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THE CEREBRAL CIRCULATION: SOME NEW POINTS IN ITS ANATOMY, PHYSIOLOGY AND PATHOLOGY *

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INTRODUCTION

It is not many years since the current teaching in regard to the cerebral circulation might be summed up in the anatomical doctrine that the vessels were 'end-arteries,' without anastomoses distal to the circle of Willis; the physiological doctrine that the cerebral vessels were without vasomotor supply, and changed their calibre only passively as a result of changes in the systemic blood pressure; and the pathological doctrine that thrombosis in the brain caused softening, and rupture of a vessel caused apoplexy. During the last two decades, a large number of investigators have approached the subject afresh along many different avenues, and have established a body of data which places the whole matter in an entirely new light. To review all of the work which has been done during this period would require far more than an evening's lecture, but although it is obvious that additional facts mean additional complications, certain broad principles stand out which have won general acceptance, and it is these that I should like to present here. Not only have the structure and function of the cerebral circulation a great theoretical importance, but they possess a considerable practical importance for diagnosis and treatment as well, and promise even more for the future.

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THE ANATOMY OF THE CEREBRAL CIRCULATION

The arrangement of the circle of Willis, the distribution of the larger arteries of the brain, and the course of the larger veins are, of course, matter of common knowledge and text-book record.

The main trunks of both arteries and veins run in the pia. The vessels within the parenchyma never reach the size of the larger pial vessels, and in general they tend to run in a direction perpendicular to the pia. Not only do the arteries spring from the surface, and, of course, ultimately from the circle of Willis or in the brainstem from the basilar, but the veins return to the pia and drain into the great sinuses. There are a few anastomoses with vessels of the scalp and face, but they are of little importance in maintaining nutrition. Even the vessels supplying and draining the choroid plexuses run in the tela choroidea, which is a fold of pia. There have been singularly few investigations of the finer anatomy. It has been accepted almost universally that there were no anastomoses between the cerebral arteries on the authority of Cohnheim. Cohnheim arrived at this conclusion from the results of experimental embolism, which produces areas of necrosis more rapidly in the brain than in any other organ of the body. He did not, however, make any extensive anatomical investigations, and those of the period (for example, in the hands of Duret and of Key and Retzius) gave a rather incomplete picture of the actual situation.

Perhaps the first to demonstrate clearly the anastomoses of the cerebral vessels was Fay¹ in 1925. He injected liquid mercury into one of the branches of the circle of Willis in a human brain after removal from the skull, and was able to demonstrate by X-ray that the injection mass would gravitate by way of anastomoses from one pole of the brain to the other and even across the midline. The subject was taken up in a more systematic manner by Pfeifer² and Cobb³ in animals, and more recently by Pfeifer⁴ in human material. By means of an injection technique, they have been able to demonstrate a rich anastomosis between capillary beds and between different systems of veins, a considerable anastomosis between neighbouring arterial systems, and even some short-circuits between arteries and veins. Pfeifer's many beautiful specimens leave no shadow of doubt that anastomoses between the various arterial systems do exist, and I have been able to confirm his findings in our own laboratory.

Not all of the details of the anatomy of the cerebral circulation need concern us here. I should, however, like to call attention to a few of the outstanding facts. In the first place, Cobb and Talbott,^{4a} extending the work of Craigie, showed that from a quantitative point of view the white matter possesses a relatively sparse blood supply, while the grey matter contains almost as many millimetres of capillary per cubic millimetre as does resting skeletal muscle, though it is far behind the cardiac muscle in its vasculature. It is probable, however, that the cerebral capillaries are more constantly

open than those of most other organs. We might say that it takes far more power to propel the ship than it does to operate the rudder and signal system, but that when steam is low, the captain's bridge is supplied first.

