

Over the ensuing seven months she had three more clinical relapses, each accompanied by reappearance in the stools of either the organism or its cytotoxin, or both. Each improvement after vancomycin (eight to 14-day-courses) was accompanied by disappearance of the organism. At one point she was given cholestyramine, but she was unable to tolerate it. Her illness was punctuated by malnutrition and episodes of heart failure. She was given no other antibiotics. After the sixth relapse maintenance treatment with oral vancomycin 125 mg eight-hourly was begun. With this regimen diarrhoea was controlled and stools over the next 10 weeks remained negative for *C difficile* and its cytotoxin. There was no adverse reaction to vancomycin throughout.

Comment

C difficile as the sole factor in the pathogenesis of pseudomembranous colitis has been questioned.⁴ Man can harbour this organism and its cytotoxin without ill effects.^{1,5} Moreover, ischaemia on the basis of capillary microthrombosis may be important in producing the mucosal necrosis seen in this condition.^{2,3} Pseudomembranous colitis is more common among patients with underlying cardiovascular diseases. In this case pseudomembranous colitis was associated with faecal presence of *C difficile* in a patient with severe chronic bowel ischaemia. She had not received antibiotics. The relapses after adequate courses of vancomycin point strongly to the role of ischaemia, which may encourage recolonisation or repopulation of *C difficile*. The patient responded well clinically to each course of vancomycin, so that development of resistant strains is unlikely.

Antibiotics should be used with caution in patients with ischaemic bowel disease. In patients presenting with the disease stools should be tested for *C difficile*. When patients with pseudomembranous colitis relapse after adequate treatment an underlying ischaemic process should be considered. As pseudomembranous colitis may be contagious patients with ischaemic bowel disease might warrant protective isolation. Finally, in this patient a small maintenance dose of vancomycin appeared to be effective and safe in preventing relapses.

¹ Larson HE, Price AB, Honour P, Barriello SP. Clostridium difficile and the aetiology of pseudomembranous colitis. *Lancet* 1978;i:1063-6.

² Bogomoletz WV. Fibrin thrombi, a cause of clindamycin-associated colitis. *Gut* 1976;17:483-7.

³ Price AB, Davies DR. Pseudomembranous colitis. *J Clin Pathol* 1977;30:1-12.

⁴ Lishman AH, Al-Jumalai IJ, Record CO. Spectrum of antibiotic associated diarrhoea. *Gut* 1981;22:34-7.

⁵ Rieta PJ, Sauterus KW, Zanen HC. Clostridial toxin in faeces of healthy infants. *Lancet* 1978;ii:319.

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Two-, six-, and 12-minute walking tests in respiratory disease

The 12-minute walking test¹ is a useful and reproducible^{1,2} measure of exercise tolerance. It provides a simple, practical guide to everyday disability and does not require expensive apparatus. Nevertheless, it is both time consuming for the investigator and exhausting for the patient. We therefore explored the possibility of using walking tests of shorter duration to assess exercise tolerance.

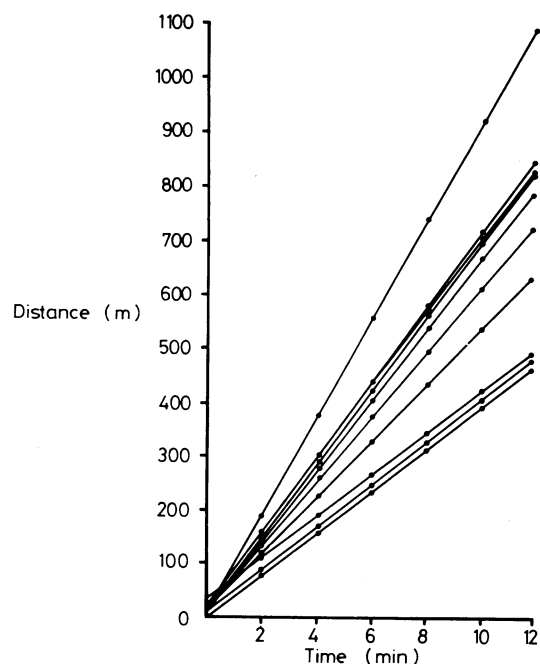
Patients, methods, and results

Walking tests were conducted as described by McGavin *et al.*¹ but the timing (at two, six, and 10 minutes) and the wording of encouragement were standardised. All patients performed two practice 12-minute tests before entry into the first two studies.

