Results of Sympathectomy in Digital Artery Disease

MARTIN BIRNSTINGL,* M.S., F.R.C.S.

Brit. med. J., 1967, 2, 601-605

In considering the natural history of patients with digital ischaemia it is useful to separate those with severe and permanent circulatory impairment due to organic arterial disease from those with purely vasospastic disorder. This can best be done on a basis of digital arteriographic findings. Furthermore, since it is recognized that what seems at first to be a primary vasospastic disorder may be followed years later by the development of organic digital disease (Johnston, Summerly, and Birnstingl, 1965), and since relapse after sympathectomy may take several years to appear (de Takats and Fowler, 1962), follow-up studies should be carried out as long as possible. The present series of 43 patients were all treated by upper thoracic sympathectomy, at the time of which they were already considered to have organic blockage of digital arteries. They have been carefully followed at least two years, and in most cases for more than five years, after this operation. The study therefore concerns the long-term results of sympathectomy in a selected group of patients with relatively severe digital ischaemia.

Material and Methods

The 43 patients (22 men and 21 women) were treated by upper thoracic sympathectomy in St. Bartholomew's Hospital during 1941-61, and subsequently followed in the peripheral vascular clinic. In over half the patients the indication for operation was the presence of terminal digital necrosis or gangrene; the rest complained of severe ischaemic symptoms, often episodic, without necrosis. Thirty-seven patients were subjected to brachial arteriography, usually carried out by me, and I also personally examined every patient during the periodic follow-up attendances at the clinic. Investigations on all patients included haematology (haemoglobin, white cell count, differential count, and erythrocyte sedimentation rate), serology (Wassermann and Kahn reactions, latex fixation, L.E. cells, antinuclear factor, and cold agglutinins), and biochemistry (serum proteins, electrophoresis, and cryoglobulins). Urinalysis, with microscopy, radiographs of chest, hands, and thoracic inlet, and supine barium swallow were also done.

The operation for sympathetic denervation was performed by the anterior (cervical) route and was usually bilateral. In most patients a T 2/3 sympathectomy of the Telford type was performed, but ganglionectomy was carried out in a few cases. The sympathectomies were performed by several different surgeons. Patients have been excluded from the series when the obstruction of the digital arteries appeared secondary to cervical rib and related lesions, other sources of embolism, cold injury, and congenital vascular malformations in the hand.

Results

The period of follow-up after operation was from 2 to 25 years, but was five years or more in 36 patients (84%). All were thought to have digital artery occlusion at the time

of sympathectomy, usually on arteriographic evidence (34 patients), but in others on clinical evidence of atherosclerosis (6 patients) or overt digital necrosis (3 patients).

For the purpose of this survey the patients are divided into two separate groups.

Group 1 comprises the patients with evidence of digital necrosis or gangrene before sympathectomy (14 men and 9 women). Group 2 comprises the patients with severe digital ischaemia before operation, without evidence of actual necrosis (8 men and 12 women). Several in this group suffered from paronychia and pulp infections, but without permanent loss of tissue.

Clinical Features

Group 1

Operation was performed for recurrent or persistent terminal digital necrosis in 23 patients (14 men and 9 women) (Figs. 1 and 2). The symptoms preceded operation for a variable period of between 2 months and 12 years (see Fig. 5). However, a short history was fairly common, being one year or less in 14 patients and under three months in six. The age of onset

FIG. 1.—Terminal necrosis of thumb and index finger of man aged 48. There is a healed scar on the middle finger. Necrosis of the thumb was a rare finding.

of the necrosis showed wide variation (Table I). Onset at or before the age of 45 was seen in 14 patients. The condition was unilateral in 12 patients, though three later developed necrosis in fingers of the opposite hand. Sometimes a single finger was involved, but more often two or three fingers, and there was a tendency for the distribution to be symmetrical in the two hands (Fig. 3). In no case was the little finger apparently affected. In most cases a small ulcer developed in the apical pulp, close to the nail. It was painful and

* Consultant Surgeon, St. Bartholomew's Hospital, London; Consultant for Peripheral Vascular Disease, Royal National Orthopaedic Hospital, London.

extremely tender, but eventually healed after many weeks, leaving a scar, or sometimes an atrophied digital pulp. Particularly in the patients with collagen disorder there was a tendency for new pulp ulcers to crop up later on other fingers. A history of thrombophlebitis was not obtained in any patient in the series.

FIG. 2.—Photograph of same hand as Fig. 1 seven years after upper thoracic sympathectomy. No further lesions. Note healed scars over digital pulp.