In the second place, I may point out that each area in the brain appears to possess peculiarities of blood supply which are as distinctive as its cellular architecture. In some instances, these peculiarities appear to be of especial pathological importance. It has long since been suggested that the selective localization of diseases of the central nervous system was in part due to regional differences in blood supply (Spielmeyer,⁵ Schwartz and Cohn⁶), and the intensive studies of recent years make this seem even more likely. Thus Pfeifer points out⁷ that the capillary dilatation which accompanies

FIG. 1.—The relatively scanty blood supply of the human substantia nigra, distinguished by its large pigmented cells (above), contrasted with that of the red nucleus (below). Injected autopsy specimen, unstained, 100 μ thick. Low power.

cerebral tuberculosis in the monkey spares the globus pallidus which is characteristically most severely damaged by a group of poisons including carbon monoxide, methyl alcohol and benzol. Pfeifer⁴ and also Finley⁸ have shown that the venous drainage of the cerebellum is peculiar, in that the white matter of the convolutions contains no large veins, while the dentate nucleus and its surroundings contain many. Finley has made a convincing attempt to correlate the localization of many acute encephalitic lesions in the latter region with the anatomical arrangement of the blood vessels. There appear to be peculiarities in the capillary supply of the substantia nigra which may explain in part its vulnerability toward epidemic encephalitis (fig. 1). This has been made the subject of special study by Finley.⁹ In a similar manner, Cobb¹⁰ has pointed out the differences in

capillary pattern between the lenticular nucleus and the cortex which may explain the localization of the lesions of paralysis agitans and carbon monoxide poisoning in the former. The list of possibilities could be extended almost indefinitely, but so far crucial investigations have been scanty. I shall return to some of the few definite practical applications of the study of vascular pattern a little further on.

NERVE-SUPPLY OF THE CEREBRAL BLOOD VESSELS

There can no longer be any doubt that the vessels of the brain are accompanied by nerves, medullated and bare. They have been demonstrated in pial vessels by Stöhr,¹¹ Hassin,¹² Penfield¹³ and others, in parenchymal vessels by Penfield,¹³ and in the choroid plexus by Clark,¹⁴ and by Ask-Upmark and Putnam.¹⁵ As will be seen below, there is every reason to believe that these nerves control the calibre of arterioles. It is not known whether they may also have a sensory function. Stimulation of the dural arteries and of the great sinuses in the human being produces pain (Fay,¹⁶ Penfield¹⁷), and there is some evidence that stimulation of the pial vessels may produce pain reactions (Fay,¹⁶ Levine and Wolff¹⁸). Certainly the choroid plexuses are insensitive, for I have applied a coagulating current to them in hydrocephalic infants under light anaesthesia on many occasions without evoking a response.

The exact connexions of the vascular nerves with the peripheral nervous system are not well known. Section of the cervical sympathetic chain produces an increase in the number of visible capillaries of the homolateral hemisphere,¹⁹ but it is not certain that the effect is permanent. A pathway for vasodilator fibres has been described, passing from the geniculate ganglion to the carotid plexus.²⁰ Sensory fibres apparently enter the trigeminal, the glossopharyngeal and the vagus roots, according to an ingenious analysis by Fay.¹⁶ Much work is still needed to elucidate this important problem, which may easily contain a clue to more efficient methods of treating the severer forms of headache, certain types of epilepsy, and even perhaps some of the structural abnormalities of the brain.

PHYSIOLOGICAL CONSIDERATIONS

No animal species could survive if its members were not provided with a mechanism for maintaining the blood supply of the brain through the ordinary vicissitudes of life. Obviously, the cerebral blood flow will be lessened if the systemic blood pressure falls, and there must exist some kind of an automatic balance between the two. Is this wholly on the part of the systemic blood pressure?

A definite answer to this question necessarily waited upon the invention of a suitable method of investigation, which was first systematically applied by Forbes and his associates.²¹ Over a series of years these investigators

have studied the pial vessels in living animals under the microscope, through an ingenious 'window' which is screwed into the burr-hole in the skull in such a way as to make a waterproof joint, thus preserving normal pressure relationships. By taking careful measurements and photographs, Forbes and his associates have shown conclusively that there is a vasomotor control of pial arterioles. They can be made to contract briskly by stimulation of the cervical sympathetic. Even more striking is their response to chemical stimuli. The presence of carbon dioxide, ether, histamine, and amyl nitrite in the blood causes a marked dilatation, while epinephrin applied locally or hypertonic solutions in the blood stream cause a contraction. Caffein causes first contraction, then dilatation.²²

