and probably advisable. Furthermore, considering Wagstaffe's(1928) report of the development of epilepsy in 1.6% of gunshot wounds of the head in which the dura was not penetrated as opposed to 18.7% in those cases in which the dura had been penetrated, it would seem particularly advisable to debride in wounds in

Fig. 38.

The brain of a monkey three months after severe wounding, left parietal region. Note absorption of damaged tissue.

Fig. 38.

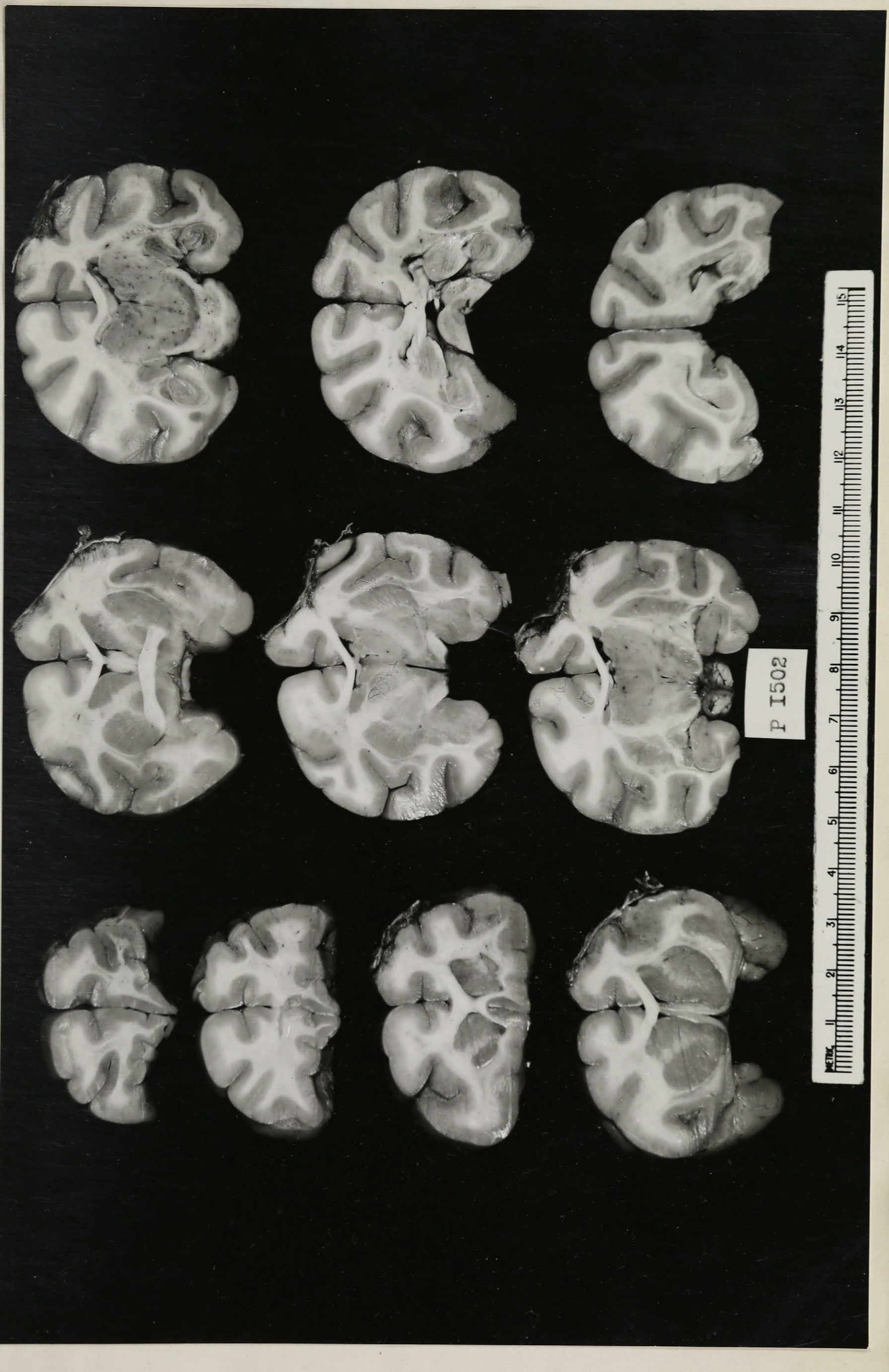
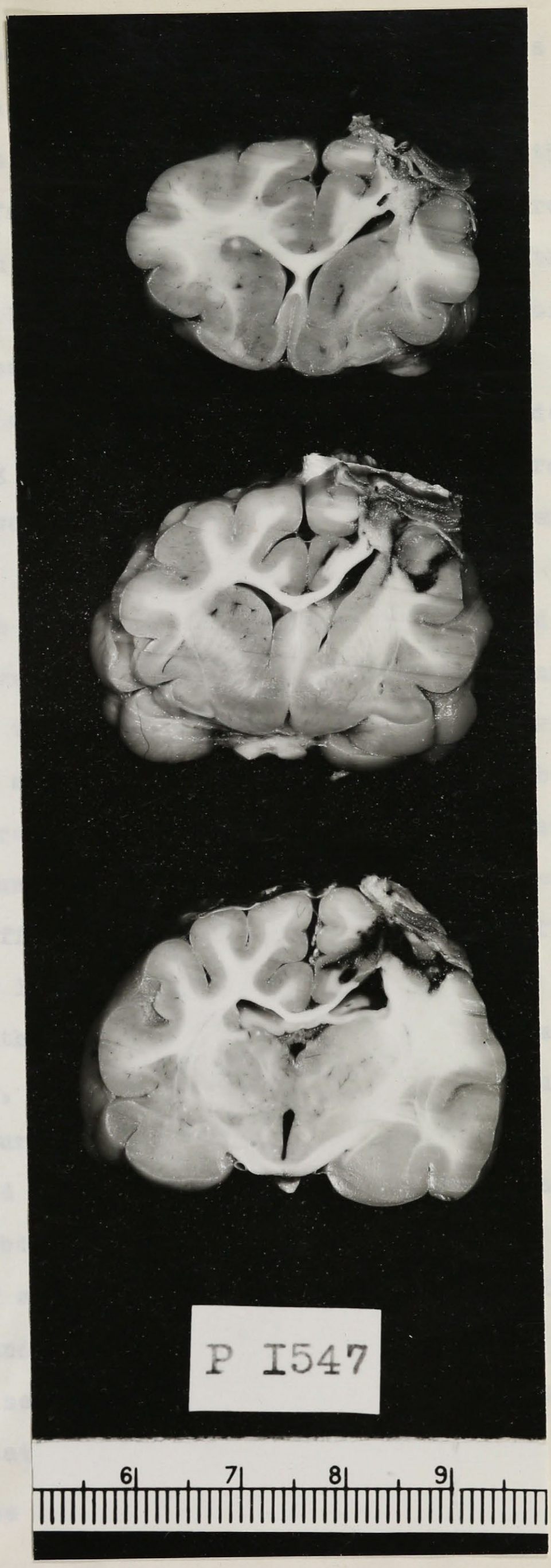


Fig. 39.

The brain of a cat three weeks after infliction of extensive left parietal region wound. Note absorption of damaged tissue.

Fig. 39.



which the dura had been torn. This is particularly true in those instances in which there may have been an open wound, leading to the possibility of infection, and in those cases which have suffered severely from shock with the resultant diminution in cerebral blood flow accompanying the lowering of systemic blood pressure; both of which factors would tend to increase the ultimate degree of scarring.

The fourth consideration, concerned with the degree of meningeal scarring and the occurrence of the "post-traumatic headache syndrome", would also argue for careful debridement of the wound.

All factors considered, then, we are in accord with the principle that severe cerebral injuries should be carefully debrided, when the actual debridement will not carry as its accompaniment a penalty disproportionate to the benefits to be gained. The presence of foreign bodies in the wound is an additional argument for radical operation in properly chosen cases (Wagstaffe, 1928, and see the discussion of this question by Pilcher, 1936).

In one of the earlier chapters the question was raised as to whether, left to nature, absorption of injured tissue would not occur, so that the final result as far as scarring is concerned would be found to be as satisfactory as that which could be produced by the surgeon. Figure 38 showing the brain of a monkey three months after the infliction of a severe wound, and figure 39 showing the brain of a cat three weeks after a severe injury, suggest, by their gross appearance, a very satisfactory end result. We have no experimental evidence drawn from a comparable series of animals,

one with injured brain operated upon, and another with injured brain in which debridement was done. However, clinical experience makes common knowledge the severe gross and histological changes found as the late result of head injury. Dr. William Cone has kindly given us permission to cite the reports of two individuals upon whom he has performed radical debridement of damaged cerebral tissue. Autopsy in these cases was obtained two and eight years after the operative procedures.

