Mussett, M. V., and Perry, W. L. M (1956). To be published.
Oliver, M. F., and Boyd, G S. (1953). *Clin. Sci.*, **12**, 293.
Opdyke, D. F., Rosenberg, A., Silber, R., Ott, W. H., and Siegel, H. (1955). *J. Lab. clin. Med.*, **45**, 270.
Piper, J. (1945). *Acta physiol. scand.*, **9**, 28.
Ricketts, C. R. (1952). *Biochem. J.*, **51**, 129.
—— and Walton, K. W. (1953). *Brit. J. Pharmacol.*, **8**, 476.
—— —— van Leuven, B. D., Birbeck, A., Brown, A., Kennedy, A. C., and Burt, C. C. (1953). *Lancet*, **2**, 1004.
Rosenberg I. N. (1952). *Proc. Soc. exp. Biol. (N.Y.)*, **80**, 751.
Scholz, D A., and Barker, N. W. (1952). *Proc. Mayo Clin.*, **27**, 332.
Seifter, J., and Begany, A. J. (1948). *Amer. J. med. Sci.*, **216**, 234.
Soffer, A., and Murray, M (1954). *Circulation*, **10**, 255.
Sorenson, C. W., and Wright, I. S. (1950). Ibid., **2**, 658.
Utz, J. P., Mann F. D., and Barker, N. W. (1953). *Proc. Mayo Clin.*, **28**, 531.
Walton, K. W. (1951). *Proc. roy. Soc. Med.*, **44**, 563.
—— (1952). *Brit. J. Pharmacol.*, **7**, 370.
—— (1953). Ibid., **8**, 340.
—— (1954) Ibid., **9**, 1.
Zinn, W. J., Field, J. B., and Griffith, G. C. (1952). *Proc. Soc. exp. Biol. (N.Y.)*, **80**, 276

PLACE OF DIRECT SURGERY IN TREATMENT OF OBLITERATIVE ARTERIAL DISEASE*

BY

CHARLES ROB, M.Chir., F.R.C.S.

Professor of Surgery, St. Mary's Hospital, London

Obliterative arterial disease may be due to a variety of causes, including thrombosis after an injury, coarctation of the aorta, thromboangiitis obliterans, an embolus, or the condition of so-called primary arterial thrombosis. I shall not discuss the place of direct surgery in the treatment of these lesions beyond mentioning that it is the best treatment for coarctation of the aorta and for thrombosis of a major artery after an injury, a good treatment for primary thrombosis and some emboli, but only occasionally possible in patients with thromboangiitis obliterans. I am concerned mainly with atherosclerosis and the place of arterial reconstruction operations in the treatment of this all too common disease.

Atherosclerosis is a general disease which affects the arteries of the whole body, and it is an important principle that an arterial reconstruction operation can have only a local effect. Therefore this type of surgery is justified only when the local manifestations of this general disease predominate to an unusual extent. In many patients symptoms arise from the occlusion of several arteries, and it is obviously a mistake to reconstruct the femoral artery of a patient who suffers from both angina pectoris and intermittent claudication. On the other hand, it is justifiable to reconstruct the femoral artery of a patient who suffers from angina pectoris and gangrene of a toe; from the patient's point of view an arterial reconstruction operation is a smaller procedure than a major amputation (Rob, Eastcott, and Owen, 1956). Fortunately, in a fair proportion of patients atherosclerosis remains relatively localized. This is particularly so in patients with occlusion of the abdominal aorta or iliac arteries, and sometimes so in those with thrombosis of the popliteal, femoral, carotid, mesenteric, renal, and subclavian vessels. In my view, at least 50% of patients with occlusion of the abdominal aorta and iliac arteries are suitable for a reconstruction operation, about 25% of those with femoro-popliteal thromboses, and probably about 5% of those with an internal carotid thrombosis, although this latter figure is merely a rough estimate.

*Carbutt Memorial Lecture delivered at Guy's Hospital on May 29, 1956.

Thrombosis of Abdominal Aorta and Iliac Arteries

The symptoms produced by this lesion are variable. One patient may be able to walk slowly for half a mile before the onset of the pain of intermittent claudication, and another with an almost identical thrombosis may have gangrene; the symptoms depend upon the efficiency of the collateral circulation. From a surgical point of view this lesion may be divided into two types—the extensive occlusion extending from the iliac arteries below to the renal arteries above (Fig. 1), and the localized occlusion usually confined to the region of the bifurcation of the abdominal aorta (Fig. 2).