Such experiments do not necessarily answer the question of the relative importance of changes of calibre in the cerebral and in the systemic vessels respectively. Forbes himself, and with Pool and Nason,²³ has pointed out that the effect of sympathetic stimulation is far greater upon the vessels of the skin and dura than upon those of the pia. On the average a given current applied to the sympathetic in the neck caused a contraction of about 8 per cent. diameter in a pial artery, and about 80 per cent. contraction in a vessel in the skin, practically obliterating it. Schmidt²⁴ has shown that if epinephrin is added to a fluid injected into the common carotid of a cat, the injection is practically confined to the brain, which remains almost uninjected otherwise. Direct measurement of the rate of flow through the monkey's internal carotid under constant pressure by Finesinger and Putnam²⁵ showed clearly that stimulation of the sympathetic or the introduction of epinephrin caused a retardation of circulation, but that this could be compensated for by raising the perfusion pressure moderately. This experiment, and also direct observation of vessels in the choroid plexus and floor of the ventricle by Ask-Upmark and Putnam,¹⁵ indicate that the vessels actually in the cerebral substance react to chemical and nervous stimuli less readily than those in the pia, which in turn show a much smaller range of contraction than those of the skin. Thus the administration of histamine, though causing a dilatation of cerebral vessels, decreases the flow through them, while epinephrin produces an increased flow.

To sum up the physiological data, we must certainly accept the fact that the cerebral vessels are capable of contracting, but this mechanism is probably to be regarded as an accessory, rather than the main one, for regulating the cerebral blood flow under ordinary circumstances.

THE QUESTION OF SPASM OF CEREBRAL VESSELS IN THE HUMAN BEING

Are there any clinical syndromes resulting from spasm of cerebral vessels? It has long since been suggested that some cases of epilepsy are due to local vasoconstriction of cerebral vessels. Penfield²⁶ has actually observed the constriction of a pial artery at the onset of a convulsion during

an operation on an epileptic patient. Some convulsant drugs are vaso-constrictors.²⁷

On the other hand, Gibbs, Lennox and Gibbs²⁸ were unable to demonstrate any alteration in internal jugular blood flow preceding a convulsion in ten patients studied by an ingenious and apparently adequate method. It is possible that a local vascular spasm may take place without materially disturbing the total rate of cerebral blood flow. Sudden occlusion of a cortical vessel may precipitate focal convulsions, and abnormalities of vascular pattern are frequently found in the brains of patients with epilepsy. To me, an attractive hypothesis is that a cortical injury of almost any type may be followed by the formation of a new capillary plexus which may acquire an abnormal innervation. It is a matter of common experience that extensive scars of the skin may show an excessive reaction to sympathetic stimuli, and that nerves caught in scars become involved with new-formed vessels. May not the vessels in areas of granulation tissue in the brain also become more sensitive to various stimuli? The subject is in need of further investigation; meanwhile, it cannot be said that attempts at therapy which are based on the conception of the vascular origin of convulsions have led to any striking clinical results.

The cause of *migraine* has also been sought in cerebral vascular spasm. The syndrome may be closely imitated by congenital aneurysm of the circle of Willis, and by thrombosis of cerebral vessels.²⁹ Spasm of retinal vessels during the attacks has been described,³⁰ but I must confess that I have never observed it. Wolff³¹ has recorded the presence of unusually large excursions of the spinal fluid when a lumbar puncture is performed during the headache produced by injection of histamine and regards them as due to excessive arterial pulsations. But the headache of migraine appears to be of a different type, and ergotamine tartrate, the most effective remedy for migraine, does not increase cerebral blood flow as much as do other drugs, e.g. adrenalin and histamine, which are therapeutically ineffective.³² So this question also must still be left open.

