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THROMBOSIS OF INTERNAL CAROTID ARTERY TREATED BY ARTERIAL SURGERY

BY

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Occlusion of the internal carotid artery is now recognized as one of the more common causes of cerebrovascular disease (Adams and Vander Eecken, 1953; Fisher, 1954). The occlusion is almost invariably due to atherosclerosis, and the arterial lesion is similar to atherosclerotic occlusions in other major arteries of the body. Many such occlusions of the aorta and peripheral arteries have been effectively treated by surgical operations designed to restore a normal blood flow. This paper describes the application of these surgical procedures to atherosclerotic occlusions involving the cervical portions of the carotid arteries. Particular attention is paid to the technical feasibility, operative risk, and early post-operative course of carotid surgery. A detailed clinical evaluation of the long-term prognosis after surgery will be the subject of a later article.

Pathogenesis

Occlusion of the internal carotid artery usually begins with the formation of an atheromatous plaque just distal to the bifurcation of the common carotid artery. As the plaque enlarges, the arterial lumen is narrowed and the blood flow is reduced. This narrowing of the lumen may be increased by haemorrhage under the plaque or by the formation of a mural thrombus. Fragments of clot may break away and form cerebral emboli, or the thrombus may extend and completely occlude the vessel. The end-result of these various processes is to decrease or abolish the blood flow through the affected vessel. This deficit in flow causes symptoms of cerebral ischaemia if (1) the cerebral collateral

circulation is inadequate, (2) there is a fall in systemic blood pressure, or (3) the patient becomes anaemic or anoxic. Whether some of these processes also interfere with the cerebral circulation by producing intracerebral vasospasm has been a matter of dispute for many years.

Three points are worth emphasizing. First, the collateral circulation is of paramount importance in determining the clinical effect of any carotid occlusion. Second, a partial occlusion can produce symptoms indistinguishable from a complete occlusion if the collateral circulation is inadequate. Third, the unpredictable nature of these pathological processes leads to great variation in the clinical course of the disease.

Clinical Features

Like atherosclerotic occlusions of other vessels, occlusions of the internal carotid artery usually occur in patients over 40 years of age and are much more common in men than in women. The commonest symptom is unilateral muscle weakness, usually associated with a disturbance of speech if the dominant hemisphere is affected. Other frequent complaints are headache and unilateral sensory disorders, particularly hypaesthesia. Transient blindness of the eye on the side of the occlusion is a characteristic sign when present, and homonymous hemianopsia is occasionally seen. Mental or emotional disorders are not uncommon.

There is considerable variation in the clinical picture, and particularly in the mode of onset. Symptoms may be mild and intermittent in character, or they may be slowly progressive to complete hemiplegia. Occasionally they may be sudden, severe, and catastrophic in onset. Some of the patients may be entirely asymptomatic, depending on the state of the collateral circulation.

There are no pathognomonic physical findings, although a decreased retinal blood pressure on the side of the occlusion is most suggestive. This can be measured directly (Thomas and Petrohelos, 1953) or indirectly by noting the ease of retinal blanching on digital pressure (Denny-Brown, 1951, 1952). Palpation of the carotid pulsation is an unreliable physical sign.

Carotid angiography is an extremely useful diagnostic procedure which yields specific information about the patency of the carotid arterial system. In many cases it is the only way in which the diagnosis can be made with assurance. Although others have emphasized its risk, there has been only one mild exacerbation of symptoms in this series after arteriography. No other investigative procedures have proved of specific value, except by excluding other disease.

For a more detailed exposition of the clinical features of initial carotid occlusions the reader is referred elsewhere (Hunt, 1914; Johnson and Walker, 1951; Behrman, 1954; Shapiro and Peyton, 1954; Millikan and Siekert, 1955).

Risks of Carotid Arterial Surgery

In discussing the treatment of internal carotid thrombosis some authors have emphasized the potential dangers associated with direct surgery on the carotid arteries. The chief fear has always been that clamping the carotid arteries for several minutes might cause ischaemic cerebral necrosis, particularly if the cortex had a poor blood supply prior to the operation. In the case of a complete internal carotid occlusion, clamping the common carotid artery temporarily deprives the cortex of the collateral circulation carried by the external carotid artery, and in the case of a partial occlusion there is the additional loss of whatever flow was passing through the internal carotid artery. In addition, the resulting vascular stasis is a theoretical opportunity for thrombosis to occur. Another potential cause of cerebral ischaemia is hypotension due to anaesthetic agents or to haemorrhage during the surgical procedure itself. A further possible complication is the production of an embolus from the operative site, and a final theoretical danger is the production of intracerebral vasospasm secondary to the operative trauma.