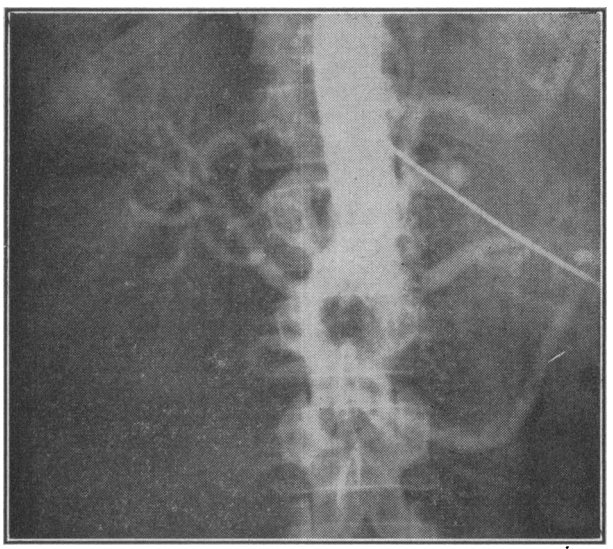

FIG. 1.—Thrombosis of the abdominal aorta in a man aged 36. The occlusion has reached the renal arteries and there is a partial occlusion of the left renal artery. The patient had grade IV hypertension with a blood pressure of 210/110.

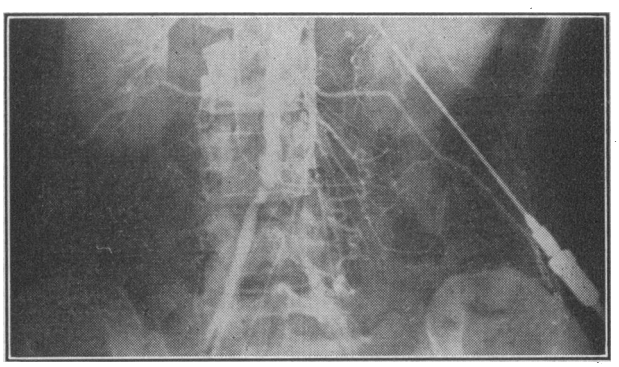

FIG. 2.—Thrombosis localized to the region of the aortic bifurcation. This patient, a woman aged 34, had gangrene of her right foot. An arterial reconstruction was successful.

It is a relatively simple matter to restore the blood flow in most of the patients with the localized type of occlusion. We have had only one death out of 28 such operations and only two recurrent thromboses, and each of these affected only one iliac artery. On the other hand, those with high occlusions present a major problem and require a major operation. For these patients it is necessary to clamp the aorta above the renal arteries and insert a plastic prosthesis or homologous arterial transplant from this level to the iliac arteries. Two of our seven patients with this lesion have died as a result of the operation, both from renal failure, but the risk of this has been reduced by using hypothermia. Because of the good results obtained with surgery in those patients with localized occlusions and the high mortality of conservative care in those with an occlusion which has

reached the mouths of the renal arteries, we now advise operation in the majority of patients with thrombosis of the abdominal aorta, exceptions being those with clinical coronary artery disease and those with evidence of active generalized atherosclerosis. It may be only after inspection of the arteries at operation that this latter group can be diagnosed.

The high mortality of occlusions which have reached the renal arteries is due to renal failure or hypertension. The former is due to occlusion of both renal arteries, with infarction of the kidneys, but the latter is of special interest. Thrombosis of the abdominal aorta at the level of the renal arteries does not cause hypertension. Fig. 3 is the blood-

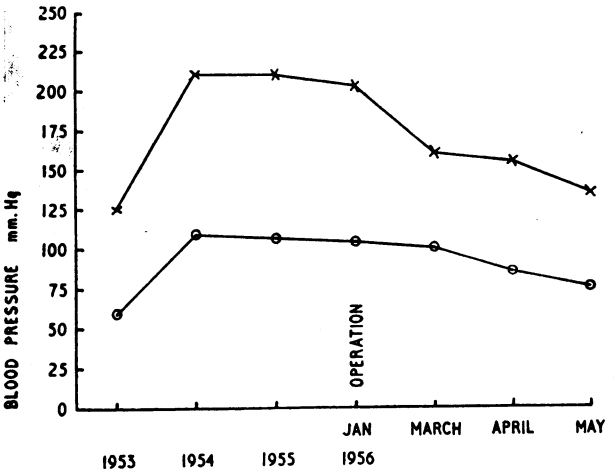

FIG. 3.—Blood-pressure chart of the patient whose aortogram is shown in Fig. 1. When he was first seen his blood pressure was normal, but following the partial occlusion of the left renal artery severe hypertension developed. This was relieved by surgery.

pressure chart of the patient whose aortogram is shown in Fig. 1. When first seen in 1953 at the age of 35 he had a normal blood pressure and an occlusion of the abdominal aorta in the region of its bifurcation. Operation was advised but refused. He was kept under observation, and in 1954 his blood pressure rose to 220/110; he still refused operation, but by late 1955 he was crippled by hypertensive headaches and his vision was failing, with papilloedema and retinal haemorrhages. The aortogram (Fig. 1) now showed a partial occlusion of the left renal artery. Reconstruction of the aorta and removal of this kidney lowered his blood pressure to normal (Fig. 3) and cured his symptoms. We have had two patients of this type; the other was successfully operated on in 1952 and is well to-day. These patients raise the interesting point of the place of atherosclerosis of the renal arteries in the production of hypertension (Howard, Berthrong, Gould, and Yendt, 1954). A partial occlusion of this type may produce a Goldblatt type of renal lesion, and in my view it is worth doing aortograms on a proportion of patients with severe essential hypertension to see if one cannot detect a localized lesion of this type.