Certain transient *paralyses* and other focal symptoms have also been ascribed to cerebral vascular spasm. It is a common observation that patients with arteriosclerosis especially may suddenly develop aphasia or hemiparesis, which lasts a few hours, and then as suddenly disappears. Such attacks are often harbingers of a more severe and more permanent recurrence, and there can be no doubt that one factor in their production is an impairment of the collateral circulation. It has been suggested by Ricker³³ and Riser, Mériel and Planques,³⁴ that the presence of an arteriosclerotic plaque may cause a mechanical stimulation and spasm of the vessel, but I know of no method of testing the hypothesis. Looking at a sclerotic vessel under the microscope, one wonders how much it could contract. The transient symptoms may also be regarded as the result of a temporary oedema resulting from a thrombus. In either case, the clinical significance of the occurrence

is the same ; the reserve capacity of the cerebral circulation has been impaired and an attempt should be made to lighten the patient's burdens, but he should be encouraged to moderate exercise.

In certain groups of cases, the existence of cerebral vascular spasm of a sufficient degree to cause focal symptoms seems extremely probable. Osler ³⁵ pointed out that transient hemiparesis and other focal signs may accompany Raynaud's disease of the extremities. Kennedy ³⁶ has called attention to the cerebral complications of the anaphylactic state. Occasionally cases are seen in which the presence of spasm of cerebral arteries seems probable, but the cause of the spasm is obscure. An example is the following :

An Italian woman of 34 was admitted to the Boston City Hospital on account of nephrolithiasis. Following operation, and without obvious cause, the left leg became cyanotic and pulseless. The femoral artery was explored on the presumption that it was occluded by an embolus, but instead it was found in a state of spasm. Later the patient developed a left hemiparesis and right hemianopia, which receded and recurred several times. It was observed that the left leg became pulseless, and the patient had an asthmatic type of breathing and complained of anginoid pains with each exacerbation of the cerebral symptoms. The symptom complex was sometimes precipitated by emotional upsets, but otherwise no cause for it was found. This case will be reported in more detail by Novak.³⁷

PATHOLOGICAL CONSIDERATIONS

The most striking fact about the cerebral circulation is that even relatively minor disturbances of it may lead to permanent and irreparable parenchymal damage. While a tourniquet may be applied to an extremity for fairly long periods without appreciable harm, and even cardiac muscle may recover from partial anæmia, or compensate for a scar by hypertrophy, the central nervous system possesses neither capacity to more than a minimal degree. Cannon and Burket ³⁸ have shown that the cells of the cerebral cortex are destroyed by 10 to 18 minutes' anæmia—a fact which has long been known to obstetricians—and that the lower nuclei have only somewhat greater resistance.

If the entire blood supply to the brain is cut off, as was done by Gildea and Cobb,³⁹ the animal goes at once into a convulsion and is completely paralysed. If the anæmia is continued for about 10 minutes, permanent damage remains. The cells of the cortex—especially the larger ones—are destroyed. The animal may show signs of focal damage or may merely become apathetic, untidy and lacking in initiative.

The results of a generalized long-continued mild asphyxia may be entirely different. They are clearly seen in the cases of congenital heart disease studied by Bodechtel.⁴⁰ There was a widespread degeneration of myelin throughout the brain, with only mild changes in the cortical cells or axis-cylinders, followed by gliosis and a slight inflammatory reaction. This picture corresponds to that known as diffuse sclerosis which, as we shall see,

may doubtless arise in other ways also. A similar histological picture was produced experimentally in dogs by Ferraro,⁴¹ by administration of sublethal doses of cyanide over a long period, which of course seriously impairs the capacity of the tissues to utilize oxygen. Similar lesions might be expected in certain types of anæmia, but they have not been reported. The degenerations in the white matter in pernicious anæmia are of another type,⁴² and

FIG. 2.—Carbon monoxide poisoning. Softening of the lenticular nucleus and disseminated lesions elsewhere in the white and grey matter, all centring about thrombosed vessels.

probably due to a more specific nutritive lack. The differences between the results of a brief, intense general anæmia of the brain and those of a mild chronic asphyxia are probably explained by the fact that the grey matter has a richer blood supply, but also a greater reducing power and need for oxygen than the white matter. If no oxygen is available, the nerve-cells are destroyed at once; if there is just enough to support the grey matter, the circulation of the white matter is insufficient to support it. Possibly

under some circumstances, for example in the medulla and spinal cord, the grey matter may actually absorb the oxygen before it can reach the white, for the vessels supplying and draining the white ordinarily run through cellular areas, and both share the same capillary network.

