

## BRAN, HYPERTRIGLYCERIDAEMIA AND URATE CLEARANCE

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Eight subjects having raised triglyceride levels associated with conditions such as diabetes, hyperuricaemia, obesity and hypothyroidism were given 50 g of bran per day to determine the effect of increasing dietary fibre on triglyceride and purine metabolism. The study was continued for two months. No significant effect was noted on the serum cholesterol or triglyceride level. There was a significant ( $P < 0.0125$ ) increase in the urate clearance during the initial two weeks of bran treatment, but serum uric acid levels did not alter.

ATHEROMA is still the major cause of mortality and morbidity in the Western world, and differences in the prevalence of atheroma between developed and underdeveloped countries have led to the suggestion that dietary factors may play a major aetiological role in the development of arterial disease. Interest has recently centred on the possible role of dietary fibre intake in the pathogenesis of atheroma.

Dietary fibre is a mixture of lignin, cellulose, chitin and other undigestible residues which pass down the gastrointestinal tract without being absorbed. An increased intake of dietary fibre in the form of whole-wheat bran has been recommended for the treatment of colonic disorders such as constipation and diverticular disease.<sup>1,2</sup> Pomare and Heaton<sup>3</sup> have shown that bran reduces the bacterial degradation of bile salts in the colon and it may increase colonic transit times, although, as Eastwood *et alii*<sup>4</sup> have pointed out, these results are difficult to interpret because of the variability of this parameter.

There have been several papers suggesting that dietary roughage may play a significant role in lipid metabolism. Moore<sup>5</sup> has shown that atheromatous degeneration in rabbits fed an athenogenic diet is reduced by the presence of dietary roughage. Recently Heaton and Pomare<sup>6</sup> showed a significant lowering of serum triglyceride and plasma calcium levels in both normal volunteers and patients with gallbladder disease when unprocessed wheat bran was added to their diet.

Connell *et alii*<sup>7</sup> have failed to demonstrate any effect of bran on cholesterol or triglyceride levels in a group of normal medical students, and we have recently reported preliminary results of the effect of bran on plasma lipid levels in patients with Type IV hypertriglyceridaemia.<sup>8</sup> In this study we were unable to show any effect of 12 weeks of bran therapy on plasma lipid levels of these patients and were also unable to show any alteration in the handling of intravenously administered triglyceride. In this paper we would like to compare the results we obtained in the patients with a primary lipid disorder with those obtained in a similar study of patients with triglyceride levels raised owing to other conditions (obesity, diabetes, hyperuricaemia

and hypothyroidism). We also took the opportunity to look at the effect of dietary fibre on serum calcium levels and on urate clearances in a number of these patients.

### PATIENTS AND METHODS

Nine male patients were selected from those attending a lipoprotein clinic (seven) and those attending a rheumatology clinic with gout (two). The patients attending the rheumatology clinic were not hyperuricaemic at the time of the study, as they were controlled on hypouricaemic therapy. No alteration was made in the drug regime of these patients during the period of study. The aim of the study was explained to them, and consent for the administration of bran and for the studies to be performed was obtained in every case. Patients were enthusiastic about participation in the trial, and we had no evidence of default. Patients were seen in the fasting state, and lipoprotein typing was performed initially on three separate occasions by full beta qualification. Serum calcium levels and 24-hour urate clearances were measured in a number of the cases. Unprocessed wheat bran in a dose of 50 g/day in two divided doses was then added to their normal dietary regime. Patients were weighed before entering the study and were then reviewed after intervals of two and eight weeks. Serum calcium levels, serum urate levels and urate clearances were measured in seven patients over the initial two weeks of the study. One patient was withdrawn from the trial because of an inability to tolerate the bran.

Eight patients completed the trial and statistical analysis of results was carried out by means of "Student's" *t* test for paired values.

TABLE 1  
Cholesterol and Triglyceride Levels of Eight Patients with Secondary Hypertriglyceridaemia During Bran Therapy

Stage of Trial	Serum Cholesterol Level (mmol/l.)	Serum Triglyceride Level (mmol/l.)
Before introduction of bran .. ..	6.5 ± 1	2.2 ± .9
After two weeks of bran therapy .. ..	6.5 ± .9	2.3 ± .9
After two months of bran therapy .. ..	6.6 ± 1.0	2.3 ± .9

### RESULTS

The eight patients who completed the trial were aged  $52 \pm 11$  years. Two suffered from hypertriglyceridaemia associated with hypothyroidism, two had obesity, two had gout and two had diabetes.

Table 1 summarizes the biochemical results of the study and shows that we were unable to demonstrate any effect of bran on the biochemical parameters measured except for urate clearance, which increased significantly in the patients in whom this parameter was studied (Table 2).

