with a peripheral obstruction, for there is no doubt that it can cause arterial spasm and may occasionally result in further infarction. The decision for or against angiography in a doubtful case, therefore, becomes in itself a diagnostic problem that merits discussion.

Having regard still to what we are going to do for the patient, the development of anticoagulant therapy makes the differential diagnosis of thrombosis from hæmorrhage of obvious practical importance. The paper by Aring and Merritt (1935) remains one of the most important contributions to this subject. It was based upon a retrospective analysis of the clinical data in a large series of cases in which hæmorrhage or infarction was revealed at autopsy and indicates that no single criterion suffices for the clinical distinction. The most reliable is a frankly blood-stained cerebrospinal fluid, found in 49 of 68 cases of cerebral hæmorrhage of their series in which lumbar puncture was performed, and in 1 of 64 cases of cerebral thrombosis.

In relation to the practical question whether in a given case anticoagulant treatment can be safely given, the important point here is not so much the rarity of blood in the cases of thrombosis as the presence of a clear fluid in more than a quarter of proven cases of hæmorrhage.

Of the other criteria mentioned in their paper the following have in my experience proved useful. Immediate loss of consciousness was twice as common in hæmorrhage as in thrombosis: severe headache at the onset, and vomiting at or shortly after the onset, were significantly more frequent in hæmorrhage than in thrombosis. Neck stiffness was present in 55% of the cases of hæmorrhage, but in only 7% of the cases of thrombosis. A systolic blood pressure of 200 or over was twice as common in the cases of hæmorrhage. Preliminary symptoms of carotid or basilar insufficiency naturally indicate the probability of thrombosis.

These criteria taken together can make the diagnosis reasonably certain in most cases, but not in all. For this reason the value of anticoagulant treatment in cerebral thrombosis needs to be proved beyond doubt, for its potential for harm in a misdiagnosed case of hæmorrhage is obvious.

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Meeting
February 5, 1959

SYMPOSIUM ON CEREBROVASCULAR DISEASE

PART II

Dr. F. A. Elliott (London):

According to the Registrar-General's report for England and Wales, deaths from cerebrovascular disease in 1937 numbered 44,366, in 1947 58,964, and in 1957 73,669. Almost a fifth of these were people under the age of 65. In the U.S.A. in 1952 44,000 out of 170,000 persons dying of cerebrovascular disease were under 65—approximately the same proportion (Wright *et al.*, 1956). Of course, these figures probably include a few cases dying, not from the effects of atherosclerosis but from conditions which can resemble them—aneurysm, tumour, angiomatous malformation, syphilis, embolism from cardiac and pulmonary sources, cerebral ischæmia due to a sudden fall of blood pressure (e.g. coronary thrombosis, hypotensive drugs, hæmorrhage), subdural hæmatoma, polyarteritis, Buerger's disease, cerebral incidents due to porphyria, hæmorrhagic disorders, the nonvascular cerebral degenerations, and so on. But this group is too small to have any significant effect on the total, and therefore there is no escaping the fact that we, in common with other populations (Riishede, 1956) are faced with a growing medical and economic problem, which has been aggravated since the introduction of antibiotics by an increased survival rate of people disabled by strokes. Clearly, since irreparable cerebral damage has often occurred by the time the patient comes under medical care, the logical objective is to prevent the development of atherosclerosis and its complications, but at the present time all that we can attempt to do is to retard the process. The subject is, of course, bedevilled by the difficulty of distinguishing with certainty between hæmorrhage, thrombosis and embolism, and until this is solved it will be impossible to assess *with precision* either the natural prognosis of these conditions or the value of any particular form of treatment.

There are five conditions which are believed to accelerate the development of atherosclerosis. Of these a raised blood pressure is thought to be the most important. If the experts are correct in this view, success in prophylaxis will be limited until hypertension can be more effectively controlled than is possible at present. It will

also have to be treated earlier, if damage to arteries is to be prevented. However, some people think that since available methods are not satisfactory, it is better to let sleeping dogs lie than to awake them to dangers from which they cannot be protected, arguing that to tell the patient that he has hypertension may simply aggravate the situation by inducing a neurosis. An opposing and perhaps more widely held view is that diet, avoidance of stress, sedation, and hypotensive agents can often help, even if they cannot cure, and that hypochondriasis is usually iatrogenic and therefore avoidable. Because overtreatment is bad, it does not necessarily follow that undertreatment is good, and it seems to me that to abstain from palliatives until symptoms of vascular insufficiency develop is wrong.

