of hypercoagulation even in patients with a relatively slender family history. Plasma or serum samples may be conveniently tested by immunodiffusion techniques, though there may be false-negative results unless a clot inhibition assay is used as well. It is reasonable to start prophylactic warfarin anticoagulation of the clinically affected. The use of heparin is to be avoided as its main effect follows binding to the antithrombin III globulin.[1] The treatment of the asymptomatic individual is undecided. Judgment can be based on the presence of further risk factors, including age, obesity, varicose veins, high oestrogen concentrations, and hypertriglyceridaemia.

The incidence of antithrombin deficiency in Norway and Massachusetts has been estimated to be about 1 in 2000.[5] In Britain several families have been recognised, though few reported, but many more probably remain to be discovered.

We thank Dr P A Harrison and Dr H S Marwick for their help in tracing and obtaining samples from this family.

[1] Lane, J L, and Biggs, R, in *Recent Advances in Blood Coagulation*, ed L Poller, 2nd edn, p 123. London, Churchill Livingstone, 1976.
[2] Filip, D J, Eckstein, J D, and Veltkamp, J J, *American Journal of Haematology*, 1976, **2**, 347.
[3] Carvalho, A, and Ellman, L, *American Journal of Medicine*, 1974, **61**, 179.
[4] Lewis, B, *The Hyperlipidaemias*, p 239. Oxford, Blackwell, 1976.
[5] Rosenberg, R D, *New England Journal of Medicine*, 1975, **292**, 146.

(*Accepted 25 November 1977*)

East Birmingham Hospital, Birmingham B9 5ST
O H B GYDE, MB, MRCPATH, consultant haematologist
M D MIDDLETON, MSC, FRCS, consultant surgeon
G R VAUGHAN, FIMLS, technician
D J FLETCHER, FIMLS, senior chief technician

Naftidrofuryl for intermittent claudication: a double-blind controlled trial

Intermittent claudication is the commonest symptom of an increasingly common disorder: obliterative arterial disease affecting the legs. Hitherto, despite the wide pharmaceutical range offered, there has been little medical treatment of proved value to prescribe and, in particular, vasodilator drugs have proved disappointing. This paper describes a double-blind controlled trial of naftidrofuryl (Praxilene), a new drug that is believed to facilitate oxygen exchange and enhance metabolism in ischaemic tissues.

Patients, methods, and results

Consecutive patients attending a peripheral vascular clinic with stable claudication were included. Once informed consent had been obtained the patient was issued with capsules in a coded container, maintaining a double-blind design. The treatment group received naftidrofuryl 100 mg thrice daily for three months; the controls received an inert placebo capsule of identical appearance. Assessment was based both on subjective and objective criteria. The patient was asked to take regular exercise and to note any improvement or deterioration. No specific instructions on smoking or diet were given during the period of observation. Clinical severity was defined according to the reported onset of claudication at normal walking pace on the level: less than 100 yards—severe; 100-200 yards—moderate; more than 200 yards—mild. A standard exercise test was performed before and one month and three months after starting treatment. Both legs were tested simultaneously by Doppler ultrasound ankle pressure ratios and gastrocnemius ^{99}mTc clearance.[1-3]

One patient who failed to attend after initial assessment was excluded. Fifty patients (25 on naftidrofuryl and 25 controls) were included. One failed to attend for the final test but was included for analysis at one month. The groups were similar in age and sex distribution. The initial severity of disease, judged clinically, showed some difference between the two groups. Among the naftidrofuryl-treated patients 15 had mild, three had moderate, and seven had severe disease. The corresponding numbers in the control group were 9, 6, and 10. Nevertheless, the level of initial clinical severity had no appreciable effect on subsequent changes in the levels of other variables. Most patients in both groups reported improvement, with a similar pattern of response in each group (see table). Few patients showed a change in clinical severity: seven improved (two on naftidrofuryl, five controls) and two showed an increase in clinical severity (one on naftidrofuryl, one control). The following variables were examined in both legs: the onset of claudication on the treadmill, the stopping time, the resting ultrasound pressure index, the post-exercise fall in pressure, and the ^{99}mTc clearance before, during, and after exercise. These measurements were examined in both legs. There were no statistically significant differences (at 5% level) between the treatment and control groups (Wilcoxon's rank sum test). No serious side effects were reported. Six patients treated with naftidrofuryl reported symptoms during treatment: vertigo (in two cases), nausea (two), and slight insomnia (two). One control reported epigastric pain, one indigestion, one constipation, and one headache with nausea.

Subjective response in the two groups

	Worse	No change	Slight improvement	Improvement
Naftidrofuryl ..	2	7	3	13
Control	2	9	1	13

Comment

The tendency for symptoms of claudication to improve during a period of observation is well known to those interested in vascular disease and probably accounts for the gross overprescribing of vasodilator or "vasoactive" drugs. This improvement occurred despite the fact that patients with apparently stable claudication were studied and that specific instructions on diet and smoking were withheld. In effect, by observing their own symptoms regularly, the patients were undertaking a programme of exercise similar to that commonly recommended for the condition.

We have been unable to show a benefit in our patients with claudication from oral naftidrofuryl. The administration of naftidrofuryl in more advanced vascular disease and by alternative routes may have different effects and requires separate study.

We are grateful for the support of Lipha UK Ltd, who also provided supplies of naftidrofuryl (Praxilene). We thank Dr Lucy Ward, Dr Margaret Bateman, and Dr John Hoyle who helped with the study.

[1] Cutajar, C L, Brown, N T C, Marston, A, *British Journal of Surgery*, 1971, **5**, 532.
[2] Smith, R C, Ferrington, C M, and Ruckley, C V, *Vasa*. In press.
[3] Yao, S T, *British Journal of Surgery*, 1970, **57**, 761.

(*Accepted 10 August 1977*)

Western General Hospital, Edinburgh EH4 2XU
C V RUCKLEY, CHM, FRCSED, consultant surgeon
M J CALLAM, MB, CHB, senior house officer, general surgical unit
C M FERRINGTON, BSC, technician, department of medical physics

Medical Computing and Statistics Group, University of Edinburgh, Edinburgh
R J PRESCOTT, MSC, PHD, lecturer

Urinary incontinence caused by prazosin

The antihypertensive effect of prazosin is thought to result primarily from arteriolar smooth muscle relaxation and consequent peripheral vasodilatation.[1] Soon after its introduction reports[2] appeared of collapse due to postural hypotension ("first dose phenomenon"), suggesting an effect on the sympathetic nervous system. Recent experimental data favour the hypothesis that prazosin interferes with α-adrenoceptor function at the postsynaptic level.[3] Our patient furnishes a new clinical argument for this hypothesis.

Case report

A 58-year-old woman was referred because of hypertension (200/118 mm Hg). She had experienced repeated urinary tract infections after a pyelitis