P.C.-R.V.H. No. 89099 was admitted to the hospital May 8th, 1934 for the first time at the age of sixteen. About two hours before admission he had been struck by an automobile. The family and past histories were reported as negative. Examination showed a boy alternating in brief periods between consciousness and stupor, presenting a laceration of the scalp in the left frontal region, and no definite neurological signs other than his stupor. X-ray studies showed a comminuted fracture of the skull in the left frontal region which, at operation - which was done as soon as possible after admission - was found to be depressed. Under avertin and local anesthesia the wound was debrided and the fragments of bone removed. Dr. Cone's operative note reads: "..... softened brain escaped through the dural laceration and large blood clots came away.... The frontal lobe had been destroyed on its ventral surface back almost to the point at which the frontal lobe joins the fissure of Sylvius.....Softened brain clots were washed out with irrigation and finally the softened brain was removed by suction.....The bleeding was controlled with silver clips.

An attempt was made to suture an opening in the dura at the base (the fracture opened into the ethmoid sinus)..... In order to drain through a clear field a left subtemporal decompression was done and a rubber dam drain was carried out through a separate stab wound.....".

A discharge note by Dr. Cone, dated June 4th, 1934, reads in part: "His post-operative course was smooth, without undue restlessness or excitement, and was characterized by steady improvement".

On November 12th, 1936, he was readmitted (M.N.I. No. 2001), having shot himself one-half hour earlier. Death occurred fifteen minutes later. Autopsy was performed and the brain was studied by Dr. W. L. Reid from whose report the following notes are taken: "The dura is adherent to brain over the left frontal pole and is thickened in this area. There is a deficiency in the left frontal pole under the area of dural adhesion, which is irregular in outline. There is no shift of the midline. Coronal sections were cut, and serial sections were taken by Dr. Cone from the left frontal pole to include the old operative scar".

Sections 4, 5a, and 5b may be taken for further description. Dr. Reid says of these: "These three sections show the most marked changes. The dura is considerably thickened. The arachnoid is also considerably thickened and irregularly disposed. There is a heaping-up of arachnoidal cells. In some areas these cells are present in fairly large groups and occasionally arranged in whorl formation, giving a distinct resemblance to a meningeal fibroblastoma. No mitotic figures have been seen in these arachnoid cells. In one area there is what appears to

be a section through a silk suture surrounded by connective tissue. There is a fairly large giant cell containing several discrete nuclei lying between the silk and the surrounding connective tissue. There is gliosis on the edge of the underlying brain tissue and in one area there is a well demonstrated meningocerebral cicatrix in which islands of glial tissue are enclosed in a delicate connective-tissue reticulum. This is connected with the overlying meninges. The architecture of the brain tissue immediately surrounding this cicatrix is disarranged and contains numerous astrocytes of the Nissl plump-cell type. There are quite a few multinucleated cells scattered through this tissue. In some areas the overlying grey matter appears fairly normal, while there is considerable destruction of the underlying white matter with loss of myelin. Most of the blood vessels of these sections are somewhat thickened and occasionally thrombosis is seen of one of the smaller vessels. There is quite marked perivascular infiltration with phagocytes - occasionally with small round cells. Many of the phagocytes appear to be compound granular corpuscles and are seen in the area of the cicatrix and in the overlying subarachnoid space. There is considerable increase in the connective-tissue content of these sections. Much of it is in relation to blood vessels but there is a large amount coming in from the meninges and extending into the areas of gliosis. Most of it is reticular in type but there are also collagenous fibers present".

Dr. Reid concludes, "On the whole, the amount of scar formation and damaged tissue is much less than would be expected had the damaged tissue not been removed. Dr. Cone commented that part of the scarring may be due to, or may be secondary to tract degeneration. In his opinion this is a healing brain

wound and there is no evidence of inflammatory reaction".

Our own review of this material leads us to concur completely in the opinion that the residual scarring must be very appreciably less than if no debridement had been done. Despite the presence of a limited amount of typical meningo-cerebral cicatrix the procedure, on a quantitative basis, seems to have been wholly justified.

The second case was treated similarly. A.M., 71 years of age at the time of his death in 1936, was originally admitted to the hospital eight years earlier (R.V.H. No.67106). The following is a synopsis of his case: "On October 4th, 1928 this patient was hit on the head by a brick; he was brought into the hospital in an unconscious state, bleeding from a large, Y-shaped lacerated wound in the right fronto-temporal region and bleeding actively from the nose. He was comatose; blood pressure 185; pulse 40. Hematoma about the right eye. Patient had been vomiting large amounts of blood. Comminuted fracture of the right fronto-parietal region with a marked depression was found. Some of the bone fragments had lacerated the dura exposing bulging, lacerated brain. Patient was operated on under local anesthesia; a wide debride-ment was done; the depressed fragments of the skull removed; bleeding points controlled and softened brain removed by light suction and irrigation. The dura was closed tightly and the wound drained through a separate stab wound. He improved from the time of operation onward and his post-operative course was rather uneventful aside from the fact that he was somewhat confused. Enquiring into his condition

over the past several years, it is ascertained from his wife that he had had no seizures; had been somewhat irritable and nervous at times. He was admitted to St. Luc's Hospital in a state of cardiac decompensation and died there on February 3rd, 1936. Autopsy was done which revealed no relevant findings." Through the co-operation of the St. Luc Hospital authorities it was possible to study the brain of this patient. Dr. Donald Coburn's notes read: "The atrophy of the right frontal lobe is quite apparent but in none of the sections is there any evidence of ventricular dilatation or distortion. There are cystic areas in the leptomeninges at the site of the dural attachment. Beneath this are small intracerebral cysts, light yellowish-brown in color. The largest measures 2.0x1.0 centimeters and has only what appears as a thin shell of cortex overlying it. There is considerable alteration of the cerebral tissue beneath the thickened leptomeninges, in addition to the cysts, and some areas have a greyish translucent appearance. The greatest involvement extends 2.3 centimeters beneath the brain surface and comes to within 0.65 centimeters of the right anterior horn. No suggestion of a cicatrix extending deep into the cerebral tissue is evident.

"Microscopic: Tissue consists of a vertical section through the right anterior lobe. The anterior horn of the ventricle is present and in the supero-lateral region is a cyst covered superficially by a thin layered membrane. The deepest part of the cyst is 1.0 centimeters from the most superficial part of the ventricle. There are smaller cysts inferior to the large one.

"The leptomeninges on the medial surface are normal. On the inferior surface in one sulcus is slight thickening of these membranes. On the superior surface there is irregular thickening, with a patchy proliferation of arachnoidal cells, with scattered psammoma bodies and whorls. The leptomeninges overlying the cystic areas are thickened as in the other regions by an increase in collagen, reticulin and scattered lymphocytes. Vessels in some areas of the thickened leptomeninges are numerous and less so elsewhere. No abnormality is noted in them.

"The cysts are covered by glial tissue with an overlying layer of leptomeninges. The walls are formed by wavy glial fibers which are well seen in the phosphotungstic acid stain. In this stain also the overlying glial tissue is seen to consist of criss-crossing heavy and light glial fibers with nuclei of glial cells scattered throughout. No nerve cells are identified here. In these cysts there are no leptomeningeal elements, and the glial fibers forming the walls are arranged in concentric fashion with no tendency to a radial arrangement.

"In two or three smaller cysts there are numerous interlacing strands of connective tissue in the walls and traversing the cavities and in spaces which are apparently subarachnoid cysts, these elements are abundant. In the Laidlaw connective-tissue stain they are seen to be collagen and reticulin fibers.

"Inferior to the lowermost cysts is a typical meningocerebral cicatrix, the leptomeninges being continuous with a

wedge-shaped interlacing network of collagen and reticulin fibers which extends slightly deeper than the adjacent sulcus. Extending out from the wedge are branching vessels and capillaries as well as fibroblasts. There are several smaller connective-tissue clumps of a similar nature. There is but moderate distortion of surrounding nervous tissue."

We are in accord with the findings described and agree with Dr. Coburn's conclusion: "We, (Dr. Cone and Dr. Coburn) feel that this (case) is ample evidence for the early debridement of contused and lacerated cerebral lesions".

Such results prove that it is possible to debride a recent cerebral wound and to obtain a late result of healing far better than one could expect were operation withheld.

Having disposed of these subjects we may now proceed to a consideration of the problem of excision of long-standing cerebral and meningocerebral cicatrices. As Foerster and Penfield (1930) point out, the test of the value of any clinical procedure rests in the clinical results that are obtained. Judged by this standard the procedure of scar excision is, in our opinion, amply justified as it has been applied to the treatment of epilepsy associated with meningo-cerebral cicatrix and areas of focal atrophy (vide Penfield, 1936). Many questions of practical and of academic interest remain unanswered, however. One would like to know, for example, what may be the appearance of the excision site some years after operation. Foerster (1936*) has stated that he has never seen at post-mortem the late results of one of his scar excision procedures. Re-exposure of operated cases has been rare in Montreal.

* Personal communication.