The results of damage by certain poisons, such as carbon monoxide and methyl alcohol, are more complicated and difficult to understand. Often their most striking feature is a necrosis of the globus pallidus (fig. 2), but focal necroses in other parts of the grey matter and in the white matter ⁴³ may occur. Not all of the changes and perhaps none of them are to be ascribed directly to general asphyxia or toxic injury, however, for the lesions may be found to contain fresh thrombi which could entirely account for them

FIG. 3.—Thrombosed vein from the above case. The dark masses are fibrin, the small spheres platelets. Masson stain. Oil immersion.

(figs. 2 and 3). The problem has more than an academic interest, for various substances such as methylene blue are often administered in carbon monoxide poisoning to combat the asphyxia. It is my personal belief, based on an extended attempt to produce lesions in animals with carbon monoxide, that such medication is unwise, on the grounds that removal of the patient into the fresh air is sufficient to overcome the asphyxia at once if ever, and that any residual symptoms are the result of a parenchymal damage which the methylene blue will not affect. Artificial respiration is far more important.

The characteristic localization in the globus pallidus is doubtless to be explained by the peculiarities of its blood supply which, as we have seen, consists of a much finer network of small capillaries than is found in other areas of grey matter (figs. 4, 5), but it is uncertain whether vascular obstruction is more easily produced in this area than elsewhere, or whether it is

more destructive, or whether the region is more susceptible to general asphyxia on account of its blood supply.

The focal lesions of carbon monoxide poisoning which may be considered a typical result of a local thrombosis lead us to a more general consideration of circumscribed vascular lesions.

The most familiar and typical result of a sudden stoppage of the blood supply to an area of the brain is a focal necrosis. All of the structures in the area—nerve- and glial cells, fibres, myelin and vessels—are destroyed.

FIG. 4.—The lenticular nucleus of a human brain, injected after removal from the skull. Note the delicacy and fineness of the capillary network as compared with that of the parietal lobe (fig. 5). Section 100μ thick, lens enlargement.

If the subject survives, phagocytosis and a 'reactive inflammation' occur, and the end result is a cyst or a scar of mixed glial and fibrous tissue. If the necrotic area includes both white and grey matter, the grey matter is usually more affected than the white matter. There are certain regions in the brain, such as the internal capsule, where such necroses are particularly common, but this is all an old story, and I shall not pursue it further.

It may not be out of place, however, to say a word about the relation between thrombosis and hæmorrhage. There is good clinical and some pathological evidence that thrombosis regularly precedes extravasation of blood in arteriosclerosis and also occasionally following head injury. Just

what is the mechanism of rupture is not always certain. It has been considered secondary to a necrosis of the vessel wall (Globus and Strauss⁴⁴) which certainly may occur, but usually only when the lumen is already filled with clot, which should prevent extravasation. In some of Alexander's cases⁴⁵ it appeared that a thrombosis in a venule—which is a common site for the formation of a thrombus—had permitted a rise in the pressure in the capillaries proximal to it sufficient to rupture them.

It is less well recognized that vascular closure may occur without causing an appreciable parenchymal damage. This was brought strikingly to my

FIG. 5.—Parietal cortex of a human brain, from the same section as that from which fig. 4 was taken. To illustrate the difference in capillary architecture.

attention a few years ago when I was studying cerebral embolism with a corn starch suspension. The starch granules are of just the right size to plug arterioles, though they pass easily through larger trunks. I was astonished to find that an appreciable quantity of starch suspension could be injected into a cat's carotid without producing parenchymal damage. In sections, the starch granules could be seen lying in the tissues without provoking any reaction.⁴⁶ This is a demonstration of the richness of the anastomoses in the cerebral circulation. It is probable that softenings only occur when a large extent of the vascular tree becomes filled with a thrombus, or when the last of the group of vessels supplying the same spot becomes closed.

There are all transitions between no permanent change and a complete

destruction of parenchyma following anoxæmia. In most instances, the injury follows a certain pattern. If a large artery becomes slowly obstructed, the changes in the area which it supplies are entirely comparable to those in the whole brain following a chronic anoxæmia, for example, of the type produced experimentally by Ferraro ⁴¹ with cyanide poisoning.