Brachial arteriography was attempted in 20 patients in this group, and was repeated after an interval in four patients. There was unsatisfactory visualization in one patient, but in the remaining 19 the digital arterial circulation was well demonstrated. In all of these segmental blockage of digital arteries was clearly seen, the usual appearance being one of abrupt termination of the column of opaque medium with a tuft of collateral vessels around the unfilled zone and re-establishment of the column in more distal parts of the finger (Fig. 4). The commonest site of blockage was opposite the proximal interphalangeal joint, but lesions sometimes originated more proximally in the metacarpal arteries. Several patients also showed blocks in the deep palmar arch and occasionally in the ulnar artery. The lesions varied in length between about 0.5 cm. and the full length of a digital artery,

TABLE I.—Age at Onset of Ischaemic Symptoms

		Group 1		Group 2	
		Range	Mean	Range	Mean
Men ..	..	29-69	49.3	37-62	50.3
Women ..	..	19-62	42.0	11-58	32.4

FIG. 3.—Photograph of small terminal ulcers in woman aged 52. The middle fingers are symmetrically involved, though healing lesions are present on right index and ring fingers.

but multiple segmental blocks in a single digital artery were not uncommon. Though the fingers with necrosis usually provide the most obvious arteriographic lesions, the rest of the fingers often revealed further filling defects, in spite of absence of ischaemic symptoms. Progression of the arteriographic changes was seen in the four patients in whom the investigation was repeated after an interval of a year or more.

FIG. 4.—Brachial arteriogram of man aged 54 with terminal necrosis of index and ring fingers. Note segmental blocks in these fingers, as well as middle finger, which was clinically normal. Further lesions in palmar arch.

However, there was again no close correlation between the severity and distribution of the clinical lesions and the radiological changes.

Histological material was obtained from amputated fingers in four patients, and at necropsy in a further two. Sections of the digital arteries confirmed the blockage shown in the arteriograms during life. The appearances were those of previous thrombosis with intimal proliferation and a variable degree of replacement fibrosis, often with the presence of multiple recanalized channels. These non-specific changes gave no indication of the nature of any systemic disease, and there was no evidence of any local arteritis in any example examined. Some sections showed infiltration of the periarterial tissues consistent with the local infection and necrosis, which necessitated amputation in these specimens. Electrocardiograms were obtained before sympathectomy in 14 patients, nine of whom revealed ischaemic changes (64%).

Group 2

The 20 patients in group 2 (8 men and 12 women) presented with symptoms of digital ischaemia between 1 and 21 years before operation (see Fig. 6). A long history was common, and in four female patients symptoms started during adolescence. However, the initial age of onset again showed wide variation (Table I). Symptoms before the age of 45 occurred in 13 patients. The presenting symptom was either intermittent digital ischaemia of the "Raynaud's phenomenon" type, or, more often, persistent blueness and coldness of the

affected fingers (acrocyanosis). In most patients the individual fingers were affected to a varying degree, but in a few the ischaemia involved the fingers equally and symmetrically. In most cases the severe arterial insufficiency in the affected fingers could be demonstrated by the reactive hyperaemia test (Catchpole, Jepson, and Kellgren, 1954).

Brachial arteriography was successfully performed in 14 patients in this group, and with inadequate visualization in a further two. The six patients in whom arteriography was omitted or unsatisfactory had either collagen disease or, in one case, a neuropathy with severe digital atrophy; the clinical evidence of organic digital artery disease appeared strong enough to justify their inclusion in this series. The segmental occlusions revealed in the arteriograms were identical with those seen in the patients in group 1, and the distribution of blocks agreed with delay in filling shown by the reactive hyperaemia test. However, the arteriographic changes tended to be more widespread than might be inferred from the distribution of the patient's symptoms.

Histological material examined from the one patient in group 2 who died showed changes in the digital vessels similar to those described in group 1. There were no digital amputations in this group of patients.

Results of Sympathectomy

Group 1

The patients were followed for between 2 and 19 years after sympathectomy (Fig. 5). During this period five patients died between one and three years after operation; the cause of death was coronary thrombosis (two patients), carcinoma of pancreas, miliary tuberculosis, and aplastic anaemia (one each). Since all of these patients were followed long enough for the early result of sympathectomy to be apparent, they are included in Table II.

The digital ischaemia remained completely cured in eight men (57%). One, who underwent unilateral sympathectomy, later developed digital necrosis in the opposite hand but remained free of ischaemia after a further sympathectomy on that side. Four men had no further necrosis but continued

to suffer mild symptoms, usually episodic and precipitated by cold. Finally, two men had persistence or return of digital necrosis during the period of follow-up. Thus, in the 14 male patients of group 1 the condition of 12 (83%) remained improved throughout the period of follow-up. None of the men required amputation of a finger.