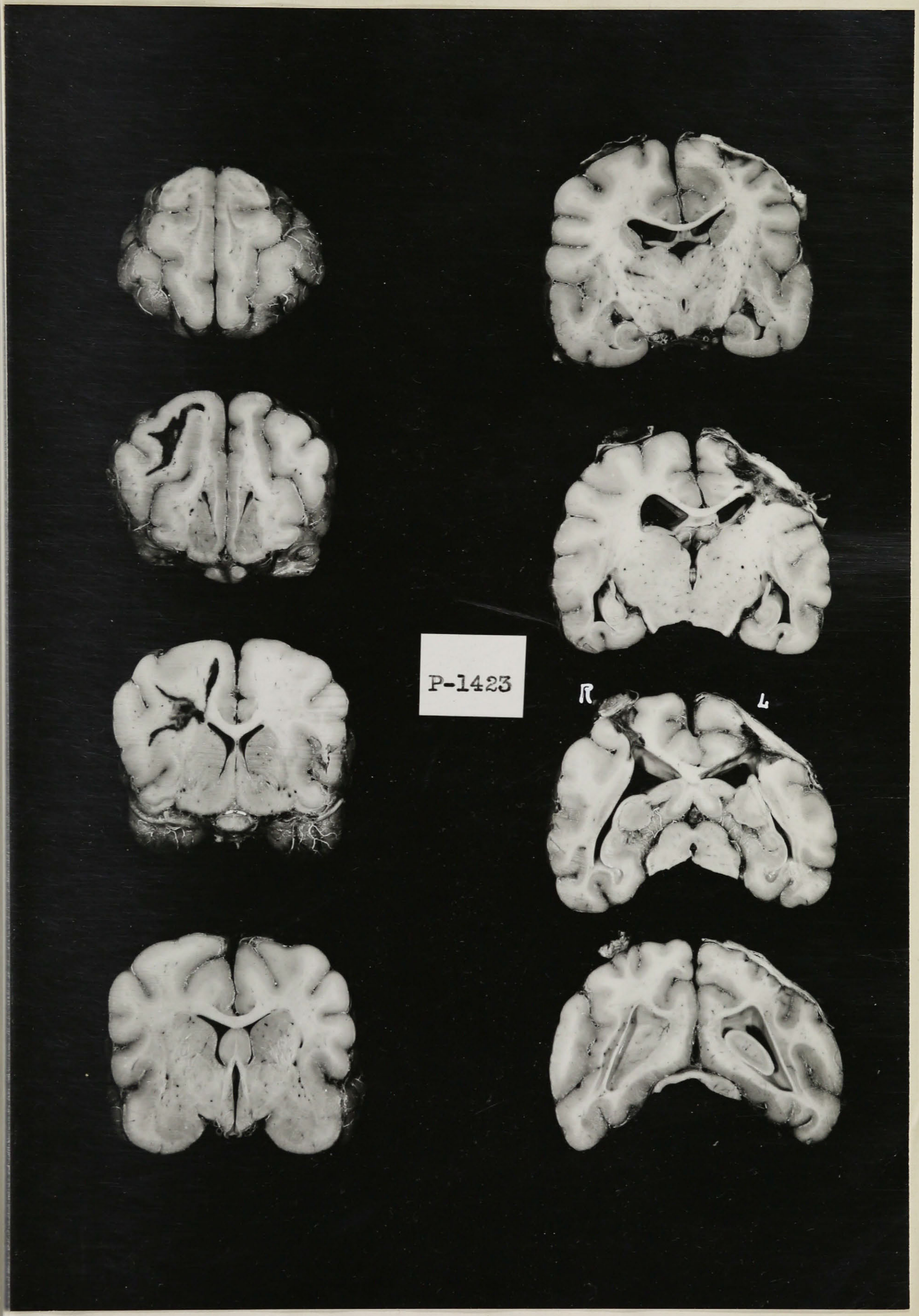
Because of the lack of histological evidence of the late results of scar excision, and because there remained unanswered other questions related to cerebral cicatrix, the author undertook in 1929, at the suggestion of Dr. Penfield, this study of cerebral cicatrix. Dr. Penfield and the author performed operations in which normal cerebral tissue was excised in cats and in monkeys. The details of the procedures need not detain us now. It will suffice to say that in a group of ten cats followed from six to two hundred and twenty-six days, histological results were obtained which were considered "good" in four animals, "poor" in six. Concurrent operations by the author upon monkeys yielded results that were no more satisfactory. In 1931 other attempts were made to excise cerebral tissue in monkeys. In a group of fifteen animals operated upon in that year by the author, eight results were obtained which were deemed satisfactory from the standpoint of relative absence of scar tissue, in five cases extensive scarring and degeneration occurred. Two cases were not suitable for analysis.

That cerebral excision may sometimes give rise to as extensive scarring as that seen in wounds is well illustrated by the following experiment: Dog, P-1423, one hundred and fifty-five days before death had removed from the left mid-parietal region through a decompression opening a block of tissue measuring slightly more than 1.6 centimeters in an antero-posterior direction, 1.4 centimeters mesio-laterally, and 1.0 centimeters in depth. To remove it two large veins

Fig. 40.

The letters indicate the wound (R) and the excision (L). See text for details.

Fig. 40.



entering the midline were clipped. Arterial supply to the remaining tissue seemed assured. A generous opening was made into the ventricle. The dura was closed. Subsequently one hundred and thirty-nine days before death a wound was made in the right parietal region through a small craniotomy. The wound was made with a pair of large scissors, inserted one and one-half centimeters into cerebral substance and moved about roughly. A large cortical vein was deliberately cut. Abraded temporal muscle was opposed to the surface of the wound. An injection of blood into the right frontal lobe ten days before death need not concern us here. The dog was sacrificed because of the development of a generalized peritonitis, probably resulting from trauma done at the time of intra-peritoneal injection of dial ten days before.

The photograph (Fig.40) shows clearly the extensive loss of bulk on the left side where the large block of cerebral tissue was removed. There is a compensatory shift of the posterior portion of the brain to the left side, which seems to be the cause of the narrowing and displacement of the lateral ventricle, rather than that these are due to cicatricial pull. There is abundant connective-tissue infiltration of the edges of the cerebral tissue. All in all, the picture is one of cerebral cicatrix. The wound area on the left shows a good deal of atrophy. The apparent up-pulling of the ventricle suggests a true pull for though this ventricle may well have enlarged to compensate for loss of bulk on the left, the wound was not made until sixteen days later and there were no adhesions

at the site of operation when it was exposed. Therefore, there is good evidence of pull with possibly an added element of atrophy.

In any event, the important point is that the result of the excision on the left is hardly more satisfactory from a histological point of view (discregarding the question of vascular nerves) than the wound in the opposite hemisphere.

Obviously some unrecognized factor was entering in to give these variable results. All the operative procedures were being carried out with, we thought, due care of the vascular supply. Yet it was quite evident that degeneration of the excision edges was sometimes occurring, and that in some instances true scar was forming as well. A chance interruption of the middle cerebral artery while amputating a temporal lobe resulted in the finding at autopsy nine months later of an important clue to the mechanism of cerebral healing. When this brain was sectioned there was found a degeneration in the course of the middle cerebral artery, which degeneration was surrounded by a minimum of scar tissue reaction, no infiltration of the brain by connective-tissue elements, and a very moderate gliosis. This lead resulted in the study of the changes following occlusion of the middle cerebral artery reported in an earlier chapter, and made possible the elucidation of the principles of cerebral healing which are there presented.

With the information gained thereby another group of animals was operated upon during the past year. In some instances the suture method of block excision was used. In other instances a portion of a gyrus was excised, with special

care to preserve vessels in the depths of a sulcus. The essential point in these experiments has been that the utmost effort has been made not to interfere with blood supply, arterial chiefly, but venous as well so far as possible.

The results of our studies of the methods of scar excision can best be presented in a sub-chapter:

The Technique of Cerebral Scar Excision.

The problem of dural exposure presents no special difficulties. Foerster (Foerster and Penfield, 1930) habitually employed craniectomy as a means of exposure. He feels that its decompressive effect may be of value. On this Continent, however, the employment of a bone flap, oftentimes of very appreciable dimensions to permit of wide exploration, has been considered preferable. Its protective and cosmetic value are of great importance and inasmuch as it can be combined with generous bony decompression in most instances, the somewhat doubtful advantage of the decompression gained by craniectomy is overweighed.

The presence or absence of dural-arachnoidal adhesions is a matter of considerable moment. Obviously penetrating wounds of the skull will be associated with generalized adhesions, and hemorrhagic extravasations into the meninges lead to them also (though we have occasionally, in animals, found no trace at later post-mortem examination of either subarachnoid or subdural bleeding). Important in the interpretation of etiology is the absence of adherence of the dura, which argues for a wholly intracerebral condition, unrelated to the meninges, and usually associated in our experience with arterial occlusion. Thickening and greying of the

arachnoid, and streaking of the vessels are probably, as first pointed out to us by Dr. Penfield, to be regarded as signs of an intracerebral degenerative process, with "dumping" of the products of destruction into the meninges. In view of what has been said in earlier chapters about the response of vessels to trauma, the necessity of separating in a gentle fashion the innumerable adhesions that may be found, is manifest.