There was no change in the weights of the patients over the study period, and there was no change in the serum cholesterol or triglyceride level.

As seen in Table 2, there was a significant increase in urate clearance during the initial two weeks of the study, despite the fact that the serum uric acid level did not change. Urate clearances were still elevated in three patients who had this parameter measured after the full two month period of bran therapy.

TABLE 2

Uric Acid, Urate Clearance and Serum Calcium Levels in Seven Patients Before and After Two Weeks of Bran Therapy

Stage of Trial	Serum Calcium Level (mmol/l.)	Serum Uric Acid Level (μmol/l.)	Urate Clearance (ml/min.)
Before introduction of bran .. .. .	2.4 ± 0.13	406 ± 83	4.9 ± 1.5
After two weeks of bran therapy .. .. .	2.4 ± 0.14	390 ± 63	8.6 ± 2.7

### DISCUSSION

There have been conflicting reports on the effect of bran on blood lipid levels, but it is often difficult to compare the results, as different types of dietary fibre are often used.

We used quite large amounts of dietary fibre in this study and this was sufficient to increase the bulk and frequency of the stool in all the patients studied. If intestinal transit time and stool bulk are significant factors in the metabolism of lipids, then we would expect to have demonstrated a change in the blood lipid levels during the period of the study.

The results show clearly that bran taken in a dose of 50 g/day for eight weeks does not alter serum cholesterol or triglyceride levels in patients with secondary hypertriglyceridaemia. These results are in accord with those reported previously by ourselves<sup>5</sup> in patients with primary Type IV hypertriglyceridaemia, and in normal volunteers by Connell *et alii*.<sup>7</sup> There have been several reports of the effect of dietary roughage on animal models of atheroma<sup>5</sup> and in humans,<sup>9, 6</sup> but, as was mentioned pre-

viously, comparison of such studies is difficult because of variation in the type of dietary fibre administered.

The increase in the urate clearance in the absence of a change in the serum uric acid level was interesting and is difficult to explain. Sorensen<sup>10</sup> has shown that alimentary degradation of uric acid by intestinal bacterial uricases accounts for about one-third of the total daily turnover of uric acid. A marked decrease in degradation has been observed when bacteriostasis is produced by broad-spectrum antibiotics.<sup>11</sup> It may well be that bran alters the *milieu intérieur* of the gut to such a degree that a large proportion of the uric acid normally excreted by the gut is handled by the kidney. This would explain the increase in urate clearance observed in these patients.

This study has failed to demonstrate any effect of bran on blood lipid levels in patients with hypertriglyceridaemia, although there is evidence that bran has significantly altered urate clearance, and we are at present investigating this aspect in more detail.

### REFERENCES

- 1 AVERY JONES, F., and GOODING, E. W. (eds.), *Management of Constipation*, Blackwell Scientific, London, 1972: 38.
- 2 PAINTER, N. S., ALMEIDA, A. Z., and COLEBOURNE, K. W., Unprocessed bran on treatment of diverticular disease of the colon, *Brit. med. J.*, 1972, 2: 137.
- 3 POMARE, E. W., and HEATON, K. W., Alterations of bile salt metabolism by dietary fibre (bran), *Brit. med. J.*, 1973, 4: 262.
- 4 EASTWOOD, M. A., FISHER, N., GREENWOOD, C. T., and HUTCHINSON, J. B., Perspectives on the bran hypothesis, *Lancet*, 1974, 1: 1029.
- 5 MOORE, J. H., The effect of the type of roughage in the diet on plasma cholesterol levels and aortic atherosclerosis in rabbits, *Brit. J. Nutr.*, 1967, 21: 207.
- 6 HEATON, K. W., and POMARE, E. W., Effect of bran on blood lipids and calcium, *Lancet*, 1974, 1: 49.
- 7 CONNELL, A. M., SMITH, C. L., and SOMSEL, M., Absence of effect of bran on blood lipids, *Lancet*, 1975, 1: 496.
- 8 BREMNER, W. F., THIRD, J. L. H. C., LAWRIE, T. D. V., and BROOKS, P. M., Bran in primary hypertriglyceridaemia. A failure of response, *Brit. med. J.*, 1975, 3: 574.
- 9 BEERSOHN, I., WALKER, A. R. D., and HIGGINSON, J., Coronary heart disease and dietary fat, *S. Afr. med. J.*, 1956, 30: 411.
- 10 SORENSEN, L. B., The elimination of uric acid in man studied by means of C<sub>14</sub> labelled uric acid uricolysis, *Scand. J. clin. Lab. Invest.*, 1960, 12, Suppl. 54: 1.
- 11 SORENSEN, L. B., Recent advances in study of uric acid metabolism and gout, *Postgrad. Med.*, 1965, 37: 659.