From the experience to date it would seem that many of the theoretical complications of carotid surgery should prove uncommon in practice provided certain routine prophylactic measures are taken. Probably the most important of these prophylactic steps is the use of hypothermia. Lowering the body temperature to 28–30° C. has been shown to decrease the cerebral metabolism (Bering *et al.*, 1956; Stone *et al.*, 1956) and allow longer periods of complete anoxia without loss of function than was formerly believed possible.

An obvious point in the prevention of cerebral damage is to shorten the arterial operating time as much as possible. In practice this means doing the simplest procedure and thoroughly checking the readiness of all instruments prior to clamping the vessels. Our procedure of choice is a thromboendarterectomy (Edwards and Rob, 1956). This was the procedure in 12 out of the 15 patients in this series in whom a good blood flow was re-established. A localized resection and end-to-end anastomosis is the next most desirable procedure (Eastcott *et al.*, 1954).

There are some technical points which are also of value in preventing complications. Heparin should be injected proximal and distal to the clamped-off arterial segment in order to decrease any tendency for thrombi to form in the areas of vascular stasis. The arterial lumen should be left as smooth as possible and should be thoroughly washed out with saline to carry away any clots or atheromatous debris. Only small stitch "bites" should be taken in the arterial wall, and these should not be pulled too tightly, since large, tightly pulled stitches narrow the lumen and produce irregularity of the wall. Since the internal carotid artery may contain a recent non-adherent thrombus, the dissection to free this vessel should be as gentle as possible. It may be advisable, on purely theoretical grounds, to strip bare a portion of the internal carotid artery in order to interrupt vasoconstricting autonomic impulses. It is obvious that more than usual care should be taken during and after the operation to see that no hypotensive episodes occur. Forty-eight hours after operation we place our patients on oral anticoagulants and, if possible, continue these for the remainder of their lives.

Turning from theoretical possibilities to practical experience, there have been two patients with post-operative cerebral complications in this series of 26 carotid explorations. One patient (Case 5) developed a post-operative hemiplegia. This improved rapidly, but he was left with a detectable weakness of the right arm. This was probably the result of cerebral ischaemia from clamping the common carotid artery for 17 minutes at normal body temperature. Another

patient (Case 9) had a post-operative hypotensive episode with an exacerbation of neurological symptoms, with recovery several hours after the blood pressure had been restored. It is possible that both of these complications might have been prevented, in one case by the use of hypothermia and in the other by closer attention to the patient's blood pressure.

It should be mentioned that one of our patients (Case 8) had a non-cerebral complication consisting of a pre-operative cardiac arrest shortly after the start of hypothermia (temperature 35° C.). Whether this was spontaneous or due to the lowered body temperature is a matter of conjecture. Fortunately prompt cardiac massage restored the heart beat and there were no sequelae. The surgical procedure was then carried out uneventfully at normal body temperature.

Operative Results of Carotid Arterial Surgery

To date (May, 1957) we have carried out direct arterial surgery on 27 patients (22 males, 5 females) with internal carotid occlusions. The operative results are given in Table I and the important features of each case are summarized in

TABLE I.—Operative Results in 27 Patients with Internal Carotid Artery Occlusions

Type of Occlusion	No. of Patients	Good Flow Established	Post-operative Course				
			Asympt.	Obj. Better	No Change	Temp. Deterioration	Death
Partial { Hypo-thermia	9	9	3	2	3*	1	0
{ Normal temp.	2	2	1	—	—	1	0
Complete	16	4	1	1	12	—	2
Total	27	15	5	3	15	2	2

* One of these patients died at home from a cerebral haemorrhage four weeks post-operatively (see text).

Table II. Of the 27 patients, 5 are asymptomatic, 4 are able to work, 8 are unable to work, 7 are permanent invalids, and 3 are dead.