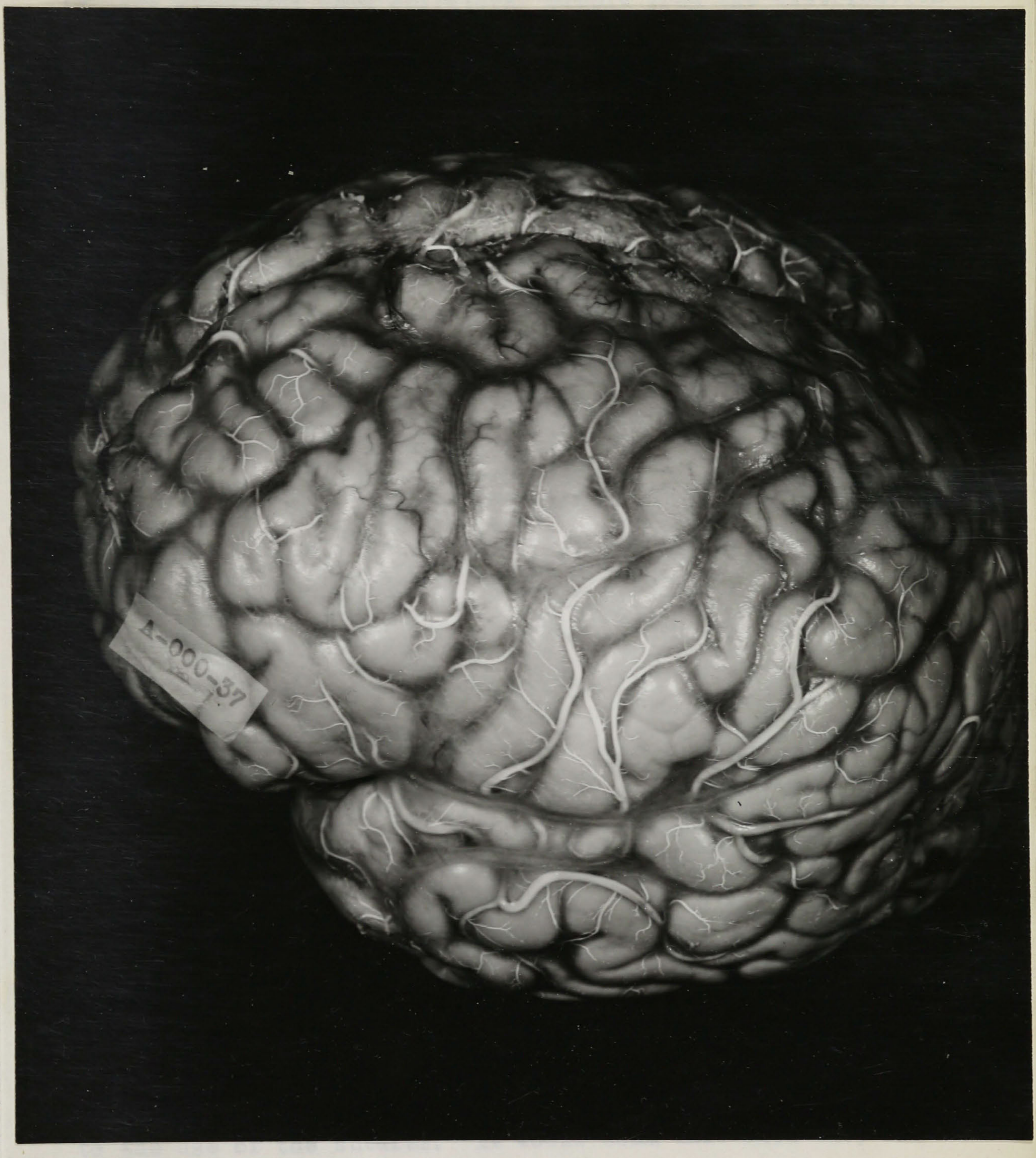
Following inspection of the brain and electrical exploration to determine the physiologically abnormal area, considerations which need not detain us here, one is faced with the important question of what principles must guide one in making the excision, and subsidiary to those principles, what is the best technique to employ.

As has been repeatedly emphasized, the essential consideration is preservation of the blood supply of the tissue left behind. Observation of the minimal reaction surrounding the cysts resulting from occlusion of the middle cerebral artery suggests that sudden, complete occlusion of the artery of supply to an area is the procedure of choice. Obviously, however, such a procedure is impractical because of the extent of the resultant lesion and because the method is not sufficiently flexible to be applied in various areas. However, these experiments do serve to demonstrate the necessity of considering the residual blood supply in the peripheral segments of the artery whose course is involved in scar tissue. For example, successful excision of a scar in the face area of the human necessitates a nice attention to the blood supply of the arm area, for judging by both experimental and clinical experience,

Fig. 41.

Human brain, injected with bismuth solution, showing the irregular surface distribution of the arteries.

Fig. 41.



the arm area will suffer both physiologically and histologically if left dependent upon collateral supply from the distribution of the anterior cerebral artery.

Whatever technique of excision is employed must, then, preserve if at all possible the main arteries of supply. In general these tend to run deep in the sulci but figure 41 which is a photograph of a human brain whose vessels have been injected with a bismuth solution (Hill, 1929) shows clearly the irregularity of distribution of the middle cerebral artery over the convexity.

Three methods of excision present themselves: The first of these employs sharp dissection of the tissue, with hemostasis dependent upon the use of silver clips, ligatures, and the electro-coagulator. It is essentially a modification of the two methods that follow. The second is the technique employed by Foerster and by Penfield, in which deep ligatures are set in the brain and then drawn, cutting cerebral tissue and gathering the vessels in a clump at the surface as the loop is drawn taut. The third employs the electro-surgical unit for dissection and for hemostasis.

As the result of our experimental work we have come to the conclusion that either the suture or the electro-surgical method is an acceptable one, the choice of which may depend upon the particular preference of the surgeon concerned. On theorectical grounds there is at least one serious objection to the use of the sutures. It would seem that when they are drawn taut in their loops they must drag severely on the vaso-astral framework, perhaps tearing small vessels and, in

Fig. 42.

The brain of a monkey 158 days following the excision of the right foot area ("sulcus technique") and 144 days following the excision of the left foot area (suture method). The extent of the excisions is shown in the next figure. See text for further description.

Fig. 42.