Femoro-Popliteal Artery

Patients with occlusion of this artery present either with the symptom of intermittent claudication as their main complaint or with rest pain and gangrene. For those with rest pain and gangrene an arterial reconstruction operation is the treatment of choice, because the alternative is usually a major amputation. It is surprising how often it is possible to save the limb of such a patient. In our experience such a procedure is possible for about 20% of patients with gangrene of the toes and feet; we have saved twenty such limbs, and two were diabetics. A patient with gangrene and clinical evidence of an aortic, iliac, or femoro-popliteal thrombosis should have an arteriogram to see if his limb could be saved. While this may well mean four or five arteriograms for each successful arterial reconstruction, the results, particularly in patients below 65 years of age, should be worth the trouble.

On the other hand, the symptom of intermittent claudication presents quite a different problem. Fully 80% of such patients have a lesion, usually of the femoro-popliteal artery, which is anatomically suitable for arterial reconstruction, but only about 25% or less should be treated surgically, and this applies to both the end-to-end and the by-pass types of operation. This latter method is the best, but in my view the selection of patients should not be relaxed, chiefly because of the general nature of this disease. Patients with femoro-popliteal thromboses often have coronary atherosclerosis. We have one simple rule: a patient with intermittent claudication due to a femoro-popliteal thrombosis should have an arterial reconstruction operation only if he is unable to work. The business man who can do his work but who cannot play golf should be treated conservatively.

Table I shows the results we have obtained with direct surgical operations in patients with obliterative arterial disease, the procedures being either thrombo-endarterectomies or arterial reconstructions by the end-to-end or by-pass technique. The follow-up is between one and six years.

TABLE I.—*Follow-up. Arterial Reconstruction Operations in* 109 *Patients with Obliterative Arterial Disease*

Artery	No. of Patients	Thrombosed in Hospital	Thrombosed Later	Now Patent
Aorta and iliacs ..	35 (3 died in hospital)	1	1 (+ 1 dead since discharge)	29
Femoral	48	11	15 (+ 2 dead since discharge)	20
Popliteal	17	1	5	11
Others..	9	2	3	4

It is of interest that patients with popliteal occlusions have done a little better than those with femoral blocks, because this is against the general trend, where the larger the vessel is the better are the results. A possible explanation of this may be that the collateral circulation is very much better around a femoral than around a popliteal thrombosis. This means that occlusion of the popliteal artery produces major symptoms early in its course, whilst a similar occlusion of the femoral artery may produce little disturbance, and so surgery becomes necessary only in those patients with marked atherosclerosis. In my view, the state of the host artery is a major factor in the late recurrence rate in these patients; in general, those with severe atherosclerosis do badly.

Carotid Arteries

Occlusion of the internal carotid artery often begins as a plaque of atheroma situated just above the carotid bifurcation. In most patients the occlusion is complete and direct surgery cannot do any good, but in a minority the occlusion is partial and the patient can be cured by surgery (Eastcott, Pickering, and Rob, 1954). These nearly complete occlusions may produce intermittent cerebral symptoms or the effects may be continuous; in either case the results of surgery may be dramatic. In one of our patients the continuous neurological abnormalities included a partial right-sided hemiplegia and the patient was unable to sign his own name; an arterial reconstruction operation has removed all his abnormal physical signs and he has returned to work in a responsible position with a shipping company. It is important to stress that many cerebral arteriograms fail to include the carotid bifurcation on the *x*-ray film, and this will fail to demonstrate such a lesion. Carotid arteriograms, in common with all other arteriograms, must show the site of needle puncture on at least one of the films.

Arteries of the Upper Limb

It is most unusual for thrombosis of one of these vessels to need a reconstruction operation, because the collateral

circulation is usually so good. However, on four occasions we have reconstructed such vessels (subclavian and axillary) in patients who were unable to work because of the symptoms of ischaemia, and the results have been worth while.

Type of Reconstruction Operation

Table II gives our results with the various arterial reconstruction operations in all our patients over the last six years irrespective of the reason for the operation, and Table III lists the disease for which the artery was reconstructed.

