Hospital Topics

Non-surgical management of peripheral vascular disease: a review

C A C CLYNE

Summary and conclusions

Although the outlook for a pronounced improvement in the ischaemic limb that cannot be surgically treated remains bleak, cessation of smoking, encouragement of exercise, and the withdrawal of vasoconstricting agents may give some symptomatic relief. There is little evidence that vasodilators or antiplatelet agents have much to offer.

Introduction

Unlike the care in the United States, the mortality from cardiovascular disease is not apparently falling in Britain, so clearly peripheral vascular disease too will remain a problem. The benefits and risks of surgery are now clearly defined,¹ but there will always be patients unsuitable for surgery because of cardiac disease or stroke, and those with extensive vascular disease not amenable to surgical correction. These patients create a therapeutic problem for general practitioner and vascular surgeon alike.

Natural history of peripheral vascular disease

The natural course of peripheral vascular disease is not usually an unremitting path leading to amputation but is more often characterised either by stable intermittent claudication or improvement of symptoms. Nevertheless, complications may be precipitated by an acute embolus or thrombosis of a segment of artery with a patient having acquired an increased walking distance to the onset of pain between the time of general practitioner referral and hospital consultation. This will be due to both clot or embolus resolution and development of collateral blood supply. Clearly then the therapeutic benefit of any regimen must be judged critically against a control group before any pronouncement may be made as to its efficacy.

Effects of smoking

Smoking is the single highest risk factor in the aetiology of peripheral vascular disease,^{3,4} the correlation being higher than

for coronary or cerebral vascular disease, but sadly there seems little public awareness of this fact. There are few data to support the contention that stopping smoking improves peripheral vascular disease, and few patients probably heed the advice (C A C Clyne *et al*, unpublished observations). Nevertheless, some evidence suggests that continuing to smoke leads to an increased risk of amputation⁶ and increased incidence of graft occlusion after surgery,⁷ but most vascular surgeons would agree that giving up smoking may be the only worthwhile conservative measure available.

Smoking may well worsen disease by causing vasoconstriction,⁸ reducing the oxygen carrying capacity of the red cells,⁹ raising blood viscosity¹⁰ by causing polycythaemia¹¹ and increasing serum fibrinogen,¹² and depressing fibrinolysis¹³—all factors that reduce blood flow and increase the tendency to thrombosis.

Effects of exercise

The long-term assessment of the effects of exercise on vascular disease are not yet available, although some benefit is likely. Exercise does improve cardiac efficiency and lower lipid concentrations.¹⁴ In patients with intermittent claudication the results of most studies confirm the benefits of exercise by increasing claudication distance,¹⁵ but this may well not be due to increased blood flow but rather to increased muscle efficiency.¹⁶ Exercise should therefore be encouraged, and supervision in a physiotherapy department may be valuable.

Modification of diet

Patients with peripheral vascular disease often have abnormal lipid patterns,¹⁷ although, as in coronary heart disease, high-density lipoprotein may offer protection, and it may well be that expressing the amount of cholesterol carried in high-density lipoprotein in relative terms provides a better index of vascular risk.¹⁸ What is lacking is evidence that modification of diet provides long-term benefit to a limb, although the achievement of biochemical normality in one study did correlate with evidence of regression of femoral artery atheroma.¹⁹ Until we know better it seems sensible to attempt correction of lipid abnormalities in the younger patient with peripheral vascular disease. The lipid/vascular argument is carefully reviewed elsewhere.²⁰

Alcohol is a well-known peripheral vasodilator—but unfortunately only for those without occluded limb arteries.²¹ It suffers from the same shortcoming as any other vasodilator and does not increase blood flow in diseased limbs. In the longer term, however, there is good evidence to suggest that alcohol may help protect against vascular disease, and even offset the effect of smoking.²²

Department of Surgery, Southampton General Hospital, Southampton

C A C CLYNE, FRCS, FRCS, lecturer in surgery

Use of drugs

If one accepts that Poiseuille's formula ($\text{flow} = (P \times r^4)/(V \times L)$), where P = pressure, r = radius of vessel, V = viscosity, and L = length of vessel; designed for the flow of Newtonian fluids, which blood is not) may have some bearing on limb blood flow, to be effective a drug must possess one of the actions listed in table I. Double-blind trials are imperative, as in most studies the placebo group will increase their distance to claudication, and techniques such as the walking test²³ allow for standard reproducible methods of assessing the state of the disease.

"Vasodilators" either deplete noradrenaline from nerve endings, block the effects of noradrenaline (α -adrenergic blockers), or exert a direct effect on the blood vessel wall.²⁴ Many will increase blood flow at rest in patients with occluded

ischaemic muscle. Beta-adrenergic blockers, however, do reduce peripheral muscle perfusion³¹ and have been reported to exacerbate and even produce claudication.³² There are even sporadic reports of peripheral gangrene due to β -blockade.³³ Symptoms of peripheral vascular disease should be closely monitored in patients taking β -blockers.