In brief, the series includes 11 patients with partial occlusions and 16 with complete occlusions. All of the patients with partial occlusions had definite arterial surgery carried out with a good blood flow at the end of the procedure. There has been no later clinical deterioration to indicate subsequent thrombosis in any of these patients.

TABLE II.—Case Summaries of 27 Patients with Occlusions of the Internal Carotid Artery

Case No.	Age and Sex	Type of Occlusion	Side of Occlusion	Mode of Onset	Symptoms					Surgery				Clinical Outcome
					Motor Weakness	Speech Disturbance	Sensory Disturbance	Visual Defect	Headache	Thromboendarterectomy	Resection and Anastomosis	Arterectomy	Flow Re-established	
1	66 F	Partial	Left	Intermittent	Yes	Yes	No	Yes	No	No	Yes	No	Yes	Asymptomatic
2	56 M	"	"	"	"	No	No	No	"	Yes	No	"	"	"
3	54 M	"	"	"	"	No	No	"	"	"	"	"	"	"
4	68 M	"	"	"	"	Yes	Yes	"	"	"	"	"	"	Able to work
5	55 M	"	"	"	"	No	No	Yes	Yes	"	"	"	"	Unable to work
6	47 M	"	Right	"	"	No	Yes	No	No	"	"	"	"	Unable to work
7	57 F	"	"	"	"	Yes	No	Yes	Yes	No	Yes	"	"	Able to work
8	48 M	"	Left	"	No	Yes	No	Yes	Yes	No	Yes	"	"	Asymptomatic
9	64 F	"	"	Sudden	Yes	No	No	No	No	Yes	No	"	"	Unable to work
10	61 M	"	"	"	"	Yes	Yes	No	No	"	"	"	"	Dead
11	60 F	"	"	Intermittent	"	Yes	No	Yes	"	"	"	"	"	Able to work
12	62 M	Complete	Right	Gradual	"	"	Yes	No	"	No	"	Yes	No	Permanent invalid
13	71 M	"	Left	Intermittent	"	"	Yes	Yes	"	"	"	"	"	Dead
14	49 M	"	Right	"	"	"	No	No	"	"	"	"	"	Unable to work
15	58 M	"	Left	Sudden	"	"	No	Yes	"	Yes	"	No	Yes	Permanent invalid
16	53 M	"	Right	"	"	No	"	No	"	No	"	Yes	No	Dead
17	58 F	"	"	"	"	"	Yes	Yes	"	"	"	"	"	Unable to work
18	50 M	"	"	"	"	Yes	Yes	No	"	"	"	"	"	Permanent invalid
19	56 M	"	Left	"	"	Yes	No	Yes	"	"	"	"	"	"
20	60 M	"	"	Intermittent	"	"	Yes	No	"	Yes	"	No	Yes	"
21	63 M	"	"	Gradual	"	No	No	Yes	Yes	No	"	Yes	No	Unable to work
22	61 M	"	"	Intermittent	"	Yes	No	"	"	Yes	"	No	Yes	Permanent invalid
23	67 M	"	"	"	"	"	"	"	No	No	"	Yes	No	Unable to work
24	54 M	"	"	Gradual	"	"	"	"	Yes	"	"	"	"	Asymptomatic
25	47 M	"	"	Intermittent	"	"	Yes	No	No	"	"	"	"	Unable to work
26	53 M	"	"	"	"	"	No	"	"	Yes	"	No	Yes	Permanent invalid
27	47 M	"	"	Sudden	"	"	"	"	"	"	"	"	"	"
Totals . .					26	18	10	13	5	12	3	12	15	

Two early post-operative arteriograms (Cases 6 and 21) and two re-explorations of the wound (Cases 5 and 7) have shown the vessel to be still patent. Six of these 11 patients have been either asymptomatic or objectively improved post-operatively. Two patients showed no change and the remaining two patients had temporary post-operative deterioration (Cases 5 and 9). One patient died at home four weeks post-operatively. Necropsy disclosed a cerebral haemorrhage on the side opposite the previous carotid occlusion. Both carotids were patent. The patient had spontaneously stopped oral anticoagulants three days before death, and it seems questionable whether or not anticoagulant treatment contributed in any way to the haemorrhage.