FIG. 6.—Post-vaccinal 'encephalitis.' There is engorgement of all vessels, but particularly of the veins, which are strikingly tortuous. Perivenous hæmorrhages, deposit of blood pigment, and destruction of myelin may be seen. Many of the veins contain platelet thrombi. Mallory's connective tissue stain, lens enlargement.

Among the cases which Alexander ⁴⁵ studied in this laboratory was one in which a thrombosis of the basilar artery and of some of its extracerebral branches had taken place, without gross obstruction of intracerebral vessels. The result was a small area of necrosis in the pons and a large area of demyelination with less severe loss of axiscylinders. Such diffuse, incomplete lesions are more frequently seen following venous thromboses. Of course, an

FIG. 7.—An atrophic area in the cortex of a case of general paralysis. Cresyl violet stain, low power. For comparison with fig. 8.

FIG. 8.—Atrophy produced in a dog's cortex by experimental capillary occlusion from the venous side. Note the similarity to the atrophy of general paralysis (fig. 7). Cresyl violet stain, low power.

extensive venous thrombosis, for example, of the longitudinal sinus and several branches, leads to a complete necrosis just as an extensive arterial closure does. But thrombosis of a small vein leads merely to a local congestion, which usually affects the white matter more than it does the more vascular grey matter, and leads principally to a loss of myelin. This can readily be demonstrated experimentally,⁴⁷ as well as in autopsy material.

Such lesions in the acute stage present all of the histological characteristics which we associate with a condition known as 'disseminated encephalomyelitis' or 'perivenous leucoencephalitis,' including the so-called 'inflamma-

FIG. 9.—Capillaries in a normal human frontal cortex. Lepehne's stain, section 100μ thick, lens enlargement (courtesy of Dr. Colin Campbell). For comparison with fig. 10.

tory' phenomena; the post-vaccinal, post-measles, and post-German measles forms of encephalitis are the best known examples of the type (fig. 6). In the later stages, the milder injuries resulting from vascular closure closely imitate the plaques of multiple sclerosis. I have elsewhere⁴⁸ given evidence which suggests that these various diseases are produced by disseminated thromboses of small cerebral vessels, and that this in turn is the result of chemical changes in the blood plasma, rather than the direct effect of a specific infectious agent. Schilder's encephalitis periaxialis diffusa and diffuse sclerosis should probably be included in the same category.

Local lesions short of complete necrosis may also occur in the grey

matter. Those due to embolism or arteriosclerotic closure are usually small, and characterized by a local loss of, or severe damage to, nerve-cells—the so-called ‘*Erbleichungsherd*’ or faded area, since in gross the distinctive colour of the grey matter is lost and it appears to merge into the white. A common cause of sudden focal destruction of nerve-cells is syphilitic endarteritis of a cortical vessel, often accompanied clinically by focal convulsions of acute onset.

It is possible to produce small areas of ‘fading’ experimentally by arterial embolism. A similar, more widespread change may be brought

FIG. 10.—A similar area from the brain of a case of general paralysis. Notice the relative poverty and flattening of the capillary network. Lepehne's stain, section 100μ thick, lens enlargement (courtesy of Dr. Colin Campbell).

about by experimental obstruction of the capillaries from the venous side, by forcing some bland material upstream into a cortical vein.⁴⁷ As a result, nerve-cells are damaged or disappear over a wide area and there is a perivascular accumulation of phagocytic and ‘inflammatory’ cells, including what appear to be plasma-cells. The glia proliferates and rod-cells appear. In short, the histological picture precisely imitates that of the cortical atrophy of general paralysis (figs. 7, 8).

There may be significance in this fact. There can, of course, be no doubt that general paralysis is ultimately the result of infection with the *treponema pallidum*. The meningitis which is usually present is a natural

enough result of the infection, but the irreparable parenchymal damage is often seen in areas in which inflammatory phenomena are mild or absent. It has seemed to Dr. H. Houston Merritt and me ⁴⁹ that possibly the disappearance of nerve-cells might be due to obstruction of capillaries by a syphilitic endarteritis. It has long been known that the capillaries in cases of general paralysis are often closed by endothelial hypertrophy, and we have been able to show that the number of capillaries containing blood is greatly diminished in atrophic areas in the cortex (figs. 9, 10). Curiously enough, the anterior horn cell destruction of syphilitic progressive muscular atrophy

FIG. 11.—Section of the brain of a case of multiple sclerosis, injected after removal from the skull. Dilated, tortuous engorged vessels in a plaque bordering on the ventricle. Section 100 μ thick, unstained, lens enlargement.

has been explained long since as the result of hypertrophy of capillary endothelium (and this we have also observed), but a similar explanation of the cortical changes has not been advanced.