The second condition I want to mention is diabetes, which is a smaller problem because it is less common and is far easier to control. All the same, a surprising number of middle-aged and elderly diabetics seem to escape detection for a long time, especially those with a high renal threshold; the remedy is, presumably, more frequent resort to glucose tolerance tests. It is scarcely necessary to add that a pseudo-diabetic curve can be found following a stroke (or other illness) which has led to a restriction of carbohydrate intake for some days, and it is also well known that hyperglycæmia and renal glycosuria can both occur, misleadingly, after a vascular accident.

The third disease worth looking for is polycythæmia, which accelerates atherosclerosis, predisposes to thrombosis, and increases the viscosity of blood to the extent of hampering the cerebral circulation. A diagnostic point of some importance is that, especially in patients from warm climates, a sallow complexion can mask a moderate degree of polycythæmia; blood counts are therefore obligatory. Treatment by radioactive phosphorus and/or repeated venesection is, of course, effective.

The fourth condition is thrombocythæmia, in which an elevation of the platelet count is the sole hæmatological abnormality. Some of these cases exhibit a paradoxical tendency to both thrombosis and hæmorrhage, while others present a succession of thrombotic incidents alone. I have seen, or at any rate recognized, 2 of these in the last three years.

Case I was a man aged 46, who, over the previous six years, had had two coronary thromboses, one cerebral thrombosis, and ischæmic ulceration of the right big toe. Three years ago his blood platelets were found to be over 1,000,000, and they were reduced to the region of 300,000 by radioactive phosphorus; since then there have been no further vascular accidents. Nevertheless, his platelets are starting to creep up again and we anticipate having to give further treatment. The red cell and white cell counts have remained normal throughout.

Case II was slightly different—he was a hypertensive male of 54, who, over a period of nine months, had first an incongruous right hemianopia, then a left hemiplegia, and finally ischæmic changes in the left little toe. His platelets numbered 1,300,000, and his red cells 6,800,000, and it is felt that his thrombotic incidents were related to the excess of platelets rather than to the modest degree of polycythæmia which was present. He has only recently come under treatment and it is too early to assess results.

Neither of these patients exhibited a tendency to bruise or to bleed excessively.

It would seem, therefore, that enumeration of the platelets is a necessary procedure in cerebrovascular disease, more especially perhaps in cases with repeated vascular accidents. Further, Moolten *et al.* (1949) and others believe that even when the platelet count is normal they may be excessively adhesive, for instance in cancer, general infection, and diets rich in animal fat and cholesterol. It remains to be seen whether such qualitative changes in platelets are of any significance in the conventional type of cerebral thrombosis.

The fifth condition to be looked for is hypercholesterolæmia, whether familial or sporadic. This can easily escape notice since not all sufferers display cutaneous xanthomatosis.

Case III.—A routine cholesterol estimation carried out in a man of 46 suffering from a slowly progressive right hemiparesis disclosed a figure of 740 mg.%. His blood pressure was normal and there was no family history of vascular disease. It was deemed inadvisable to carry out angiography, which might or might not have substantiated the clinical diagnosis of high carotid stenosis. He improved to a striking degree and quite rapidly while on anticoagulants. During a further three months, when he received no treatment of any kind, his condition again slowly deteriorated, but it started to improve and has continued to do so, since he has been on a low-fat, low-cholesterol, low-carbohydrate diet. Now, at the end of a year, he is very much better than he was when treatment was first started, and his blood cholesterol is maintained in the neighbourhood of between 400 and 500 mg.%.

It is more difficult to assess the significance of cholesterol levels in the region of 300 and 400 mg.%, which are not uncommon even in the absence of myxœdema, nephrosis and diabetes, and as far as I know there is, as yet, no really accurate information as to whether clinical benefit accrues from lowering the cholesterol level in such cases. Methods which can lower blood cholesterol, apart from diet, include the administration of sitosterol (Best and Duncan,

1956), phenyl ethyl acetamide (Loeper, 1956), nicotinic acid (Altschul *et al.*, 1955; Galbraith *et al.*, 1959) and cerebroside (Jones, 1956).

Acute porphyria, well known as a cause of acute polyneuropathy, is reported by Peters *et al.* (1958) to be an occasional cause of acute cerebral incidents in young adults. This is mentioned in passing, not as a contributory factor in the production of atherosclerotic vascular accidents, but as a biochemical entity which has to be remembered. Recognition of the condition is of more than academic interest because these authors, following Schrumpf (1953), find that chelating agents such as BAL and EDTA reduce the mortality of this very serious disease.