FIG. 6.—Duration of presenting symptom and postoperative follow-up in group 2 (digital ischaemia without necrosis).

Only one female patient (11%) remained permanently cured of ischaemic symptoms after operation, while four continued to have mild symptoms without further necrosis. In four women necrosis persisted or returned after sympathectomy; in three of these it was severe enough to demand amputation of one or more fingers. Contralateral sympathectomies were performed in two women who had previously undergone unilateral operations. In the nine women of group 1 5 (56%) remained improved in that they suffered no further necrosis after sympathectomy.

Group 2

The patients were followed for between 3 and 25 years after operation, during which time only one died from ischaemic heart disease. Table II shows the final assessment of the result of sympathectomy upon the digital ischaemia. Five men remained completely cured when reviewed six or more years after operation. However, the remaining three underwent gradual relapse, so that their eventual condition became worse than before operation.

One of the women was completely cured of her symptoms for 25 years after operation. Five women were either uninfluenced or underwent relapse to their preoperative state. In a further six women the final state was worse than before operation. Thus, although five men (63%) were completely relieved by operation, cure was achieved in only one woman

TABLE II.—Final Result after Sympathectomy

Group 1			Group 2		
State at Final Review	M	F	State at Final Review	M	F
Cured	8	1	Cured	5	1
Ischaemia without necrosis	4	4	Same	0	5
Necrosis persists	2	4	Worse	3	6
Total	14	9	Total	8	12

FIG. 5.—Duration of presenting symptom and postoperative follow-up in group 1 (digital ischaemia with necrosis). The diagram indicates state of fingers after operation and final pathological diagnosis.

(8%). The remaining 11 women either relapsed or became finally worse than their original state, and it is doubtful if their sympathectomy served any useful purpose.

Aetiology of Digital Ischaemia

The diagnosis of the underlying condition considered responsible for the digital ischaemia is shown in Table III. The diagnosis was regarded as *atherosclerosis* where apparent thrombosis of the digital arteries was unaccompanied during the period of study by any features of underlying collagen disorder or other generalized medical condition. Atherosclerosis characteristically produced the maximum degree of ischaemia at onset of the occlusion, and later progression was uncommon. However, eight of the men developed evidence of arterial obstruction of the lower limbs during the period of study. The term "acrosclerosis" designates digital vascular disease with scleroderma-like features such as macular telangiectases on the hands or lips, often with oedema or thickening of the skin of the fingers or hand but without any other evidence of systemic involvement. This term seems preferable to the rather cumbersome "primary Raynaud's disease with scleroderma-like features" used in a previous article (Johnston *et al.*, 1965).

TABLE III.—Final Clinical Diagnosis

	Group 1		Group 2	
	M	F	M	F
Atherosclerosis	12	2	7	2
Acrosclerosis	0	5	0	7
Systemic scleroderma	2	2	1	1
Miscellaneous	0	0	0	2
Total	14	9	8	12

A final clinical diagnosis of digital thrombosis due to atherosclerosis was made in 19 men and 4 women. Results of treatment were variable, but all the men in whom clinical cures were recorded fell under this diagnosis. In the 12 women with acrosclerosis results of treatment again varied, though the two clinical cures in women both had this diagnosis. The digital ischaemia before sympathectomy showed a marked tendency to chronicity in these patients. A diagnosis of *systemic scleroderma* was made in three men and three women, and the uniformly poor prognosis of this condition is shown by the ultimate relapse of all of these. However, five showed improvement for between one and six years after sympathectomy, and even the eventual recurrence of digital necrosis did not necessarily indicate that operation had been valueless, since the patients often noticed slight permanent improvement in the grossly impaired circulation of their hands. The diagnoses in the Miscellaneous group in Table III were *rheumatoid arthritis* with arterial occlusion, confirmed arteriographically, and an obscure *neuropathy* with marked symmetrical digital atrophy. Both patients relapsed after sympathectomy.

Discussion

In this series of 43 patients histological examination of the digital arteries was possible in only a few instances. Biopsy of an actual digital artery was avoided because of the risk of increasing the ischaemia, while biopsy of digital skin (Phillips and Burch, 1958) has not been found useful in the few cases of digital artery occlusion investigated in this way. However, clinical observation over a period of years allowed the aetiology to be established with reasonable accuracy. Table III shows the marked difference in the underlying pathology in the two sexes. In 19 of the 22 males the disease in the fingers was thought to be atherosclerosis, whereas this condition was responsible in only four of the 21 women. Conversely, collagen

disorder arose in at least 15 of the women, compared with three men. However, the six examples of systemic sclerosis, exemplifying the more severe form of this disorder, were distributed equally between the two sexes.

