The Lancet · Saturday 10 March 1979

SYMPTOMLESS DIVERTICULAR DISEASE AND INTAKE OF DIETARY FIBRE

J. S. S. GEAR
P. FURSDON
D. J. NOLAN
A. WARE
J. I. MANN
A. J. M. BRODRIBB
M. P. VESSEY

Departments of Social and Community Medicine and Radiology, University of Oxford and Radcliffe Infirmary, Oxford

Summary A study is reported in which the prevalence of symptomless diverticular disease of the colon is related to the consumption of dietary fibre in vegetarians and non-vegetarians. Vegetarians had a significantly higher mean fibre intake (41·5 g/day) than non-vegetarians (21·4 g/day). Diverticular disease was commoner in non-vegetarians (33%) than in vegetarians (12%). Comparison of subjects with and without diverticular disease in the vegetarian and non-vegetarian groups provided some further evidence that a low intake of cereal fibre is associated with the presence of diverticular disease.

Introduction

DIVERTICULAR disease of the colon occurs frequently in westernised populations eating little dietary fibre and rarely, if at all, in African communities where fibre consumption is high.[1] The incidence of the disorder is also believed to have risen during the past 100 years in a number of western countries as the intake of dietary fibre has fallen.[1] These reported associations do not necessarily imply a cause-and-effect relation between a low intake of dietary fibre and the risk of diverticular disease, not only because the population groups contrasted have differed from one another in many ways other than fibre intake,[2] but also because the data on which the analyses have been based are of doubtful quality.

Patients with proven diverticular disease have been reported to have a lower crude fibre intake than healthy controls;[3] however, the findings related to diet after the onset of symptoms, and fibre intake may have been altered as a result of the disease. We have, therefore, studied dietary fibre intake in symptomless volunteers living in southern England in relation to the presence or absence of diverticular disease shown by radiology.

Subjects and Methods

Volunteers

Two groups of subjects aged 45 years and over were studied. The first group was intended to be broadly representative of the general population and comprised 264 patients (selected from the lists of Oxford general practitioners) who agreed to submit to a barium follow-through examination. The second group comprised 56 symptomless members of the Vegetarian Society of the United Kingdom living in southern England. 12 of these had been vegetarians since childhood, 14 for more than 25 years, and the remainder for at least 10 years. The age and sex distribution of the two groups of subjects is shown in table I.

TABLE I—AGE AND SEX DISTRIBUTION OF VOLUNTEERS IN THE TWO STUDY GROUPS

	45–59 yr		60–74 yr		>74 yr		Total	
Group	Male	Female	Male	Female	Male	Female	Male	Female
Non-vegetarian	62	82	56	64	..	..	118	146
Vegetarian	14	19	5	11	3	4	22	34

Dietary Methods

Full details of dietary methods will be published elsewhere. Briefly, two approaches were used—a comprehensive questionnaire, based on the principles described by Burke[4] and concerned with recent food consumption; and a 3-week dietary diary which was kept by 12 of the subjects under study and used to validate the questionnaire. The questionnaire was completed during a semistructured interview (conducted by A. W. or J. G.) for 189 non-vegetarians and 55 vegetarians. Proximate food constituents and fibre content were calculated from standard values obtained from the tables published by McCance and Widdowson.[5] Daily dietary fibre intake esti-

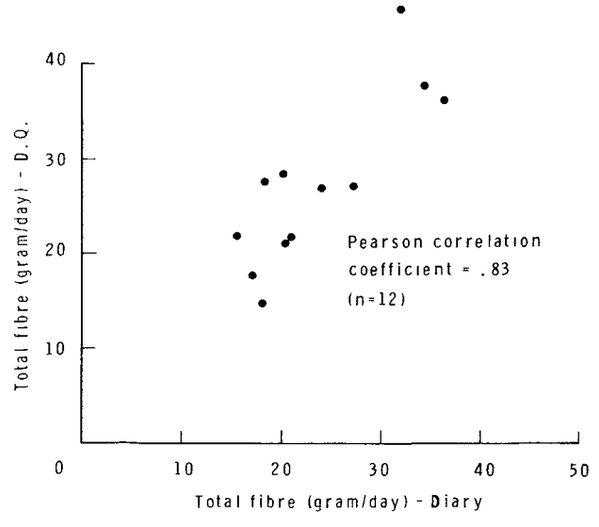

Fig. 1—Total fibre intake estimated from the dietary questionnaire (D. Q.) in relation to total fibre intake estimated from dietary diary.

mated from the questionnaire correlated closely with that from the 3-week diary (fig. 1).