Although these chemical and hæmatological abnormalities are relatively uncommon, it seems likely that, as more is discovered about the deposition and removal of thrombi the list will lengthen, as will the opportunities for rational treatment.

At the moment, however, the main therapeutic emphasis is on anticoagulants, dietetic restriction, and the use of fibrinolytic agents.

Most of the work on diet has been concerned with coronary disease, but it seems reasonable to assume that it applies to all anatomical variations of atherosclerosis. The case against cholesterol and unsaturated animal fats is based on numerous observations of which I will mention only a few. First, a high cholesterol diet induces atheroma in certain experimental animals, and according to Maslova (1956) the effect is increased by the simultaneous administration of nicotine. Secondly, Fullerton *et al.* (1953) find that a meal high in animal fat shortens the coagulation time in man, but other workers, using different methods, contest this finding. Thirdly, Cullen and Swank (1954) reported that in hamsters a fatty meal slows the capillary circulation and increases the adhesiveness of both red cells and platelets. Fourthly, as reported by Greig (1956) and confirmed by Buckell and Elliott (1959) the ingestion of butter fat usually inhibits fibrinolytic activity in man; that is, it inhibits the enzymes which are partly responsible for the removal of fibrin deposits in blood vessels. This is consistent with Bornstein's (1956) discovery that lipoproteins inhibit certain enzymes, though not all. The fifth and last point is particularly impressive to the clinician, and that is the frequency with which patients with either cerebrovascular or coronary disease often improve on a low-fat, low-carbohydrate diet, and sometimes relapse when they forsake a frugal regime. I have observed this, in rather desultory fashion, on many occasions, while Milton Plotz (1949) found that of 27 cases of coronary disease who also had peptic ulcers, and were therefore placed on a Sippy regime with a high fat intake, 9 died of coronary thrombosis within seven months, 12 suffered from increasing degrees of angina, and only 6 were unaffected. It will be interesting to see the outcome of systematic studies, at present proceeding in America, on the incidence of vascular disease in pure vegetarians, and in vegetarians who also use milk and eggs. Pending the results of this and other studies it would seem prudent to restrict animal fats, whether saturated or unsaturated, foods rich in cholesterol, and carbohydrates.

The fibrinolytic activity of the plasma has excited much interest in recent years. It is measured by complex and unsatisfactory techniques and the whole subject is overloaded with hypotheses. However, Buckell and Elliott (1959) have confirmed Fearnley's observation (Fearnley *et al.*, 1957) that fibrinolytic activity fluctuates during the day; *as a rule* it rises during the daylight hours and comes back to a low level sometime during the night, which is interesting in view of the liability to retinal, cerebral and coronary thrombosis during the early hours of the morning. Further, we have found that, in general, fibrinolytic activity is greater in normal males aged 20 to 22 than in males aged 38 to 50 (Buckell and Elliott, 1959); that is to say, it seems to decrease with age. I have already mentioned that it is usually reduced by a meal high in animal fats—in our work by 50 grams of butter. If these *in vitro* observations are a true reflection of what happens *in vivo*, there would seem to be a certain hazard about an elderly man having a meal rich in fat late at night, because the apex of his lipæmic curve will probably occur at about the same time as his fibrinolytic activity is at its lowest ebb. Another suggestive observation is that of Cromwell and Smith (1956) who found that the capacity of dogs to withstand arrest of the cerebral circulation is increased by the administration of a fibrinolytic activator, and they attribute this to the prevention of clotting during the period of stasis. Whether this explanation is correct or not, raising the fibrinolytic titre of the plasma seemed to afford some degree of protection to the brain in these experiments. The last point I want to make is that physical exercise has been found to increase fibrinolytic activity (Biggs and Macfarlane, 1947; Greig, 1956).

Arising out of these and other observations, attempts are being made by various workers to treat thrombo-embolic disease with fibrinolytic agents. Meneghini (1958), von Kaulla (1958) and others have succeeded in raising the fibrinolytic activity in man by repeated intravenous injections of protein-free pyrogens

derived from *Salmonella abortus* and *E. coli*, and this is being used as a method of treating thrombo-embolic incidents. Others, including Moser (1958) and Fishman and Kline (1956), are using plasmin, a fibrinolytic agent derived from human blood, while Stephanini and Marin (1958) have isolated a fibrinolytic agent from nonpathogenic fungi and are at present evaluating its effect in thrombotic disease in man. What is really needed, however, from the prophylactic point of view, is a method of increasing fibrinolytic activity on a long-term basis, but in the meantime it would seem that regular and adequate physical exercise and restriction of fat appear to be the best method of doing so.