For patients with obliterative arterial disease it is only occasionally possible to resect the occluded segment and restore continuity by a direct end-to-end anastomosis, but when this can be done it is the best procedure. In my view the next most satisfactory operation is thrombo-endarterectomy. This is of particular value in localized occlusions of the aorta and iliac arteries, but it is sometimes of value in vessels as small as the popliteal. Two important

TABLE II.—*Method Used in* 228 *Arterial Reconstruction Operations*

Operation	No. of Patients	Thrombosed Early and Late	Dead (including Operation Deaths)	Now Patent
Direct suture	25	1	3	21
Thrombo-endarterectomy ..	24	5	1	18
Autogenous vein ..	25	15	4	6
Homologous artery ..	109	34	10	65
Plastic cloth	19	0	5	14
Polyvinyl alcohol ..	26	9	5	12

TABLE III.—*Reason for Operation in the* 228 *Patients Listed in Table II*

Reason	No. of Patients	Thrombosed Early and Late	Dead (including Operation Deaths)	Now Patent
Injury	17	5	4	8
Congenital abnormality	12	0	0	12
Aneurysm or A-V fistula	85	19	16	50
Obliterative disease ..	109	39	6	64
Malignancy	5	1	2	2

points in choosing patients for this procedure are the size of the thrombosed segment and the state of the vessel wall proximal and distal to the occlusion, but, as the tables show, with careful selection the results have been very good. In our hands autogenous vein grafts have given disappointing results in patients with atherosclerosis. The tables show that homologous arteries have been satisfactory, and most of the thromboses in this group have been in patients with obliterative disease of the femoral and popliteal arteries; but the maintenance of an artery bank is by no means easy, and so we use a plastic prosthesis, either of plastic cloth or of polyvinyl alcohol sponge, for the reconstruction of the aorta and iliac arteries.

Anticoagulants

We use anticoagulants locally during the operation, and then from the third or fourth post-operative day as a long-term measure in patients with obliterative arterial disease. The idea is that these patients are likely to thrombose their arteries, either the one which has been reconstructed or another such as the coronary. Long-term anticoagulant therapy possibly reduces the incidence of this. Since 1952 we have kept many of our patients on phenindione (" dindevan ") in sufficient dosage to prolong the prothrombin time to just less than twice the patient's control level. It has caused little trouble beyond the need for regular control, and we now do not even stop the drug for such procedures as another surgical operation. With the prothrombin time at this level one can operate and fail to notice any change in the patient's bleeding. The value of this measure is still unproved.

Conclusion

Our follow-up shows that with careful selection the results of direct surgery in the treatment of obliterative arterial disease can be good. They are best in patients with occlusions of the aorta and iliac arteries and they are most gratifying in patients with gangrene of the toes and feet, cerebral symptoms due to partial internal carotid occlusion, or hypertension. Good results also follow the reconstruction of the femoro-popliteal artery in patients with intermittent claudication, but here selection is particularly important. In my view the by-pass type of operation is the best procedure for occlusions of this vessel, but its reintroduction has not widened the indications for surgery in patients with this general disease, unless the reason for operating is gangrene or rest pain.

REFERENCES

Eastcott, H. H. G., Pickering, G. W., and Rob, C. G. (1954). *Lancet*, 2, 994.

Howard, J. E., Berthrong, M., Gould, D. M., and Yendt, E. R. (1954). *Bull. Johns Hopk. Hosp.*, 94, 51.

Rob, C. G., Eastcott, H. H. G., and Owen, K. (1956). *Brit. J. Surg.*, 43, 449.

SOME DELAYED COMPLICATIONS OF INOCULATION

BY

PHILIP W. ROBERTSON, M.D., M.R.C.P.

Wing Commander, Medical Specialist, R.A.F.

AND

BRIAN J. LEONARD, M.D.

Late Squadron Leader, R.A.F.

For several years we have been aware of a number of curious disturbances which may occur during the first or second week after inoculation or vaccination. This paper is based upon a large number of clinical observations; no attempt is made to offer a detailed explanation of these disturbances, but rather to consider in what way they fit into the disease pattern of other syndromes and what is their long-term significance.

It has long been known that reactions could follow various inoculation procedures, and such reactions have usually been considered under " immediate reactions," as the delayed " serum sickness " type of reaction, or as anaphylactic reactions. We have not been particularly concerned with immediate reactions and have not met with any true anaphylactic reactions, but in the group of conditions related to serum sickness we have found the greatest variety of disease syndromes.

Present Investigation

With few exceptions, our observations were made upon young healthy adult recruits between the ages of 18 and 20. Within the first few weeks in the Service these recruits received various inoculations and all were vaccinated. As a rule, the first T.A.B.T. injection was given at the same time as the vaccination, and most of our observations were made in the period one to two weeks after this double procedure. A second T.A.B.T. injection was given six weeks after the first, following which only occasional reactions were seen. This can be attributed to various factors, but chiefly to the fact that those who reacted to the first injection were not usually subjected to a second, while those who did