This conception may have a practical application. The treatment of general paralysis with fever is one of the great therapeutic advances of modern neurology. Fever is an efficient agent in dilating cerebral capillaries. It is possible that the success of the treatment is in part due to the hyperæmia of the cortex and that even more effective agents may be found by search.

I have so far mentioned only the results of vascular obstruction. The circumstances under which cerebral vessels dilate and multiply is an almost

unexplored field. A brilliant beginning has been made by Pfeifer,⁷ who has demonstrated an apparently specific type of capillary dilatation in tuberculous monkeys. The plaques of multiple sclerosis often exhibit an extraordinary increase of vessels, and sometimes characteristic vascular patterns (fig. 11). Abnormal proliferation of cortical vessels almost angiomatous in character is occasionally observed following head injuries. But all these matters still contain obscure points.

CONCLUSIONS

In the present survey I have attempted to call attention to some of the directions along which the newer information about the cerebral circulation has aided in our understanding of diseases of the nervous system. Some of the interpretations which I have suggested still await confirmation—for example, the hypotheses concerning multiple sclerosis, encephalitis and general paralysis. But whether they are confirmed or not, I have not the slightest doubt that there are more to come, if we but look for them. If syphilitic progressive muscular atrophy is due to capillary closure, so may the nonsyphilitic form be also, not to mention acute poliomyelitis. The selective localization of the lesions of paralysis agitans in the corpus striatum, and of the lesions of tabes in the dorsal columns and the pupillary reflex centres are only a few of the problems which urgently deserve investigation. It is perhaps not too much to say that aside from congenital anomalies and the effects of tumours and suppurative processes, there are few pathological processes in the central nervous system which are not directly or indirectly the result of circulatory disturbances. I hesitate even to speculate on the possibilities in the field of mental disease.

SUMMARY

1. A survey of recent investigations of the anatomy, physiology and pathology of the cerebral circulation is presented.
2. It has been conclusively demonstrated by various investigators that the cerebral arteries are not end-arteries but possess a rich system of anastomoses. The vulnerability of the brain toward vascular disturbances is due rather to the sensitiveness of the parenchyma than to deficiency in blood supply.
3. Different regions in the brain are characterized by marked differences in pattern of blood supply. Some of the local peculiarities may be of significance in the localization of disease-processes.
4. The cerebral vessels bear nerves and are under vasomotor control by the sympathetic. The vasomotor activity of the arterioles of the brain is much less than that of those elsewhere, so that passive changes in the cerebral circulation outweigh active ones, at least under ordinary conditions.
5. The cerebral vessels react much more strongly to chemical stimuli than to nervous impulses. Carbon dioxide is a particularly active vasodilator.

6. While it is probable that spasm of cerebral vessels may cause symptoms, cases in which such an explanation appears likely are rare. The rôle of vasospasm in epilepsy and migraine is doubtful.

7. In addition to the familiar cysts of softening caused by vascular obstruction, milder types of injury may occur.

8. A diffuse loss of myelin may be produced by a mild general anoxæmia, and local loss of myelin by a mild local asphyxia—for example, following venous thrombosis. The lesions which result simulate closely those of 'perivenous encephalomyelitis,' multiple sclerosis, and diffuse sclerosis. It is suggested that the lesions in these diseases are thrombotic in origin.

9. Partial anoxæmia of the cortex leads to a loss of nerve-cells without softening. Evidence is advanced that the parenchymal atrophy in general paralysis is a similar diffuse process, the result of endothelial hypertrophy in capillaries.

10. The apparently specific vascular dilatation of cerebral tuberculosis and the characteristic vascular abnormalities of multiple sclerosis are briefly referred to.

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