Study 1. Pacing during 12-minute test—Ten patients of mean age 61 (\pm SD 11) years with limited exercise tolerance owing to stable chronic airflow obstruction were studied. Their 12-minute walking distance ranged from 400 to 1100 m. The test was performed on five occasions at four-week intervals, always at the same time of day. The distance covered at two-minute intervals throughout the test was noted. Patients generally walked further during the first two minutes of the test (figure) than during any

subsequent two-minute period, when they covered remarkably constant distances (mean correlation coefficient=1.000, range 0.996 to 1.000, $n=50$).

Study 2. Comparison of two-, six-, and 12-minute tests—Thirty patients of mean age 61 (\pm 12) years with stable chronic respiratory disability owing to various diseases were studied (forced expiratory volume in one second = 1.28 ± 0.66 l, forced vital capacity = 2.29 ± 0.78 l). Twelve-minute walking distances ranged from 345 to 1215 m. Each patient performed one two-minute, one six-minute, and one 12-minute test in a randomised cross-over design. The walks were made on three consecutive days but at the same time of day. The mean distances walked during the tests were 149 ± 35 m, 413 ± 107 m, and 774 ± 229 m, respectively. The three tests were highly correlated: six-minute *v* 12-minute, $r=0.955$; two-minute *v* 12-minute, $r=0.864$; and two-minute *v* six-minute, $r=0.892$ ($n=30$). The linear regression equations were: 12-minute distance = 2.04 (six-minute distance)



Distance walked during 12-minute walk test, measured at two-minute intervals. Each line represents mean of five walks in a particular patient.

— 67.7 m; 12-minute distance = 5.70 (two-minute distance) — 73.3 m; six-minute distance = 2.76 (two-minute distance) + 3.12 m. The variance ($=100$ SD/mean) for the two-minute, six-minute, and 12-minute tests respectively was 23.4, 26.0, and 29.6 m.

Study 3. Reproducibility of two-minute test—Thirteen patients of mean age 51 ± 14 years with a range of respiratory disease (forced expiratory volume in one second 0.98 ± 0.25 l, forced vital capacity 2.24 ± 1.02 l) and exercise tolerance (two-minute walking distance 54–215 m) were studied. No patient had performed a walking test previously. Patients performed four two-minute tests, with at least an hour in between walks; mean distances of consecutive walks were 137 ± 46 m, 141 ± 43 m, 146 ± 41 m, and 147 ± 40 m.

Comment

The 12-minute walking test was based on a 12-minute running test described by Cooper³ as a guide to physical fitness in healthy young men. We thought that in patients with severe disability a test of shorter duration might be adequate. Our first study, of the 12-minute test, showed that, after a slight initial burst of speed, patients walked at constant speed, suggesting that shorter tests would be as good. Subjects showed a remarkable ability to pace themselves during this test.

The high correlation coefficients between the two-minute, six-minute, and 12-minute tests indicated that they were similar measures of exercise tolerance. The variance of the 12-minute test was slightly greater than that of the six-minute test, which was slightly greater than that of the two-minute test—that is, the longer the patients walked the greater was the spread of results. Although this might reflect greater random variation, it probably indicates that the longer tests are more discriminating. In practice the differences were not large.

The 12-minute distance is highly reproducible.³ The two-minute distance is equally reproducible and similarly requires two practice

walks because of the initial training effect. The time chosen to assess exercise tolerance by walking tests is not critical. Shorter times are easier for both patient and investigator and are as reproducible but discriminate slightly less well and have less of a training role. The six-minute walk may represent a sensible compromise.

- ¹ McGavin CR, Gupta SP, McHardy GJR. Twelve minute walking test for assessing disability in chronic bronchitis. *Br Med J* 1976;i:822-3.
- ² Mungall IPF, Hainsworth R. Assessment of respiratory function in patients with chronic airways disease. *Thorax* 1979;34:254-8.
- ³ Cooper KH. A means of assessing maximal oxygen intake. *JAMA* 1968; 203:201-4.

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Effect of high-fibre diet on haemostatic variables in diabetes

Raised values of factor VIIc, factor VIIIc, and fibrinogen are associated with increased cardiovascular mortality.¹ Treatment of hyperlipidaemia with a fat-modified diet causes substantial falls in plasma factors VIIc, VIIIc, and Xc, and an increase in fibrinolytic activity.² Patients with diabetes have a greatly increased risk of cardiovascular morbidity and mortality; values of factors VIIc and fibrinogen are significantly higher in diabetics than in non-diabetics, especially those with retinopathy or proteinuria.³ We report a randomised crossover study of the effects of dietary treatment of diabetes on haemostatic function.