The aetiology of the digital disease has been shown to influence the outcome in the individual patient as regards both the general and local manifestations of the disorder (Birnstingl, 1967). For instance, in three of the six patients who died the cause of death was ischaemic heart disease, and all of these had digital atherosclerosis. Similarly, 64% of the patients for whom electrocardiograms were available showed ischaemic heart disease, mostly in those with digital atherosclerosis; and atherosclerotic disease in the lower limbs was present in 30% of the patients with digital atherosclerosis, whereas none was found in relation to the other diagnoses. However, in considering the local manifestations, the underlying condition failed to influence the degree of digital ischaemia in any predictable way, the exception being diffuse scleroderma, which was invariably associated with a poor final result in the fingers. Nevertheless, pathology had important bearings upon the result of sympathectomy.

The arbitrary division into groups 1 and 2 according to presence or absence of digital necrosis did not reflect any difference in the underlying pathology. Necrosis presumably occurred only when severe ischaemia was produced by sudden closure of the corresponding digital arteries. Rapidity of onset appeared to be more important than the extent of the thrombosis, because little correlation was found between the arteriographic changes and clinical severity. This is also supported by the short history of many of the patients with necrosis, which was less than three months in six patients.

A surprising finding was the similarity of arteriographic appearances in patients with differing underlying pathology. This justifies Jepson's (1956) concept of "digital artery occlusion" as a clinical entity, regardless of the precise underlying pathology, since the ischaemia is invariably due to closure at the digital artery level. Nevertheless, when faced with a patient with severe digital ischaemia it is clearly important to investigate the aetiology, and in this respect it is interesting that a diagnosis of thromboangiitis obliterans was not sustained in a single patient, and that this condition, though not uncommon in the feet, is a rare cause of severe ischaemia in the hands.

The term "atherosclerosis" has been used to describe the common lesion found in the digital arteries of men. TK's seemed more appropriate than the alternative "idiopathic digital artery thrombosis," accepting the accumulating evidence for a thrombogenic mechanism for arterial disease and using atherosclerosis in the wide sense in which it was introduced by Marchand (1904) (Lewis and Pickering, 1934; Mitchell and Schwartz, 1965).

It remains to consider the influence of upper thoracic sympathectomy. During the period in which the operations were performed it was my policy to advise sympathectomy in all patients with severe digital ischaemia. Consequently there is no clue to the natural history of such patients when surgical treatment is withheld. It is clear that the final long-term result after sympathectomy is much better in men than in women, whatever the original indication for operation. Thus in the men 57% in group 1 and 63% in group 2 remained completely cured throughout the period of follow-up, whereas in the women the respective percentages were 11 and 8. Partial improvement was evident in a few more patients with digital necrosis, so that 83% of the men and 56% of the women in group 1 did not develop further episodes of necrosis, though they continued to have some degree of ischaemia. The differing results after sympathectomy in the two sexes is mainly explained in the underlying pathological condition. Of the 22 men 19 had atherosclerosis of the digital arteries; most improved after sympathectomy, and more than half were completely cured. It is possible that some would have improved

without operation. Of the 21 women 15 had collagen disorder, which, though varying in tempo in the individual patient, had a tendency towards marked chronicity in the hands. It was also characteristically resistant to sympathectomy, with the proviso that the operation allowed the fingers to remain healed in more than half the patients with actual tissue necrosis.

Until more is known of the prognosis of digital necrosis in the untreated patient it seems reasonable to continue to recommend sympathectomy to all patients of both sexes with trophic changes, bearing in mind that amelioration rather than cure is the best that can be expected in most women. This advice applies whatever the nature of the underlying condition, since, as already mentioned, some permanent improvement can be expected even in severe collagen disorder. In view of the poor prognosis in women without actual necrosis, 11 out of 12 (92%) being uninfluenced or eventually worse, it seems doubtful if the operation should be advised in these circumstances.

Summary

Forty-three patients are reviewed in whom upper thoracic sympathectomy was performed for severe digital ischaemia due to digital artery obstruction, confirmed by arteriography in 34. The extent of digital artery blockage failed to correlate with the severity of the symptoms. The probable underlying pathological conditions at final review was atherosclerosis in 23, acrosclerosis in 12, systemic scleroderma in six, and neuropathy and rheumatoid arthritis in one each.