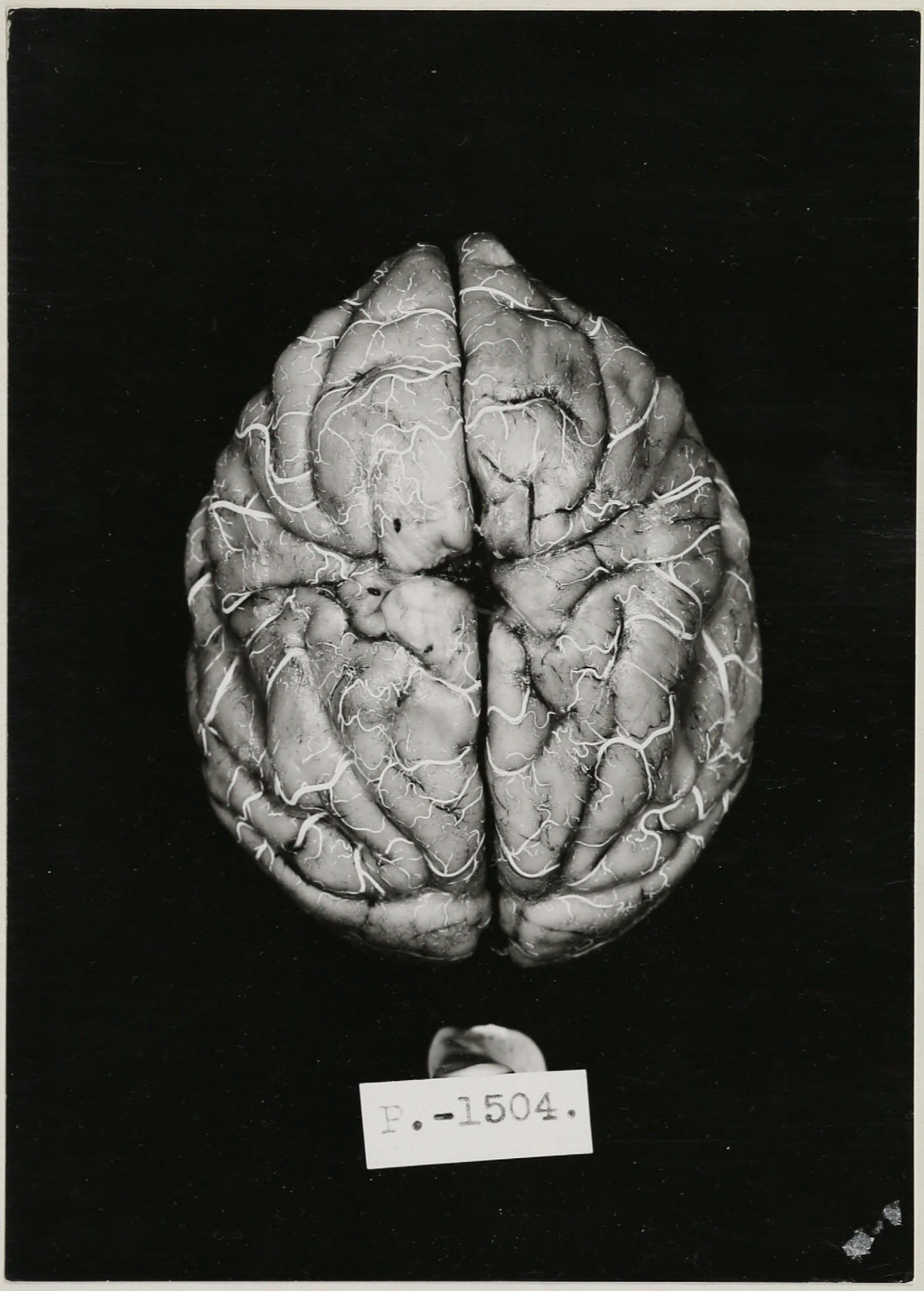
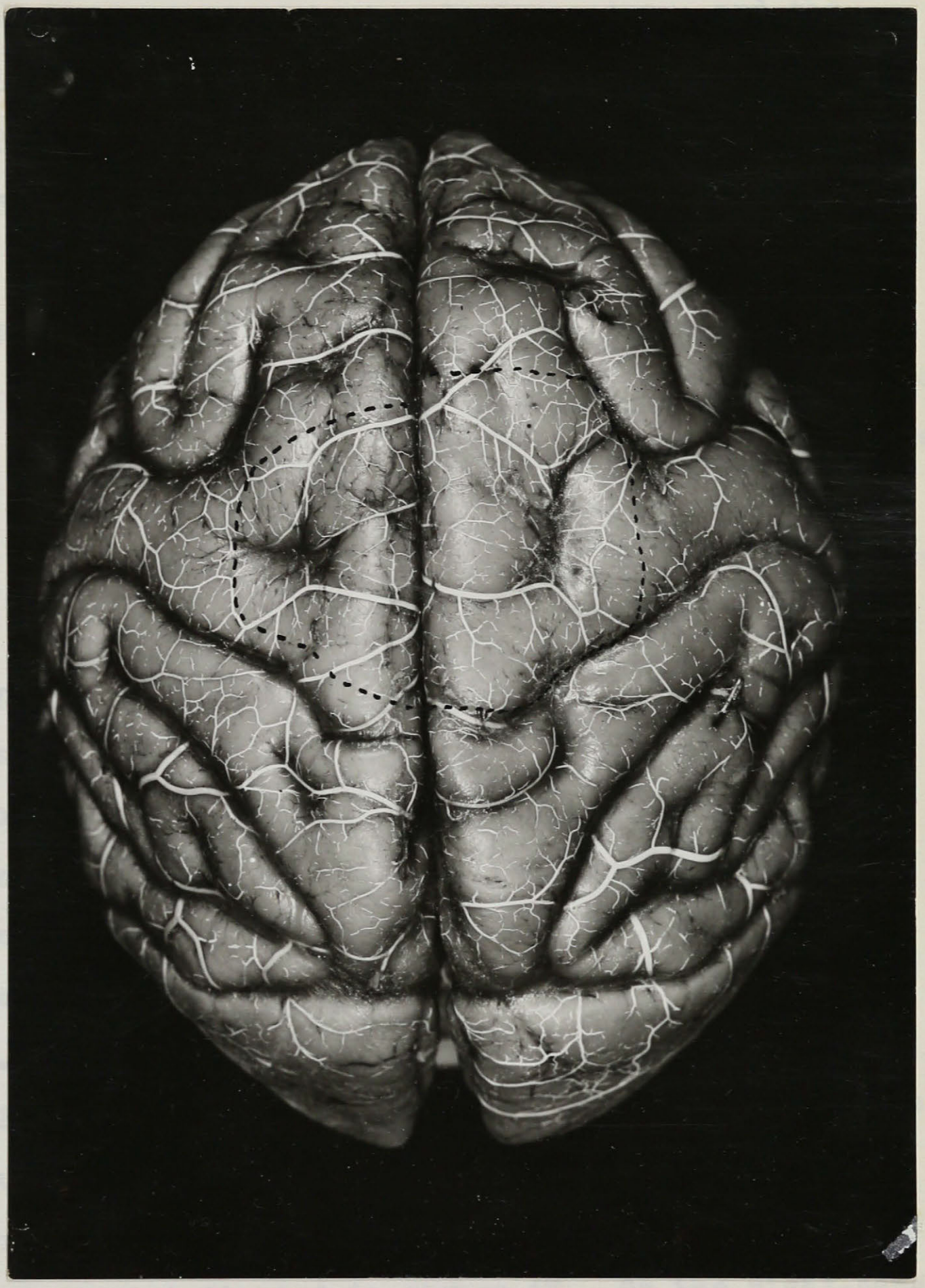


Fig. 43.

The extent of the excisions whose end results are shown in fig. 42.

Fig. 43.



addition, initiating serious vasomotor disturbances. We have therefore, observed microscopically the meningeal vessels before and after tying of the loops. There is no greater evidence of meningeal vascular disturbance in these cases than when the meninges are incised with the electrocautery, and the late histological results do not suggest more damage in the cerebral substance itself.

Thanks to the kindness of Dr. John Fulton of Yale University, Dr. Cone and the author have had the opportunity of studying the brains of a large number of animals from his laboratory in which he has excised various cerebral areas. Our conclusion at the time of this study was that the results were such as to justify the use of the electrocautery in such experiments, and a review of the data in the light of more recent experience confirms this opinion, any extensive degeneration found being attributable to vascular disturbances apparently unrelated to the use of the electrocautery. As a result of these and other studies made at the time, we reached the conclusion that the zone of damage due to the direct effect of the heat generated by the high frequency current passing through the tissue, extended little if any further than one millimeter.

Hence the author believes that either method may be used. Figure 42 is the photograph of the brain of a monkey (P-1504) from which cerebral tissue was excised on the right and on the left as indicated in figure 43. On the right-hand side the central and superior precentral sulci were utilized so far as possible as cleavage planes and the electrocautery was used for incising tissue only when necessary. The

Fig. 44.

Coronal sections of the brain shown in fig. 42.

Fig. 44.

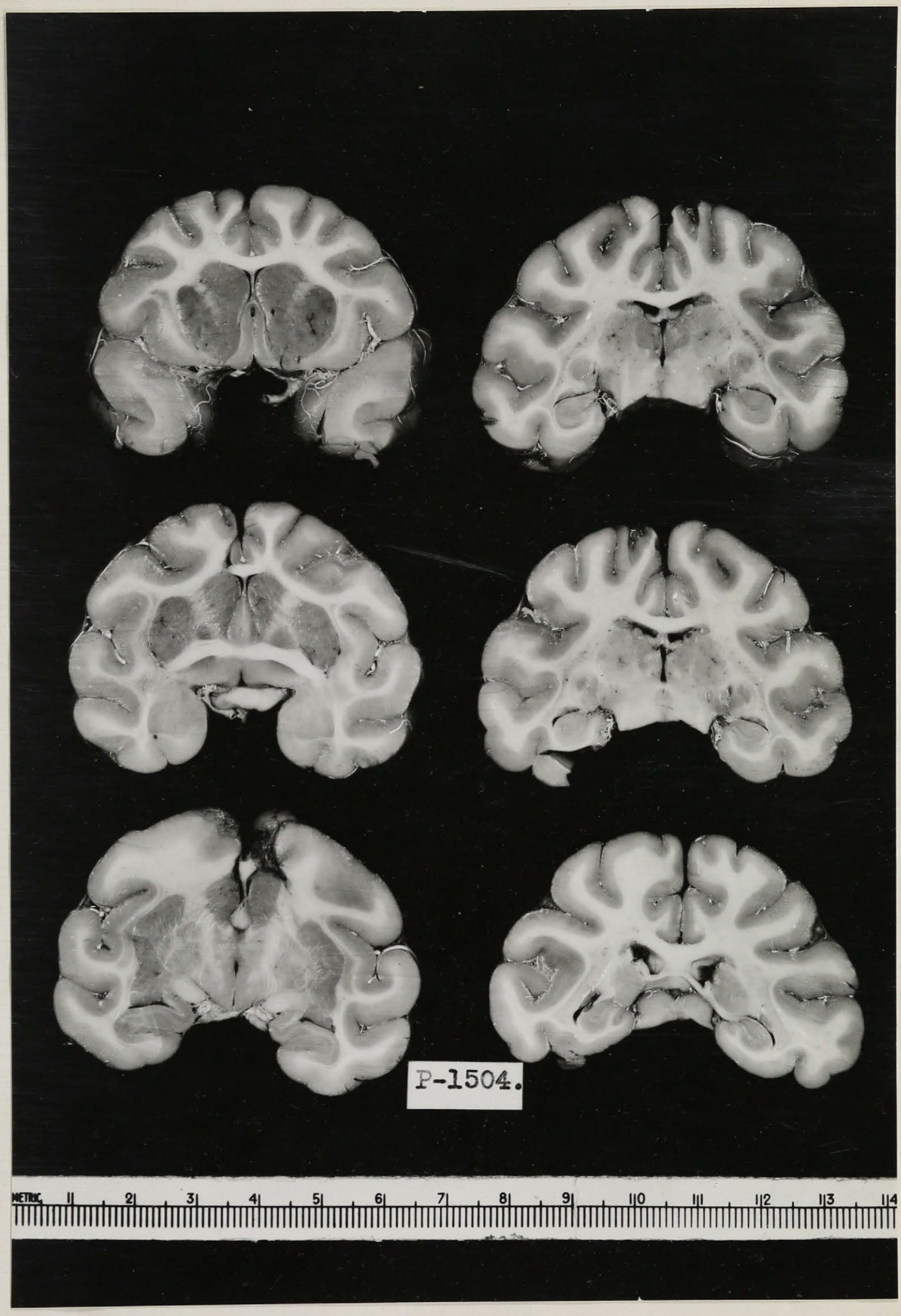


Fig. 45.

