

Secondly, the incidence of bleeding was 4.9% amongst which seven fatal cerebral haemorrhages occurred.

However, neither the incidence of spontaneous disobliteration nor the optimal dose and duration of SK therapy have yet been established. Furthermore, no controlled and randomized study is available comparing in this condition the value of SK treatment to other current therapeutic regimens.

Since the introduction of Fogarty's catheter (Fogarty, Cranley, Krause, Strasser, and Hafner, 1963) the possibilities of vascular surgery have been

extended, and this method represents an important alternative for the treatment of patients with an arterial embolism and to minor extent arterial thrombosis in atherosclerotic arteries. There is therefore an urgent need to organize a well designed co-operative trial comparing the immediate and late outcome of recent occlusions of limb arteries treated with heparin, Fogarty catheter, streptokinase, or urokinase in homogenous groups of patients allocated at random to one of four treatment schedules. Separate groups should be made for arterial emboli and arterial thrombosis in young patients.

Treatment of chronic arterial occlusions with streptokinase

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Previous studies have demonstrated that fibrinolytic therapy with streptokinase is successful in patients with acute arterial occlusion. However, this form of therapy is generally considered to be ineffective in the treatment of longstanding arterial occlusions, in which conservative therapeutic efforts have been directed mainly at the establishment of collateral circulation and not at establishing flow in the occluded vessel itself.

Gottlob, Blümel, Piza Brücke, and Böhmig (1968), in experiments *in vitro*, demonstrated lysis of thrombi removed from patients with chronic arterial occlusions. Encouraged by these results, Schoop, Martin, and Zeitler (1968), Ehringer and Fischer (1968), and our own group started clinical investigations into the thrombolytic treatment of chronic arterial occlusions (Poliwoda, Alexander, Buhl, Holsten, and Wagner, 1969).

Patients

One hundred and thirty-two patients (118 men and 14 women, 36 to 77 years of age) were treated with streptokinase. All had longstanding arterial occlu-

sion, the duration of the disease as indicated by intermittent claudication varying from four weeks to 16 years. In all patients, the clinical findings were supported by oscillography, light plethysmography, and arteriography. These investigations were performed before and after streptokinase therapy, and the results compared.

Therapeutic Programme

The initial dose of streptokinase was determined by the streptokinase resistance test. The enzyme was given by intravenous infusion over a period of 20 minutes and followed by a dose of 125 000 units per hour for 16 hours by continuous intravenous infusion. Therapy was interrupted for eight hours during the night. The effect of streptokinase therapy was controlled by the thrombin time (normal 18 to 20 seconds). A twofold to threefold prolongation of the normal value was considered optimal. After the third day the thrombin time usually returned towards normal (less than 35 seconds) and treatment with heparin was begun, administered by continuous intravenous infusion, in a dose of 30 000 units over

24 hours. Treatment with coumarin (Marcumar) was usually begun at the same time. But the dose was reduced before the repeat angiography to adjust the Quick one-stage prothrombin time to 40 to 60%.

After this coumarin therapy was continued to maintain the prothrombin time between 20 and 25%.

The response to treatment was followed by daily oscillography and daily clinical examination; arteriography was repeated four to six days after streptokinase therapy was stopped.

All patients were checked biweekly in our out-patient clinic after release from the hospital.

Results

The results of therapy are summarized in Table I.

Of the 11 patients with pelvic arterial occlusions, six gave definite signs of resolution after streptokinase therapy. One of the six also had evidence of marked improvement in femoral artery flow on the both sides after streptokinase therapy. There were 74 femoral artery occlusions in 57 patients. In 24, flow was restored after streptokinase therapy. In three other cases a complete obstruction was partly relieved to reveal a severe stenotic lesion. Out of nine patients with 13 femoral artery stenoses, flow was restored completely in seven, whereas in five others it remained unchanged, and in one complete obliteration occurred.

The seven successfully treated peripheral arterial occlusions may be attributed to the short duration of the occlusions. That is to say, none of the occlusions was more than 14 days old. The most recent was seven days old. All of the occlusions which had existed for more than 14 days were resistant to therapy.

All the patients who responded favourably in therapy had had an exacerbation of symptoms within the last four months before therapy was begun, and was responsible in most patients for the hospital admission. None of the patients who had long-standing clinical symptoms of arterial occlusion without any recent acute episode gave evidence of

resolution on arteriography after streptokinase therapy.

All patients with evidence of improvement on arteriography also showed considerable clinical improvement and a marked increase in the distance that they could walk without claudication. During streptokinase therapy many patients volunteered the information that there was improvement in the coldness and numbness of their limbs and some reported an increase in the distance that they could walk without claudication from 50 to 1 500 yards. This improvement occurred even in patients in whom repeat angiography demonstrated no improvement.

Table II shows the complications observed during the treatment of 59 patients. Thirty-four of 59

	Day of Treatment					
	1	2	3	4	5	6
Fever	3	5	8	12	11	6
Thrombophlebitis	—	—	5	8	4	—
Early reaction	7	—	—	—	—	—
Macroscopic haematuria	—	1	3	4	—	—
Haematoma	—	2	3	—	—	—
Haemorrhage	1	—	3	1	—	—

Table II Side effects during streptokinase treatment in 59 patients

patients had febrile episodes between the first and seventh day of therapy. In these patients, the temperature rose between 38 and 40°C. Nine of 59 patients had macroscopic haematuria during streptokinase therapy, 14 had bleeding from the nose or mouth, and three complained of joint pain.

In six of 120 patients complications made it necessary to discontinue therapy and three of them died of cerebral haemorrhage.

The practical implications of these results are that a large number of patients who were formerly considered unsuitable for fibrinolytic therapy may benefit from such therapy. But this form of therapy should be considered for such patients whose symptoms have been exacerbated within the last months.

	No. of Patients	No. of Occlusions or Stenoses	Restored	Unaffected	Worse
Pelvic arterial stenosis	14	21	9 (42%)	12	—
Pelvic arterial occlusion	11	15	6 (40%)	9	—
Femoral arterial stenosis	9	13	5 (38%)	7	1
Femoral arterial occlusion	57	74	24 (30%)	48	2
Popliteal arterial occlusion	8	9	3 (33%)	6	—
Peripheral arterial stenosis	9	16	2 (12%)	14	—
Peripheral arterial occlusion	24	38	7 (18%)	31	—
Total	132	186	56 (30%)	127	3

Table I Results of therapy