Actual necrosis of one or more fingers was the presenting symptom in 23 patients and severe episodic ischaemia without

necrosis in 20, but this variation in symptomatology related to rapidity of onset of the thrombosis rather than to the underlying pathology.

The late results of sympathectomy were best in men, about 60% of whom were completely cured of their symptoms. Of the women 56% were cured of necrosis, but milder ischaemic symptoms usually persisted; when sympathectomy was performed in the absence of necrosis, only 8% of women received permanent benefit.

When digital necrosis is present upper thoracic sympathectomy can be expected to confer permanent benefit in rather more than half the patients, even in the presence of collagen disorder. Sympathectomy should not be advised in women when digital ischaemia is unaccompanied by local necrosis.

I would like to thank Professor G. W. Taylor for permission to study a number of patients under his care.

REFERENCES

- Birnstingl, M. (1967). In *Vascular Surgery and Reticuloendothelial System*, edited by G. W. Taylor and J. F. Wilkinson, Chap. 6. London. In press.
- Catchpole, B. N., Jepson, R. P., and Kellgren, J. H. (1954). *Ann. rheum. Dis.*, 13, 302.
- de Takats, G., and Fowler, E. F. (1962). *J. Amer. med. Ass.*, 179, 1.
- Jepson, R. P. (1956). *Circulation*, 14, 1084.
- Johnston, E. N. M., Summerly, R., and Birnstingl, M. (1965). *Brit. med. J.*, 1, 962.
- Lewis, T., and Pickering, G. W. (1934). *Clin. Sci.*, 1, 327.
- Marchand, F. (1904). *Verh. dtsch. Kongr. inn. Med.*, 21, 23.
- Mitchell, J. R. A., and Schwartz, C. J. (1965). *Arterial Disease*. Oxford.
- Phillips, J., and Burch, G. E. (1958). *Amer. J. med. Sci.*, 235, 668.

Total Dose Imferon (Iron-dextran Complex) Infusion Therapy in Severe Hookworm Anaemia

KANTI M. PATEL,* M.B., B.S., M.R.C.P.ED., M.R.C.P.GLASG., D.C.H., D.T.M.&H.
J. A. TULLOCH,† M.C., M.D., M.R.C.P., F.R.C.P.ED.

Brit. med. J., 1967, 2, 605-607

Anaemia is one of the commonest medical problems in Uganda, East Africa. Most cases are of iron-deficiency type, and hookworm infection is an important cause (Meredith and Eyekeze, 1962). A large section of the population of East Africa are infected with hookworm, usually *Necator americanus* (Wilks and Patel, 1967). Anaemia caused by hookworm infection is often very severe. Along with the eradication of the infestation, oral iron is important for satisfactory treatment. Unless treatment is continued conscientiously for several months after the haemoglobin level is restored to normal there is no chance of replenishing the iron reserves, which are necessary to protect against relapse when reinfection with hookworm occurs (Pritchard and Mason, 1964). Reinfection is exceedingly common in Uganda. Continuance of outpatient supervision is difficult to arrange. Many of these patients stop taking oral iron when they leave hospital, and do not return to the outpatient clinic until severe anaemia has recurred. This problem of uncertainty prompted us to investigate the effectiveness of a

single intravenous infusion of iron. The preparation used was iron-dextran complex (Imferon). This was chosen because of its extremely low toxicity, high stability, freedom from ionic iron, and established response in haemoglobin increase (Varde, 1964).

Patients and Methods

Sixty patients were included in the study. Their haemoglobin was 4 g./100 ml. or less, their faeces contained more than 200 worms—that is, 30,000 hookworm ova per gramme of faeces—and there was no other obvious cause for the anaemia. Iron-deficiency anaemia was established in each case by peripheral blood film and bone marrow. All patients were in hospital. Eight additional patients were originally included in the comparative study but were withdrawn because of complicating conditions—for example, cirrhosis of the liver and pulmonary tuberculosis. Forty-five patients were treated with intravenous infusion of Imferon. The amount given was determined on a body-weight and haemoglobin-deficit basis from the table supplied by the manufacturers; the single doses ranged from 1,250 to 3,750 mg. Dilution was with normal saline, and the solution was never stronger than 5% v/v. The first 50 n.l.

* Senior Lecturer in Medicine, Makerere University College Medical School, Kampala, Uganda, E. Africa.

† Formerly Professor of Medicine, Makerere University College Medical School, Kampala, Uganda, East Africa. Now Consultant Physician, Stracathro Hospital, Brechin, Scotland.