Hematoxylin and van Gieson preparation of the two excision sites. There is little difference in the histological end result of the two excisions, one done by the "sulcus technique", the other by the "suture method".

Fig. 45.

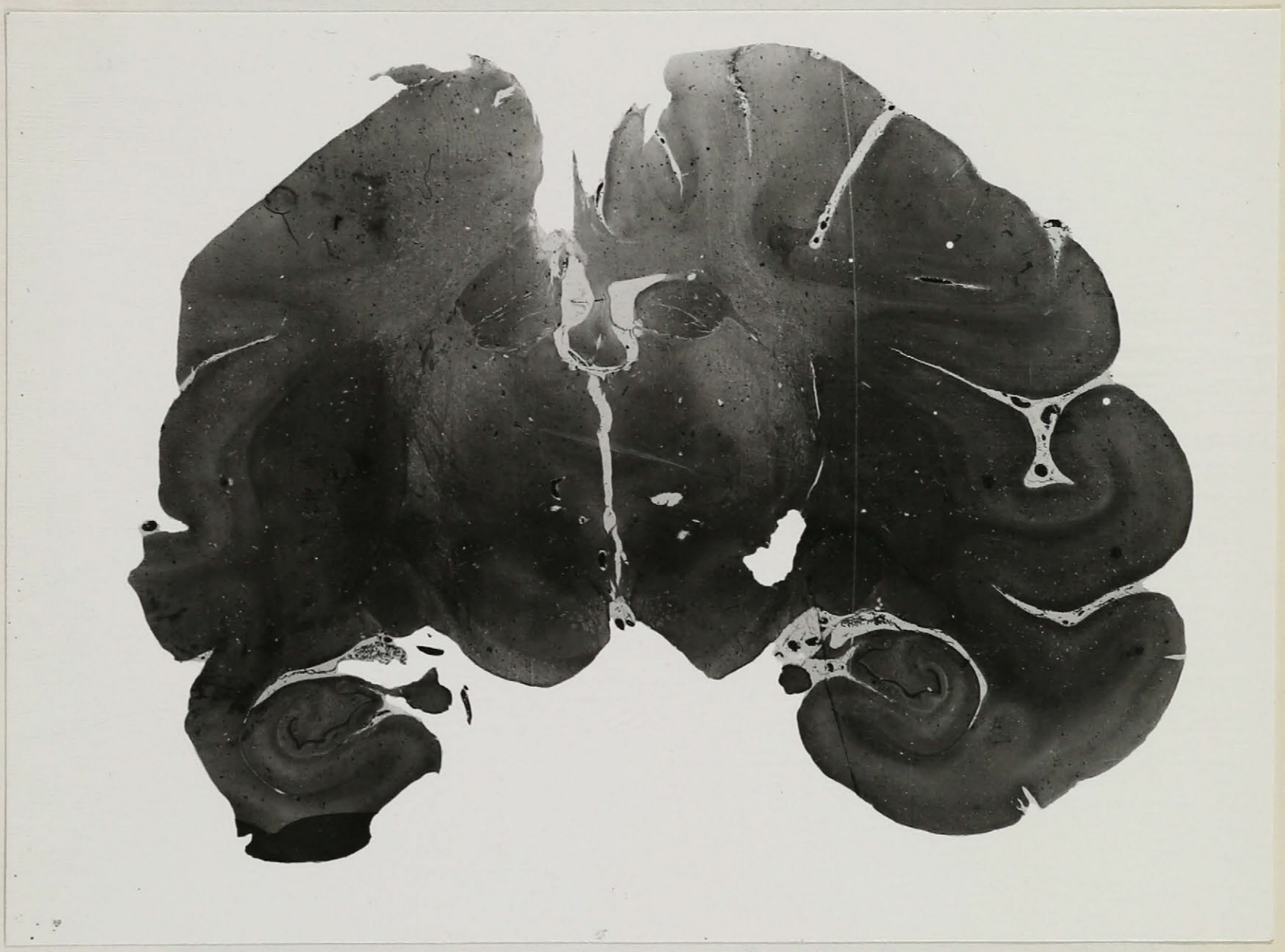
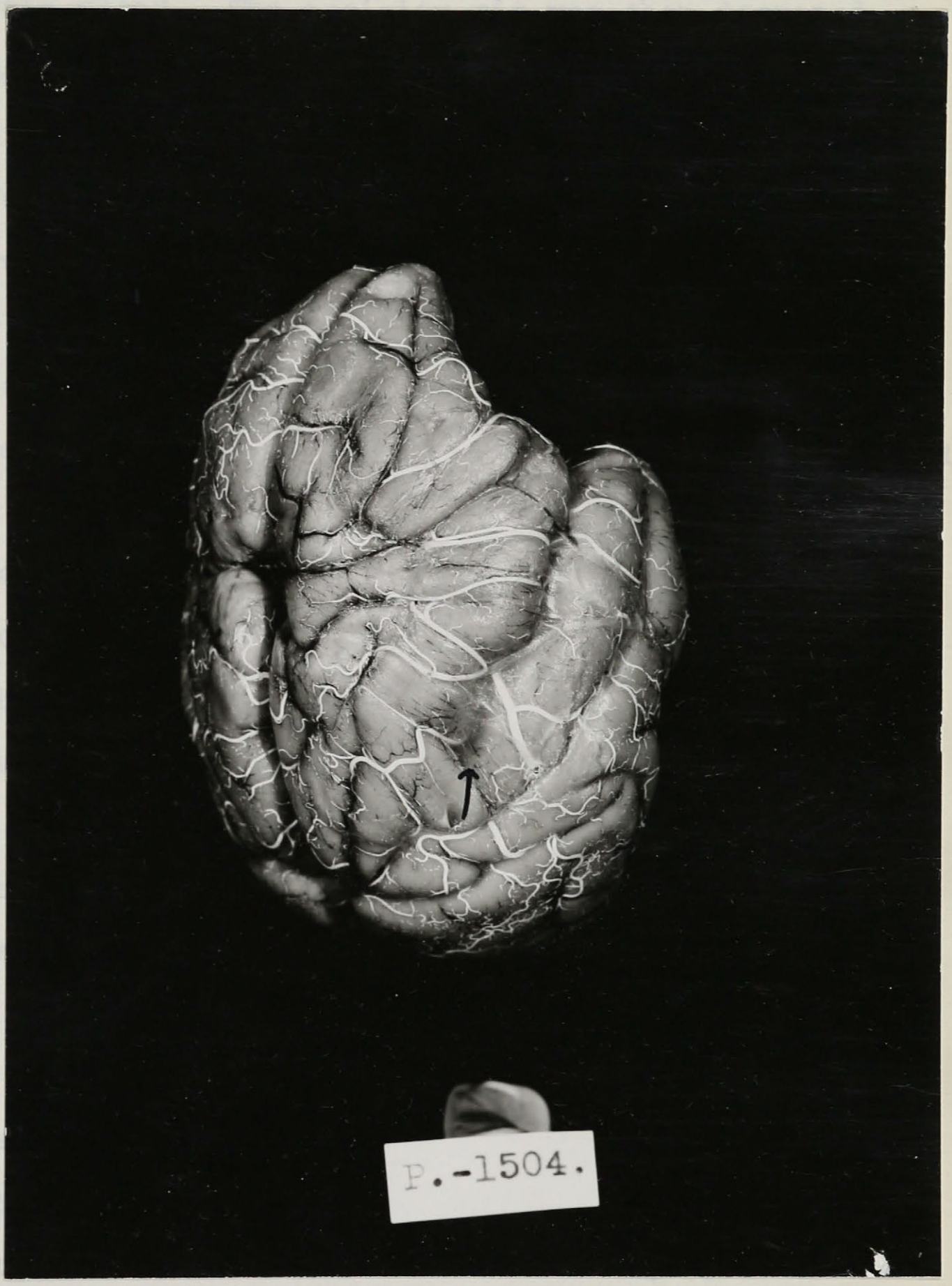


Fig. 46.

The arrow indicates the widening of the Sylvian fissure which has resulted from the shift of the brain toward the excision. Note also the tendency of the arteries to approximate one another as they approach the excision site, another result of the shift.

Fig. 46.



excision block was removed with a brain spatula and the pit was deepened into the ventricle by the use of the sucker. On the left the deep-cutting sutures were set along the lines indicated in the figure, and the block of tissue was lifted out with a brain spoon. The excision pit was then deepened and an opening was made into the lateral ventricle. The animal was sacrificed one hundred and fifty-eight days and one hundred and forty-four days after the first and second operation respectively. The brain is shown in figure 44 in coronal section. The picture shows to disadvantage the left side (suture method) but microscopic examination of the two excision sites showed little to be chosen between, as demonstrated in figure 45.