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Dr. John Marshall and **Dr. David A. Shaw** (London):

Anticoagulant Therapy in Cerebrovascular Disease

Anticoagulant therapy has been used in the treatment of cerebrovascular disease for some time past, yet it is true to say that the indications for its use are far from clear. Indeed it would not be an overstatement to declare that the question is still very much in doubt as to whether or not anticoagulants have any place at all in this therapeutic field. This situation obtains despite the rapidly expanding literature on the subject which already contains references to many hundreds of patients with cerebrovascular disease so treated. The reasons for this persisting uncertainty are manifold and chief among them is undoubtedly our lack of precise knowledge about the disease process itself. The first part of this symposium, which dealt so admirably with the pathology, the pathogenesis and the clinical diagnosis, nevertheless acknowledged in all departments fundamental gaps in our understanding which will require to be filled before truly rational therapeutic concepts can be formulated.

In the particular case of anticoagulant therapy there is the additional anxiety on the debit side about the hazard of treatment. In addition to our inability to distinguish with complete certainty between a small intracerebral hæmorrhage and an occlusion of a cerebral vessel, the former obviously contraindicating the use of anticoagulants, there is the possibility, supported by some experimental work in animals (Wood *et al.*, 1958; Sibley *et al.*, 1957), that white infarcts may become hæmorrhagic under the influence of anticoagulants. Fortunately, most clinical experience does not suggest that this is a frequent occurrence and it is encouraging that cerebral hæmorrhage is an uncommon complication in the anticoagulant treatment of coronary artery disease where it is reasonable to assume that a proportion of patients also have diseased cerebral arteries and hypertension.

Yet another fact which, in our view, renders difficult the interpretation of reported results is that many authorities base their evaluation of treatment on a comparison of clinical progress before and after the institution of anticoagulant therapy. This presupposes a precise knowledge of the natural history of the disease which in fact we do not possess. Millikan *et al.* (1955) treated 26 patients with basilar insufficiency or thrombosis with anticoagulants and compared the results with those obtained in an untreated group with the same diagnosis. They chose this condition for study because they had observed that thrombus in the basilar territory was frequently laminated, and that patients tended to have recurrent clinical episodes. It seemed reasonable to correlate the clinical episodes with the laying down of further laminæ of thrombus. The authors concluded that the number of episodes was reduced following the institution of anticoagulant therapy. In 1958, Fisher reported the results of treating a group of 58 patients with cerebral thrombosis by means of

anticoagulants, and concluded that patients with attacks of circulatory insufficiency and those with ingravescent strokes were benefited. Conclusions were based mainly on comparison of progress before and after the start of treatment. McDevitt (1955, 1958) in two symposia on cerebrovascular disease reported on the treatment of a group of patients, with various cerebrovascular lesions, and thought the incidence of further attacks was diminished. Carter (1957) reported treating 26 patients with cerebral embolism with immediate anticoagulant therapy comparing them with a group of patients treated conservatively or by stellate ganglion block in previous years. He considered that anticoagulant therapy was beneficial. In the present state of knowledge it seems to us in the Academic Unit of the Institute of Neurology that two things are required, first the clear establishment of the facts about the natural history of cerebrovascular disease, and secondly the conducting of properly designed and controlled clinical trials of anticoagulant therapy. This, with the co-operation of Professor Bradford Hill, we have undertaken and this communication is by way of an interim report.

With regard to the first problem we have followed up 251 patients who were discharged from Queen Square in the years 1950 to 1954 with a firm diagnosis of cerebrovascular disease. A full report of the results will be given elsewhere, but two observations seem relevant to the present discussion. Table I shows the mortality figures

TABLE I.—MORTALITY AT THE TIME OF FOLLOW-UP IN VARIOUS CLINICAL GROUPS

	No. of patients	No. died	Percentage mortality
Diffuse disease of hemisphere	77	56	73
Focal hemisphere "thrombosis"	114	65	57
Internal carotid occlusion ..	23	12	52
Brain-stem "thrombosis" ..	30	14	47