Alterations in blood rheology

Much evidence supports the concept of increased blood viscosity in patients with peripheral vascular disease,³⁴ and this is usually due to increased serum fibrinogen.³⁵ Defibrination may be achieved with ancrod³⁶ or clofibrate,³⁷ which may give clinical improvement. Even plasma exchange causing a rapid fall

TABLE I—Drugs for vascular disease—modes of action

Proprietary name	Registered name	Primary "vascular" action	Other effects
Isoxsuprine	Duvadilan	α -adrenergic blockers	β -adrenergic stimulant
Cyclandelate	Defencin		β -adrenergic stimulant
	Cyclospasmol		
Thymoxamine	Cyclobral		
Phenoxybenzamine	Opilon		
Tolazoline	Dibenyline		
Nicotinic acid	Priscol	Direct effects on vessel wall	Effects on lipid metabolism
(and related substances)	Hexopal		
	Bradilan		
Bamethan	Ronicol		
Nicotinic acid	Vasculit	Effects on lipid metabolism	
(and related substances)	Hexopal		
	Bradilan		
	Ronicol		
Vasolastine	Vasolastine	Effects on blood viscosity	Reduces serum fibrinogen
Clofibrate	Atomid-S		
Oxpentifylline	Trental	Effects on muscle metabolism	Antihistamine and labyrinth depressant
Cinnarizine	Stugeron		
Naftidrofuryl	Praxilene		

arteries, but no drug has yet been shown to increase muscle flow during exercise.²⁵ Their value to the patient with claudication must therefore be doubtful, even ignoring arguments about "steal" of blood into more healthy limbs during exercise with a vascular system more amenable to vasodilatation and therefore able to allow a greater increase in blood flow.²⁶ In a review similar to this one in 1952 many vasodilators available today were already in production²⁷ but, despite this, the number of prescriptions and their relative cost continue to increase (table II). Possibly in the painful resting ischaemic limb vasodilators may improve blood flow enough to give clinical amelioration,²⁸ but I am unaware of any satisfactory controlled clinical studies confirming drug-induced increased walking distance in the patient with claudication.

TABLE II—Cost of "top five vasodilators" based on a sample of 1 in 200 prescriptions written by general practitioners and dispensed in chemists' establishments and by appliance contractors

Year:	1976	1977	1978
Cost	£4 182 800	£6 444 700	£8 079 500
No of prescriptions ..	878 700	1 048 700	1 128 600

Alterations of blood pressure

Induced hypertension is not a widely practised method of managing peripheral vascular disease for obvious reasons.²⁹ Angiotensin and steroids have been used with some objective improvement in patients with rest pain, but each drug has severe unwanted effects.³⁰ The importance of maintaining systolic blood pressure to perfuse the peripheries in older people is fraught with pharmacological argument as hypertension is probably maintained by vascular constriction proximal to the

in blood viscosity has been tried,³⁸ but it appears to be of more value in Raynaud's phenomenon.³⁹ Increased viscosity due to paraproteinaemia will occasionally give rise to peripheral vascular symptoms, and these may regress with treatment.⁴⁰

Polycythaemia rubra vera is an occasional cause of peripheral vascular symptoms,⁴¹ but more commonly secondary polycythaemia and pseudopolycythaemia will be found.⁴² Improvement may be expected to accompany a reduced packed cell volume in all these groups using simple dilution techniques⁴³ and phlebotomy, but it is unlikely that reducing the packed cell volume to abnormally low concentrations will offer any satisfactory practical long-term improvement. Many drugs used to treat peripheral vascular disease have been recently shown to decrease blood viscosity, but clinical trials have failed to show any benefit from these agents.⁴⁴ Even the red cell itself appears to be abnormally rigid in peripheral vascular disease⁴⁵ and drugs said to alter this are available,⁴⁶ although evidence of their benefit to the ischaemic limb is not.

The long-term use of anticoagulants in occlusive vascular disease of the leg confers little benefit,⁴⁷ although patients with enlarged arteries may be protected from distal emboli. Similarly, the place of antiplatelet agents, such as aspirin and dipyridamole,⁴⁸ is not yet established, although some encouraging results are available from the use of aspirin to protect the cerebral circulation.⁴⁹

Increasing metabolic efficiency

If it is possible it would seem sensible to make more efficient use of the blood available to an exercising ischaemic limb in which an absolute increase in blood flow may be impossible. The "untrained" ischaemic limb may not be functioning at maximum metabolic capability,¹⁶ and an agent aimed at improving metabolic efficiency, naftidrofuryl (Praxilene), may offer some help to the older patient with claudication.^{50 51}

More invasive techniques

Phenol injection of the lumbar sympathetic chain, if successful, should offer results comparable with surgical sympathectomy⁵² without the hazards of general anaesthesia. This procedure is available in most district hospitals and requires little in the way of equipment, although radiological screening may improve accuracy.

Percutaneous transluminal dilatation of arteries fills most surgeons with horror, but favourable reports are emerging which suggest that peripheral arteries⁵³ (and indeed coronary arteries⁵⁴) may be effectively dilated via a transfemoral route under local anaesthetic. Better results without complications must be achieved than those reported by workers using the original Dotter technique⁵⁵ before this could become an accepted procedure.