Of the 16 patients with complete occlusions, in only four were we able to restore the blood flow (Cases 16, 21, 23, and 27). None of the patients with complete occlusions demonstrated improvement which was not consistent with the normal progress of the disease. There were two deaths, necropsy showing a pulmonary embolus and a myocardial infarction as the presumptive causes of death (Cases 13 and 16).

It is not possible to analyse statistically such a small series of cases, particularly in a disease with as variable a course as carotid thrombosis. We believe, however, that there are theoretical considerations in favour of direct arterial surgery which are supported by a study of the patients in this series. The most appealing theoretical advantage of direct arterial surgery is the chance to interrupt a pathological chain of events which frequently ends in irreversible cerebral damage. There is no way to know if the surgically corrected incomplete occlusions in this series would otherwise have progressed to complete occlusions and severe loss of function. It is undeniable, however, that some of the cases of complete occlusion with hemiplegia had previous symptomatic partial occlusions which were operable before the occlusion became complete (Cases 12, 13, 23, and 26).

Another theoretical advantage of arterial surgery is the ability to relieve symptoms of cerebrovascular insufficiency by improving the cerebral blood flow. This has definitely been borne out in practice (Cases 1 and 2).

A further theoretical advantage of carotid arterial surgery is the ability to improve the cerebral blood flow and provide a better collateral circulation should future vascular occlusions occur elsewhere in the cerebral arterial system.

Patients with internal carotid thrombosis have been shown frequently to have atherosclerotic disease in the other carotid artery and in the vertebral arteries (Hutchinson and Yates, 1957).

Conclusions

Direct arterial surgery attempting to restore normal blood flow has been the primary method of treatment for 27 patients with symptomatic occlusions of the internal carotid artery. The ability to restore blood flow has been found to depend largely on whether the occlusion is partial or complete. In complete occlusions blood flow can be re-established only during the short time before the clot extends into the cranial cavity. Even then, irreversible cortical damage may have occurred (Cases 5, 21, and 23). In partial occlusions a good blood flow can nearly always be re-established. The risk of surgery is not great, only 2 out of 27 patients having any post-operative exacerbation of their neurological symptoms.

At present we feel that the patients most likely to benefit from surgery are those with incomplete occlusions who first come to a doctor because of symptoms of cerebrovascular insufficiency. Restoring flow in these patients not only frequently relieves the symptoms of cerebrovascular insufficiency but may prevent the later development of complete thrombosis and irreversible cerebral damage.

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SICKLE-CELL DISEASE: NEW METHOD OF TREATMENT

PRELIMINARY REPORT

BY

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Sickle-cell disease is an inherited malady with a poor prognosis. The misshapen erythrocytes are destroyed in the body, resulting in a haemolytic anaemia, and they adhere to each other to form intravascular thrombi with infarctions of various tissues.

The defect resides in the haemoglobin, which, when deprived of its oxygen by the respiring tissues, undergoes molecular rearrangement to form long rod-like particles with resulting alteration of the erythrocyte contour. The only treatment of value is blood transfusion, which may be life-saving during a haemolytic crisis. Anti-coagulants do not prevent the thrombotic phenomena.

Sickled cells are not usually seen in blood obtained from a patient by venepuncture, because in the process of examination the blood becomes re-oxygenated and the erythrocytes are restored to their normal shape (Hahn, 1928). The usual method by which sickled cells are demonstrated is that of sealing a drop of blood under a coverslip on a slide. The consumption of oxygen in such a preparation by the respiring erythrocytes, leucocytes, and contaminating bacteria results in the reduction of the haemoglobin and consequent alteration in the shape of the red cells.

Tomlinson and Jacob (1945) washed the red cells from a patient with sickle-cell disease repeatedly in normal saline and then resuspended them in the patient's plasma. They made sealed preparations and demonstrated that the red cells failed to sickle. They showed also that the addition of zinc acetate or sodium cyanide solutions to blood from a patient prevented the occurrence of sickling. These substances are known inhibitors of the enzyme carbonic anhydrase. These workers concluded that they had removed a factor necessary for sickling from the erythrocytes by washing, and suggested that this factor might be carbonic anhydrase.