in various clinical groups, not including cerebral hæmorrhage, over a follow-up period ranging from four to nine years. The highest mortality was in those with diffuse cerebrovascular disease of the hemispheres; next were patients with focal "thrombosis" in the hemisphere; thirdly, those with occlusion of the internal carotid artery; and finally, those suffering from thrombosis of the brain-stem. This contrasts strikingly with the commonly held view that the brain-stem vascular lesions are the most lethal. Among the 97 patients who had survived to the time of follow-up, 90 had experienced no recurrence, 4 had had one further attack and 3 more than one. This is again contrary to all expectation and especially in the 16 patients with brain-stem lesions none of whom had had further attacks. Unfortunately information about recurrences in those who had died was not available. If the recurrence rate was the same as in the survivors then our concept of the natural history of the condition requires revision; on the other hand if they had a high recurrence rate prior to death it suggests that there may be two groups of patients, one with a benign course after a cerebrovascular accident and the other with a downhill course punctuated by further accidents. This can only be ascertained satisfactorily by a prospective study which we are now undertaking. These observations indicate the difficulty of assessing the effects of treatment in a condition in which we are so uncertain of the natural history.

Our clinical trial of anticoagulant therapy in cerebrovascular disease is divided into two parts: the short-term treatment of the acute stroke, that is within seventy-two hours of its onset, and the long-term prevention of further strokes in patients who are not seen until twenty-one days or more after their last incident. The patients in the acute trial are examined immediately on admission and a clinical diagnosis is made. Lumbar puncture is then carried out and arteriography of the appropriate cerebral vessel performed. The diagnosis is then modified if necessary. The patients who are diagnosed as suffering from a non-embolic cerebral infarction are then admitted to the trial and allotted at random to treated or control groups. The treated patients are started on phenylindanedione (Dindevan) immediately and intravenous heparin is given for the first twenty-four hours. Treatment is continued for twenty-one days, the prothrombin time being maintained at two and a half to three times the normal control time. In all other respects the patients in the treatment and control groups are managed identically by the same team of nurses and physiotherapists. This aspect is important when factors such as the maintenance of an airway, the avoidance of respiratory infection and the control of water balance have such a great influence on mortality. The results to date, which are being followed by a method of restricted sequential analysis are shown in Table II, and are not as yet significant. Table II shows only mortality, but functional

TABLE II.—INTERIM RESULTS IN PATIENTS WITH ACUTE NON-EMBOLIC CEREBRAL INFARCTION TREATED WITH ANTICOAGULANTS

	No. of patients	No. of deaths
Treatment group ..	18	4
Control group ..	18	2

assessments at one, three and six months are also being made. 2 of the 4 deaths in the treated group were due to intracerebral hæmorrhage. One of these patients had a further, fatal, accident on the twenty-first day of treatment and

autopsy revealed that the initial lesion had been a hæmorrhage but that a recent cerebral hæmorrhage was present in another part of the brain and had clearly been responsible for the death. Her history showed that a left hemiparesis had developed one afternoon over a period of an hour and a half without headache or vomiting. By the time she reached hospital she was comatose. Her cerebrospinal fluid was not blood-stained, but arteriography showed the anterior cerebral artery to be displaced 3 mm. to the left. In retrospect this shift and the coma should have been otherwise interpreted. The history of the second patient showed that the hemiparesis had come on gradually over several hours, without headache or vomiting and he was quite alert when he reached hospital. The cerebrospinal fluid was not blood-stained and there was no displacement of vessels in the arteriogram. Twenty-four hours after admission his condition began to deteriorate and he died within seventy-two hours. At autopsy there was an intracerebral hæmorrhage. Despite the careful application of the accepted clinical criteria for distinguishing cerebral thrombosis from hæmorrhage, coupled with examination of the cerebrospinal fluid and arteriography, there were misdiagnoses. Anticoagulant therapy will have to offer considerable advantages to offset the misdiagnoses which are bound to occur with the present available diagnostic methods.

The patients in the chronic trial, which has now been running for fifteen months, are treated entirely on an out-patient basis. They attend initially for one day during which serial readings of the blood pressure are made along with assessments of cerebral, cardiac and renal function. If there are no contraindications to long-term anticoagulant therapy the patients are then admitted to the trial and allotted at random to treatment or control groups. The patients in the treatment group are started on phenylindanedione (Dindevan) and thereafter attend at regular intervals for estimation of the prothrombin level. The types of lesion are shown in Table III and the results to date are shown in Table IV. It will be seen that there have been 3 deaths in the treatment group, 2 from cerebral hæmorrhage and 1 from a cardiac infarct, and none in the control group. There have been 5 further cerebrovascular accidents (including the 2 fatal ones) in the treatment group and 2 in the controls. Again these results are not significant. Gratifying features are the small number of defaulters, namely 3, and the low incidence of hæmorrhagic complications, none of them fatal, and only 2 necessitating the permanent cessation of treatment. This compares favourably with reported results in other series, as for example