Spinal cord stimulation by electrodes implanted into the epidural space may relieve limb pain and improve muscle tone in several diseases.⁵⁶ Some reports of its possible role in the management of symptoms from an ischaemic limb exist,^{57 58} and these are now being evaluated in a proper clinical and scientific background.⁵⁹

Finally, some believe help may soon be to hand with the discovery of prostacyclin and its analogues.⁶⁰ These agents appear to influence intravascular thrombosis through inhibition of platelet aggregation by stimulation of adenylate-cyclase leading to an increased concentration of cyclic 3'5' adenosine monophosphate in the platelets. They might offer short-term help in the acutely ischaemic limb⁶¹ but, of more importance, they could improve our ability to prevent vascular disease through a better understanding of blood vessel pathophysiology.

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Reading for Pleasure

O Absalom

DOUGLAS HUBBLE

If we put aside the Oedipal hypothesis the conflicts between sons and their fathers are commonly caused by the distance between maturity and adolescence, authority and revolt, established convention and new mores. The traditional battlegrounds are sexual, vocational, financial, and religious. Hundreds of autobiographies have been written by suffering sons when they have escaped from paternal control.

James Boswell's diaries, for example, are filled with the accounts of the contests between himself and Lord Auchinleck, which were conducted on all four fronts. He hated the law (his father was a judge) and wished to join the Army. He was sexually promiscuous. For a time he became a Roman Catholic; Auchinleck was an orthodox Presbyterian who extolled Cromwell to Dr Johnson as the man "who taught kings that they had a lith in their necks." James was a spendthrift who begged continually for additional funds. Their conflicts were exacerbated by profound differences in character and temperament. James was volatile, friendly, idle, and indiscreet. His father was rigid, stern, industrious, and close. "James, Jamie," protested the outraged Auchinleck, "if ye'd shat your breeches ye'd tell the world." Auchinleck made a second marriage and there was an unpleasant threat of what Samuel Butler was later to describe in *The Way of All Flesh* as "will-shaking."

Few daughters seem to have found it necessary to get their fathers out of their systems by writing a book about them. I can recall only two. Dame Daphne du Maurier wrote *Gerald* (actor-manager, 1878-1934), and Sarah Campion wrote *Father* (G G Coulton, Cambridge ecclesiastical historian, 1853-1947). Both authors were novelists and their recollections were affectionate, honest, and merciless. Let no father forget that there may be a cherished female child in the family circle taking invisible notes.

Father and son

Hostilities engendered solely by religious differences are now outmoded, but in *Father and Son* Edmund Gosse related a nine-

teenth century example with consummate skill. He was born in 1849, the only child of middle-aged parents who were Plymouth Brethren of the strictest sect. They found in this esoteric, evangelical religion, and in the constant study of the Bible—with a lively expectation of the Second Coming when the redeemed would "meet their Lord in the air"—their predominating interest. *Father*, Philip Henry Gosse, FRS, was a distinguished zoologist and at his death the *Son* wrote 4½ columns about him in the *Dictionary of National Biography*, giving only two lines to the matters that had been the subject of his famous book, first published in 1907—16 years after his father's death. Philip Gosse was profoundly disquieted when, in 1856, Darwin began the essay that was to become *The Origin of Species*. After earnest consultation with friends of like mind and prayerful discussion with his wife, who was then suffering from her final illness, he decided to write a book entitled *Omphalos* (1857) in which he argued that the geological evidence substantiated the account of creation as described in *Genesis*. None of his scientific friends supported him and he was publicly derided for holding the belief that God had put the fossils in the rocks to test the faith of geologists.

Father and son (then aged 8) lived together at Marychurch in south Devon. Both of them were engaged in active biological research on the beaches. Before he was 10 years old, Edmund had added a new genus to British fauna, *phellia microcincta*, the walled corklet. His spiritual progress was equally dramatic. His father, who was the leader of the small local congregation of Brethren, persuaded the "saints," as they dubbed themselves, that Edmund on his tenth birthday should "take up his cross" in public baptism by immersion, a ritual usually permitted only to adults. The faithful came from all over south Devon to watch so unique a ceremony. Edmund's regeneration may not have been complete for he was afterwards seen to put out his tongue at other boys not yet considered worthy to "break bread at the Lord's table."

A little later his father told him, somewhat nervously, that he was to have a new mother. "Papa," he asked, "is she one of the Lord's children and has she taken up her cross in baptism?" Philip Gosse had to admit that she had not yet been baptised. The story, told with living restraint, irony, and humour, moves on to its inevitable climax. When Edmund was 16, Charles Kingsley obtained for him an appointment at the British Museum. He was pursued, almost daily, by long, closely argued theological letters from his father: "When I left you in

Thirtover, Cold Ash, Newbury, Berkshire RG16 9JE

SIR DOUGLAS HUBBLE, MD, FRCP, formerly professor of paediatrics and child health and dean of the medical faculty, University of Birmingham