Patients, methods, and results

We studied 11 non-insulin dependent and 10 insulin-dependent patients with diabetes mellitus. Each group was randomised to the control or trial diet. The control low-fibre diet was a traditional diabetic diet, giving 40% of energy as carbohydrate and containing not more than 20 g/day of fibre. In the trial diet carbohydrate provided 60% of total energy, and the mean fibre content was 95 g/day,⁴ mainly from leguminous vegetables. The two diets were isocaloric.

After six weeks the patients were admitted to hospital for 24 hours to assess diabetic control. Two samples of blood were taken for estimating plasma clotting factors. Patients were discharged taking the alternative diet to return six weeks later for a second admission and blood sampling. Fibrinogen concentrations were measured at once. Plasma aliquots were stored in liquid nitrogen for assays of biological or clotting activity of factors VIIc, VIIIc, and Xc. Factor VIII-related antigen (VIIIaG) was also measured. The same standard was used throughout. Full details of clinical and laboratory methods are given elsewhere.^{1,4} The results were assessed by analysis

Mean values of clotting factors in non-insulin-dependent and insulin-dependent diabetics after high-fibre (trial) and low-fibre (control) diets for six weeks. Results pooled for each period

	Factor VIIc (%)	Factor VIIIc (%)	Factor VIIIaG (%)	Factor Xc (%)	Fibrinogen (g/l)
Non-insulin dependent					
High fibre	92.7	87.4	40.3	82.7	3.56
Low fibre	115.4	82.3	48.9	95.3	3.57
Change	-22.7**	5.1	-8.6	-12.6**	-0.01
SE of change	6.21	3.26	2.42	3.56	0.12
Insulin dependent					
High fibre	110.0	85.2	65.8	69.9	3.09
Low fibre	108.9	83.2	76.4	76.8	3.25
Change	1.1	2.0	-10.6*	-6.9	-0.16
SE of change	11.58	12.86	4.73	4.65	0.26

Clotting factor values expressed as percentage of one standard; not directly comparable with values in other reports on Northwick Park Heart Study based on other standards.

* $p < 0.05$.

** $p < 0.01$.

of variance for dietary effects, for any effects of order of treatment, and for sex differences in response to treatment.

The main findings were based on the replicates at the end of each six-week period from all the patients, according to whether they were on the high-fibre or low-fibre diet. The effect of the high-fibre diet on factor VIIc in the non-insulin-dependent group was a fall of over 20%. (The fall was more pronounced in the five men, in whom it was about 30%.) The high-fibre diet also caused a significant fall in factor Xc in the non-insulin-dependent group, though in this case there was no difference between the sexes. There were no changes in the non-insulin-dependent group in factor VIIIc or fibrinogen. In the insulin-dependent group, the only significant effect attributable to the high-fibre diet was a fall in factor VIIIaG. Diabetic control improved significantly on the high-fibre diet in both groups.⁴

Comment

The results show that some plasma clotting factor values can be reduced by diet alone. Since most patients had previously had a low-fibre intake, the changes can reasonably be described as decreases due to the high-fibre rather than increases due to the low-fibre content. The effects of the high-fibre diet on factors VIIc and Xc in the non-insulin-dependent group were similar to changes seen after the dietary treatment of hyperlipidaemia.² In some circumstances, therefore, dietary modifications may exert clinical benefits partly through their effects on clotting factor values. There is other evidence⁵ for this possibility. The lack of any effect of high-fibre on factors VIIc and Xc in the insulin-dependent group may be due to the nature of insulin-dependent diabetes or to an effect of exogenous insulin.

This study and the study of men with hyperlipidaemia² were both in small numbers of patients. There is a strong case for larger studies on the dietary control of clotting factor values and of the extent to which any effects of diet on the incidence of ischaemic heart disease are mediated through haemostatic function.

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² Elkeles RS, Chakrabarti R, Vickers M, Stirling Y, Meade TW. Effect of treatment of hyperlipidaemia on haemostatic variables. *Br Med J* 1980;281:973-4.

³ Fuller JH, Keen H, Jarrett RJ, *et al.* Haemostatic variables associated with diabetes and its complications. *Br Med J* 1979;ii:964-6.

⁴ Simpson HCR, Lousley S, Geekie M, *et al.* A high carbohydrate leguminous fibre diet improves all aspects of diabetic control. *Lancet* 1981;ii:1-5.

⁵ Meade TW. Diet, haemostatic function and ischaemic heart disease. In: Turner MR. *Nutrition and health*. Lancaster: MTP Press, 1982.

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Correction

Smoking habits and inflammatory bowel disease: effect on nutrition

An error occurred in this paper by Dr A D Harries and others (17 April, p 1161). In the table the heading "Mid-arm circumference" should have read "Mid-arm muscle circumference."