TABLE III.—DIAGNOSES OF 114 PATIENTS ON LONG-TERM ANTICOAGULANT THERAPY

	Treatment	Control	Total
Diffuse disease of hemisphere..	6	4	10
Focal hemisphere "thrombosis"	38	37	75
Brain-stem "thrombosis"	11	13	24
Internal carotid occlusion ..	2	3	5
	57	57	114

TABLE IV.—INTERIM RESULTS IN 114 PATIENTS ON LONG-TERM ANTICOAGULANT THERAPY

	Treatment	Control
No. of patients	57	57
Further cerebrovascular accidents..	5*	2
Progressive deterioration	1	—
Deaths	3	—
Defaulters	—	3
Hæmorrhagic complications:		
Treatment resumed	9	—
Treatment abandoned	2	—

*Two of these were fatal and are included in the deaths.

McDevitt (1958), where there were 35 hæmorrhages in 26 patients in a series of 91 under treatment.

No conclusions can be drawn at present from the results of these studies as to the place of anticoagulant therapy in the treatment of acute and chronic cerebrovascular disease. The trial has, however, been carefully designed to supply, in due course, an answer which will either prevent the introduction of a method of treatment which may be valueless or even harmful or establish that anticoagulant therapy has a place in the treatment of this increasingly common disease.

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Professor Charles Rob (London):

The Surgical Treatment of Stenosis and Thrombosis of the Internal Carotid, Vertebral and Common Carotid Arteries

The surgical approach to cerebral thrombosis has changed during the last few years. This change has been caused by the more general appreciation of the fact that the thrombosis is often situated in the cervical portions of the carotid and vertebral arteries, by the greater use of arteriography and by the fact that arterial surgery has progressed to the point where vessels such as the cervical portions of the carotid and vertebral arteries can be efficiently reconstructed.

TABLE I.—OPERATIVE RESULTS IN 70 PATIENTS WITH INTERNAL CAROTID ARTERY OCCLUSIONS

Type of occlusion	No. of patients	Good flow established	Post-operative course				
			Asymptomatic	Objectively better	No change	Temporary deterioration	Death
Partial:							
With hypothermia ..	51	51	31	10	8	2	—
At normal temperature ..	2	2	1	—	—	1	—
Complete	17	4	1	1	12	—	3
Total	70	57	33	11	20	3	3

The surgical treatment of thrombosis of the internal carotid artery has developed along two lines; first, measures designed to increase the efficiency of the collateral circulation around the arterial occlusion, and second, arterial reconstruction operations designed to restore a normal blood flow. Amongst the first group may be included arterectomy (Chao *et al.*, 1938) and sympathectomy (Johnson and Walker, 1951). Our experience with these operations agrees with that of others in that we think that the post-operative course has not been different from the natural tendency to improvement seen in many patients with this condition. In 1954 Eastcott, Pickering and Rob reported the first successful arterial reconstruction operation for internal carotid stenosis; in 1956 Edwards and Rob reported another case where the relief of neurological symptoms and signs was more pronounced; in 1957 Rob and Wheeler reviewed their experience with 27 patients and in 1958 Crawford *et al.* reported the first reconstruction of the vertebral artery for this lesion. Here I shall discuss the treatment of internal carotid and vertebral arterial occlusion in the light of the experience obtained with the patients referred to in our previous publications, plus 43 others, making a total of 70 operated on at St. Mary's Hospital, London.

The Internal Carotid Arteries

The pathology of internal carotid and vertebral arterial occlusion has already been discussed by Professor Crawford, but I wish to stress a few points. The brain is supplied by 4 arteries, the 2 carotids and the 2 vertebrals. As Hutchinson and Yates (1956, 1957) have so clearly shown, atheroma occurs mainly at 3 places, the origin of the internal carotid artery, the origin of the vertebral artery and the middle cerebral artery (Fig. 1). In their series of 87 patients fully examined at autopsy, occlusion of the cervical segments of the carotid and vertebral arteries was common and they noted a surprising degree of atheroma of the extracranial, in contrast to the intracranial, portions of the cerebral arteries.