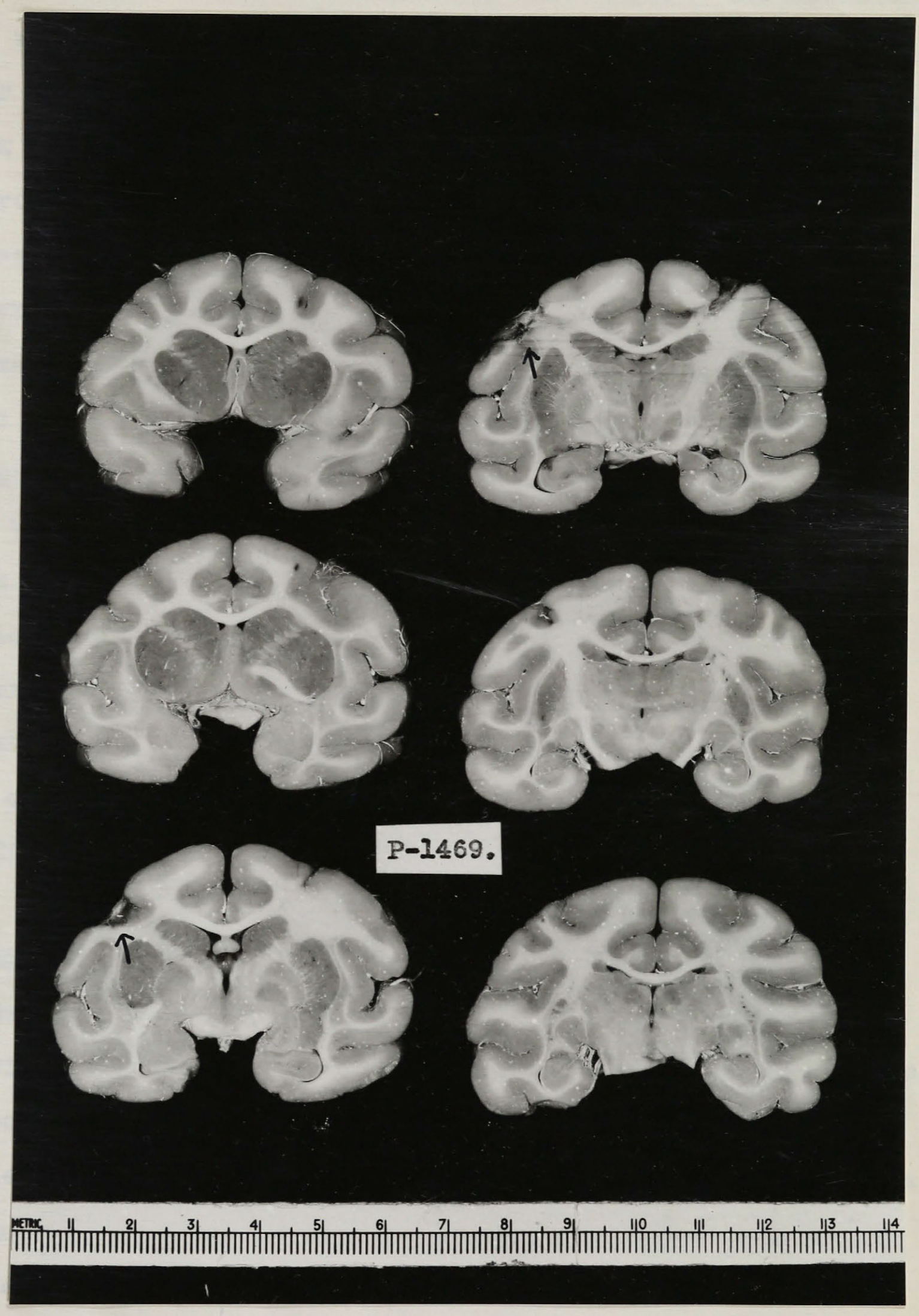
The obvious shift of the brain, in the absence of any appreciable scarring, is quite evident in figure 42 already referred to. The three black dots on the left hemisphere are the fine sutures used for removal of the tissue, and they show well how the brain has shifted mesially. The deep Sylvian sulcus just evident on each convexity shows that the shift is compensated for by widening of the sulci. It is evident, then, that widened sulci need not be an indication of <u>local</u> atrophy, since the gyri here are of good size. Figure 46 shows again the widened sulcus and demonstrates the alignment of the vessels toward the excision site.

In those instances in which we have employed the cautery for removal, its use has been limited. An example of the technique used is presented by the study of another

Fig. 47.

The gross result of excision of the motor gyrus (hand area) by the "sulcus technique". One hundred and sixty-four day survival.

Fig. 47.



monkey (P-1469). It was planned to remove almost the entire hand representation in the precentral gyrus. Figure 47 shows the result at one hundred and sixty-four days. The operative note reads, "The central sulcus was freed from the upper to the lower limits (of the hand area). This manoeuvre precipitated brisk hemorrhage laterally and a silver clip was necessary to control it, necessitating some local trauma. The precentral sulcus was similarly freed - this time with moderate venous hemorrhage, easily controlled by pledgets and warm saline. The mesial edge of the excision was cut to the depth of the gyrus with the Majestic unit, the lateral edge similarly. The pia arachnoid deep in the precentral and central sulci was then incised with a sharp knife and with a small brain spoon a level cut was carried across the base of the freed section of the gyrus from before and from behind, and the isolated section was lifted out. A small attachment deep in the antero-medial angle was cut with the Majestic unit. The base of the excision pit appeared very reasonably clean. The field was left very dry".

Microscopic observations of the arachnoidal circulation immediately after the excision are reported in the following note: "Definite pulsation could be seen in the arteries on the anterior face of the postcentral gyrus, and on the posterior face of the frontal gyrus, so that circulation in these two gyri appeared undisturbed. Moreover, there was a minimum of evidence of trauma to these gyri. The medial edge of the excision was clean cut, and the circulation in the

Fig. 48.

Hematoxylin and van Gieson preparation of the brain shown in fig. 47. The preparation passes through the excision area.

Fig. 48.

Fig. 49.

The right frontal pole of this monkey was amputated 143 days before death along the line indicated by the interrupted line on the left hemisphere. Note the shift of the brain forward, and the arachnoid free area, indicated by the arrow, where the cut face of brain has approached the surface.

Fig. 49.

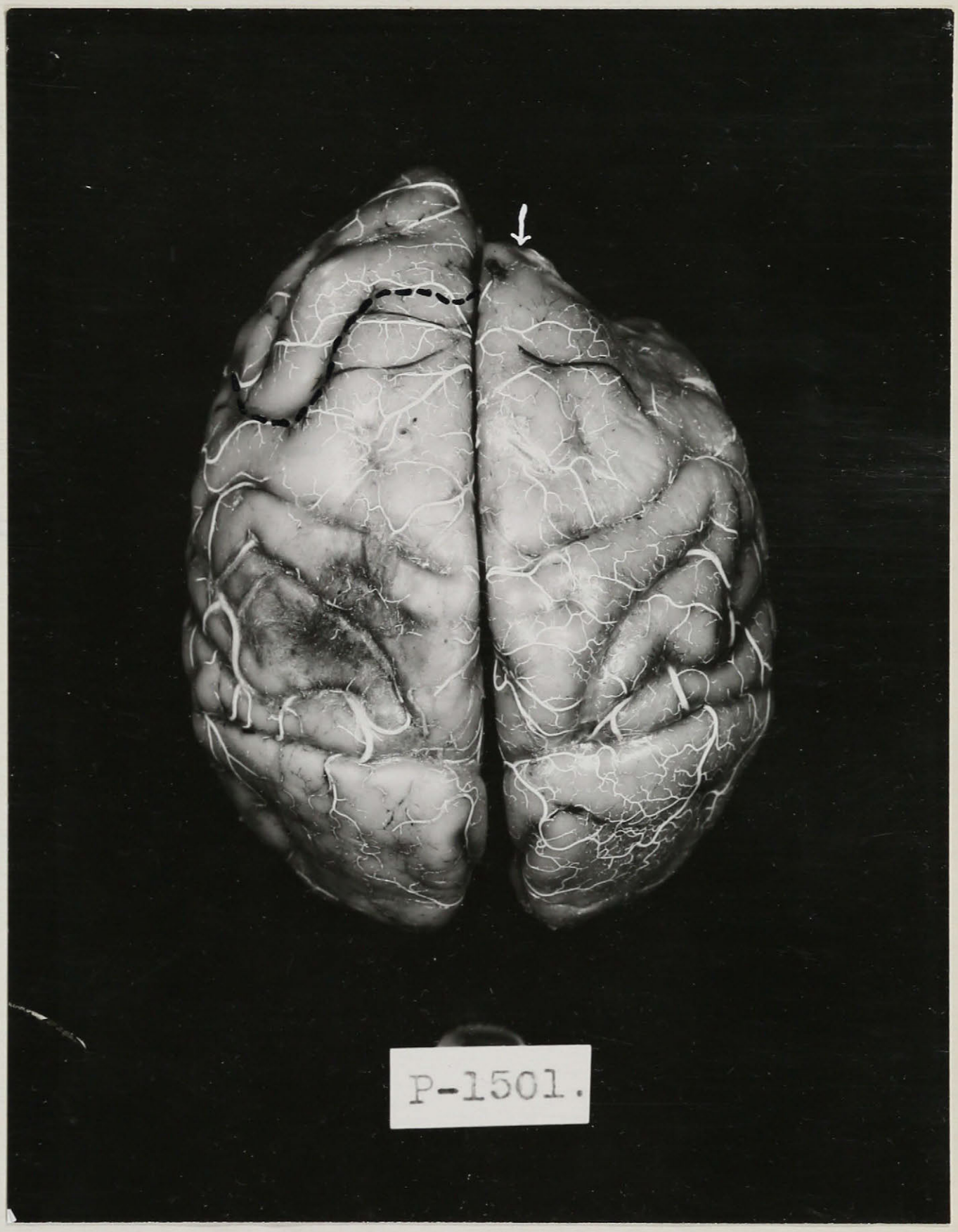


Fig. 50.