From the surgeon's point of view occlusions of the internal carotid artery may be partial or complete and it is of importance for me to stress that good results usually follow surgery when

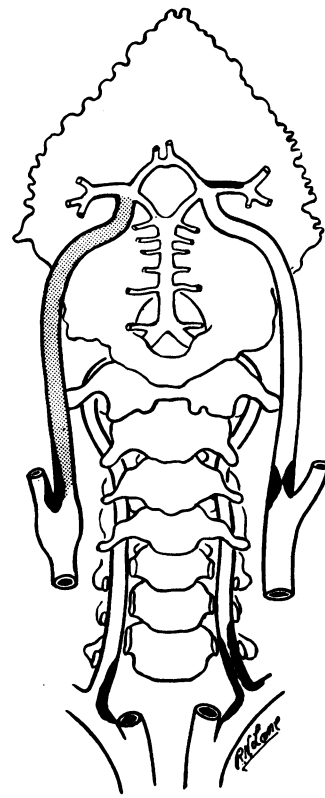

FIG. 1.—Diagram modified from one made by Hutchinson and Yates (1957) showing the main sites for atheromatous stenosis and subsequent thrombotic occlusion of the carotid, vertebral and cerebral arteries.

the occlusion is partial and poor results when it is complete. My own opinion is that if we could operate on more of the complete occlusions early as emergencies we might do good in this group, but confirmation of this opinion must await the clinical experience.

Table I summarizes the results which we have obtained in 70 patients operated on since 1954.

Complete occlusions.—In these patients the surgeon can only reconstruct the artery when it is still possible to obtain a good back flow from the artery distal to the occlusion; once the thrombosis has extended into the skull and become adherent this becomes impossible, at

least until we can reconstruct the intracranial part of the internal carotid artery. But, as Table I shows, we have upon several occasions been able to restore a good blood flow in patients with complete occlusions.

Partial occlusions.—From the diagnostic standpoint I wish to stress the value of auscultation of the arteries in the neck—in about 25% of partial occlusions there is a systolic bruit—and to stress again that a partial occlusion may be indistinguishable clinically from a complete occlusion, and that a firm diagnosis has to be made arteriographically or surgically.

Partial occlusions may produce their clinical effects in one or more of the following ways (Fig. 2): first, the stenosed artery may thrombose

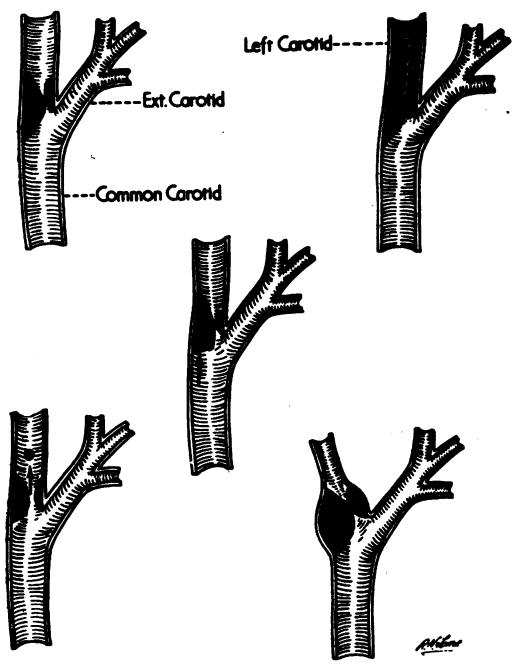

FIG. 2.—There are at least six ways in which a stenosed internal carotid artery can cause symptoms. Five are shown here, including the build up of clot on the surface of an atheromatous stenosis, the formation of a complete thrombosis, hæmorrhage behind a plaque of atheroma, the production of a distal embolus and spasm beyond the narrowed segment. The sixth is by a change in the patient's general state which reduces the blood flow through the stenosed segment.

and a complete occlusion result; second, the occlusion may become nearly complete as clot builds up on the stenosed segment; third, a hæmorrhage may occur behind a plaque of atheroma and this may produce a transitory phase of nearly complete occlusion; fourth, some general change such as an attack of paroxysmal tachycardia or even a hot bath may reduce the flow through a previously narrowed artery; fifth, an embolus may become dislodged from the stenosed segment, and sixth, the vessels peripheral to the stenosis may contract due to arterial spasm. We have not seen a proven example of either the fifth or sixth possibility and have merely included them for completeness.

The surgery of partial occlusions is to a large extent prophylactic and in particular it aims at preventing a complete occlusion followed by irreversible cerebral damage. As Hutchinson and Yates have shown, stenosis of the carotid arteries is often bilateral and may be found in association with stenosis of the vertebral arteries. The potential efficiency of the collateral circulation through the circle of Willis may be reduced in patients with multiple stenoses; this in our view is an added reason for restoring a normal flow where possible.

Surgical technique.—When the occlusion is complete no special precautions to protect the brain from the effects of ischæmia are needed. But for partial occlusions we use either hypothermia or a temporary shunt, with a strong preference for the former. The patient's body temperature is reduced to 29° C. or 30° C. by external cooling. At this temperature it is safe to clamp one internal carotid or vertebral artery for at least half an hour, a time which is quite sufficient for an arterial reconstruction operation.

The artery may be reconstructed by: resection of the stenosed segment and a direct end-to-end anastomosis; the insertion of a blood vessel graft or transplant; the operation of thrombo-endarterectomy; or the insertion of a by-pass graft around the occlusion. Of these we find the operation of thrombo-endarterectomy to be the most useful, but when the anatomical features of the occlusion permit we prefer to resect the stenosed segment and perform a direct end-to-end anastomosis. We reserve blood vessel grafts and transplants for the occasional case in which neither of the above procedures is possible and so far have not used the fourth procedure, a by-pass graft in this situation, although Denman *et al.* (1955) have recorded a success with this operation.

Risks of carotid surgery.—In the past, authors have emphasized the potential dangers of direct surgery on the carotid arteries. The chief fears have been that clamping the carotid arteries might cause ischæmic cerebral necrosis or that emboli might arise from the operation site. As Table I shows, this has not occurred. Two patients showed temporary deterioration after the operation. One case was in our view attributable to a fall of blood pressure and recovery was rapid and complete; the other was in a patient whose partially occluded internal

carotid artery was clamped at normal body temperature for seventeen minutes. With hypothermia and relatively rapid but adequate surgery the operation is safe. We believe that with practice it is possible to reconstruct the internal carotid artery in under twenty minutes in more than 90% of patients and that the period of occlusion only slightly exceeds this in the remaining patients. The surgeon's technique should be meticulous and careful: in this type of operation technique is of considerable importance. There have only been three hospital deaths which means that in this admittedly selected group the mortality of operation has been considerably less than that of medical management. The cause of death in one patient was myocardial infarction, in one pulmonary embolism and in one pneumonia.

The Vertebral Arteries

As Hutchinson and Yates have shown, stenosis of the vertebral arteries frequently occurs at, or close to, their origin from the subclavian arteries before they have entered their bony canal. This means that this lesion occurs at a point where this artery is relatively accessible to surgery (Fig. 1). Our experience is that most patients with atheromatous stenosis of the carotid and vertebral arteries respond adequately to surgical correction of the carotid stenosis which is a simpler operation. In only 7 of Hutchinson and Yates' 83 patients was vertebral artery stenosis present without carotid stenosis.

The Common Carotid Arteries

Atheromatous stenosis of these arteries is not common; we have only operated upon 2 patients. There is, however, one special type of atheroma which occludes the common carotid arteries and that is the sheet-like plaque which spreads across the dome of the arch of the aorta and involves the origins of the innominate, common carotid and subclavian arteries. This type of atheromatous occlusion is one cause of the syndrome known as "pulseless disease" first described by Takayusu (1908). Several such patients have now been successfully treated by an arterial reconstruction operation (Warren and Triedman, 1957).

Post-operative Course

The first essentials are to return the patient's body temperature to normal, if hypothermia has been used, and to ensure that the blood pressure does not fall. Apart from these steps few special precautions are required. It is of importance to stress that from the patient's point of view an internal carotid reconstruction under hypothermia is a minor operation, the patient gets up the next day and can go home in five to seven days; when the neurological abnormality has permitted, the majority have returned to work within one month of the operation. As already stated, the operation has technical difficulties, but these are not apparent to the patient.

Anticoagulants.—Many authorities, including Millikan and Siekert (1955), have recommended long-term anticoagulant therapy for the treatment of carotid atheroma. We have used long-term anticoagulant therapy in a number of patients who have had an arterial reconstruction operation for an atheromatous stenosis or thrombosis, including those of the internal carotid artery. The hope is to prevent not only thrombosis of the artery which has been reconstructed, but of other vessels such as the coronaries. But in the case of internal carotid and vertebral stenosis there is some evidence that there is an increased incidence of cerebral hæmorrhage; for this reason we have abandoned this treatment at least as a routine measure in such patients. We always use anticoagulants in the form of local heparin during the operation.

Late Results and Follow Up

Dr. Harold Edwards will shortly be publishing a paper dealing with the follow-up of our first 28 patients. Our experience is that the reconstructed artery stays open; late sequelæ are usually due to vascular accidents elsewhere. Our first patient is fit and well four years later; her age is now 72.

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