Hematoxylin and van Gieson preparation of a longitudinal section through the brain following amputation of the frontal pole, as shown in fig. 49.

Fig. 50.

gyrus, as judged by its color, appeared undisturbed. However, no definite pulsation of vessels could be seen and the rate of flow could not be determined, and we could not say with positive assurance that the circulation in the mesial portion of the precentral gyrus was normal, or even approximately so. The same observations held for the lateral portion of the precentral gyrus.....Nevertheless, this portion of the gyrus appeared grossly unaffected".

Figure 48 is a low-power view of the excision site at one hundred and sixty-four days. This would appear to be a reasonably satisfactory excision result, though other sections showed some softening and connective tissue proliferation beneath the floor of the excision pit, suggesting interference with vascular supply in that area.

Figure 49 shows the brain of a monkey (P-1501) whose right frontal pole was amputated as indicated by the interrupted line on the left hemisphere. The precentral gyrus was dissected free by the "sulcus technique" just described and the cautery was used only to incise the pia arachnoid at the mesial convexity. The actual cutting of brain tissue was done with a brain spatula. Care was taken to avoid the anterior cerebral artery. To be noted in the picture is the extent to which the right hemisphere has shifted forward. Figure 50 is a low-power preparation showing the minimal scar tissue reaction along the excision face one hundred and forty-three days after operation.

A word should be said about the use of silver clips. Their indiscriminate use is to be deprecated for we have observed marked glial and connective-tissue reaction about them on frequent occasions.

Concerning the advisability of making a permanent opening into the ventricle we have little to say. The question is of particular concern if it bears a relationship to the occurrence of seizures, a question not relevant at the moment. Experimentally we have not reproduced the ventricular dilatation so common in clinical cases. Monkey P-1504 demonstrates the difficulty of maintaining ventricular communication in a small brain with small ventricles. It is our impression that with large ventricles the opening into the ventricle should remain permanent; but that there is established in all, or even in most cases, a communication between the fluid in this large "cystic" space and the subarachnoid space at its periphery seems unlikely, for the meningeal adhesions seen in experimental animals are such as to lead one to think that the subarachnoid space at the cyst edge is usually obliterated. From the standpoint of cerebral healing the opening is probably of advantage because of a possible decompressive effect. Probably not much actual necrosed tissue is carried off directly into the fluid, for the excision walls, in the course of a day or two, become lined by an extensive mesothelial carpet under which phagocytic activity is carried on, evidently completely isolated from the "cyst" proper.

The subject of the employment of drains we do not propose to discuss because of the fact that experimentally, drainage of a wound is practically impossible, because of the danger of infection. We, therefore, have no direct evidence bearing upon the problem.

The handling of the leptomeninges is a matter of importance for exposure to drying and to other forms of trauma

undoubtedly facilitates the formation of adhesions even in the absence of hemorrhage. Hemorrhage itself, both subarachnoid and subdural, sometimes vanishes mysteriously leaving no residual adhesions. The factors governing this reaction are unknown to us, but we suspect that such absorption occurs if the meninges are untraumatized. Rupture of leptomeningeal continuity at any point leads to adhesions along the line of rupture as we have already indicated and as was earlier shown by Lear and Harvey (1924). Such adhesions may be very firm. We know of no way to eliminate them entirely. They seem to represent an invariable histological sequence. Gentle handling of tissue reduces their occurrence to a minimum.

Dural closure should be meticulous, for though a new mesothelial lining can be supplied for defects of a few millimeters' extent it is easy for edematous brain to insinuate itself through dural gaps and thus traumatize itself further.

The bone flap is customarily replaced and fixed with wire sutures, provision generally being made for a bony decompression.

No surgical procedure of the sort outlined can be considered sufficient of itself. Due attention must be given to the factors arbitrarily termed "medical" in the first portion of this chapter. Only by an intelligent, comprehensive consideration of all the problems involved can the optimum therapeutic result be obtained.

SUMMARY:

There have been considered in this chapter the various "medical" and "surgical" procedures which tend to reduce or to eliminate the vascular disturbances attendant upon the various forms of acute cerebral injury - thrombosis, shock, and direct trauma. An understanding of the early stages of change in these conditions is of great importance in trying to reduce the amount of ultimate damage resulting from the injuries. In the second half of the chapter the indications for and the technique of surgical removal of long-standing cerebral cicatrix have been considered.

SUMMARY.

1.

In the introductory chapter there is presented a general outline of the argument developed in the later chapters. It is proposed that the various cicatrices found in cases of cerebral arterial occlusion, cerebral hemorrhage, and cerebral contusion and laceration are all closely related in the essential element concerned in their development, i.e., interruption of normal vascular supply. Three benefits of the study are foreseen: 1) A better understanding of the cellular changes involved in cerebral scarring; 2) A clearer differentiation among the late histological stages resulting from various types of cerebral insult; and 3) A clearer conception of the principles of therapy, both medical and surgical, necessary for the satisfactory treatment of this important group of cerebral conditions.

II.

In the second chapter are reviewed the anatomical features of the cerebral vascular system that are essential to the development of a collateral circulation. The possibility of and the mechanism for functional circulatory disturbances are next discussed and the special susceptibility of brain tissue to deprivation of oxygen is stressed. Evidence from experimental work is presented to bear out the view that vascular disturbances may occur as the result of variation in neurovascular tone.

III.

The work detailed in Chapter III on cerebral arterial occlusion forms the physiological and histological groundwork on which are based the later conclusions. The summary of Chapter III is here quoted from page 38 of the text:

1. Various stages in the development of the late anatomical changes resulting from experimental occlusion of the main branches of the middle cerebral artery are described.
2. Three clinical cases are presented for comparison with the experimental material.
3. It is suggested that the anatomical end result of occlusion of the middle cerebral artery or its branches gives a definite anatomical picture.
4. It seems possible that the gradations in the histological picture found in such cases may be due to the relative rate of occlusion of the middle cerebral artery, i.e., that sudden occlusion with massive softening leads to cyst formation, that slow occlusion provides opportunity for the establishment of collateral circulation in the periphery of the softened area and thereby allows proliferative glial and connective-tissue changes to take place. As a result, greater cicatrization is found in such cases.
5. Sudden complete occlusion of the middle cerebral artery in monkeys possessed of a normal vascular tree is unaccompanied by red infarction. It is suggested that

the diminished circulation persisting after the occlusion, though insufficient to support the life of the parenchymal tissue, is adequate to preserve the vessel walls and to prevent diapedesis. It follows as a probable corollary that "red infarction" occurs clinically when the vessel walls are so diseased that the impaired circulation following sudden occlusion is still further impaired by pre-existing vascular disease with the result that the vessel walls are so poorly nourished that diapedesis occurs through them.

IV.

The fourth chapter deals briefly with the subject of intracerebral hemorrhage. The theory that most cases result from a circulatory insufficiency giving rise to prestasis and to diapedetic hemorrhage, is accepted. So far as scarring is concerned, this process is not unlike that which is produced by the experimental injection of blood. The late histological changes resulting from the injection of blood are described and compared with the pictures seen in clinical cases. Finally, these changes are correlated with the mechanical and functional vascular disturbances that we believe occur in association with hemorrhage.

V.

In Chapter V. cerebral concussion is defined and is separated as a physiological and clinical entity from cerebral contusion. The essential anatomical feature of

contusion is perivascular hemorrhage. Cerebral contusion is then, so far as the mechanism of scarring is concerned, essentially the same condition as intracerebral hemorrhage, complicated similarly by associated disturbances in cerebral circulation.

VI.

Cerebral laceration and cicatrix are discussed in Chapter VI. and it is pointed out that laceration is very closely related to contusion - both in the circulatory disturbances that must accompany it, and in the conditions which predetermine the ultimate nature of the scar. Thus, to the static histological description already given in the literature is added the conception of cerebral scarring as a dynamic process dependent essentially upon disturbances in circulation.

VII.

In the final chapter use is made of the foregoing dynamic conception in discussing therapeutic problems. The importance of an adequate circulation and the effects of anoxemia on cerebral tissue are reviewed. The factors producing an inadequate circulation and the means of preserving or improving cerebral circulation are then considered. The question of radical debridement of cerebral wounds is discussed and the clinical importance of cerebral cicatrix is considered. Finally the technique of cerebral scar excision is reviewed in detail and the advantages and disadvantages of various methods are discussed.

VIII.

The study gives, it is hoped, a better understanding of the pathogenesis of cerebral cicatrix, a clearer differentiation of the lesions resulting from various types of cerebral insult, and a clearer conception of the principles essential to optimum therapeutic results.

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* Footnote: References marked with an* refer to papers which have not been read in detail but which are included in this list for the sake of completeness of bibliography.

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