Radiological Methods

Details of the method used and its validation have been published.[6] Each participant ingested 120 ml of barium sulphate ('Baritop 100') in three divided doses, 6–8 h apart, 5 days before a simple supine radiograph of the abdomen was taken. In a few instances a second radiograph was necessary because retention of large amounts of barium in the lumen of the colon might have obscured diverticula. The technique used ensured that the radiation doses involved were in line with the recommendations of the World Health Organisation for volunteers in a research project.[7]

The radiographs were examined by a consultant radiologist (D. N.) and a physician (J. G.) who had no knowledge of either the dietary-fibre intake or the identity of the individual concerned. Diverticular disease was considered to be present if any diverticula were detected in the transverse, descending, or sigmoid colon.

Results

The total dietary fibre intake of the vegetarians was much greater on average than that of the non-vegetarians (fig. 2). Mean (±S.D.) total dietary fibre intake for the vegetarians was 41·5 (±12·6) g and that for the non-vegetarians was 21·4 (±8·2) g; t=13·9, P<0·001. Diverticular disease was consistently found more frequently amongst the non-vegetarians (table II), the overall difference between the two groups being significant at the 1% level (χ^2_1=9·93, P<0·01). There was a strong association between age and diverticular disease in the non-vegetarian group (fig. 3), and also a suggestion that diverticular disease in both vegetarians and non-vegetarians occurred more frequently in men than women in the younger age-group, but more frequently in women than men in the older age-group (table II); however, this difference is not statistically significant.

Vegetarians with diverticular disease appeared to have a lower mean intake of cereal (and total) fibre than those unaffected by the disease (table III), but this difference did not reach statistical significance. Non-vegetarians without diverticular disease consumed significantly less vegetable fibre than those with the disorder (table III).

Because of the important association between diver-

TABLE II—PREVALENCE OF DIVERTICULAR DISEASE IN NON-VEGETARIANS AND VEGETARIANS BY AGE AND SEX

Subjects	45–59 yr		>59 yr	
	No. with diverticular disease	Total no. studied	No. with diverticular disease	Total no. studied
Males				
Non-vegetarians	19 *(31)*	62	21 *(38)*	56
Vegetarians	2 *(14)*	14	1 *(13)*	8
Females				
Non-vegetarians	17 *(21)*	82	31 *(48)*	64
Vegetarians	0	19	4 *(27)*	15

Nos. in parentheses refer to percentages.

TABLE III—MEAN FIBRE CONSUMPTION OF 189 NON-VEGETARIANS AND 55 VEGETARIANS WITH AND WITHOUT DIVERTICULAR DISEASE

Type of fibre	Non-vegetarians		Vegetarians	
	With diverticular disease (n=84)	Without diverticular disease (n=105)	With diverticular disease (n=7)	Without diverticular disease (n=48)
Total dietary fibre	21·8±7·4	22·1±8·4	33·7±13·0	42·8±12·3†
Cereal fibre	7·4±5·6	8·7±6·3	10·7± 6·0	17·5±10·2‡
Vegetable fibre	10·7±4·2	9·2±4·9*	14·3±11·7	14·4± 5·7
Fruit fibre	2·5±2·1	2·7±2·1	8·2± 2·5	9·6± 4·5

Results given in g±S.D.
Difference between subjects with and without diverticular disease: *t=2·24, P=0·026; †t=1·80, N.S.; ‡t=1·74, N.S.

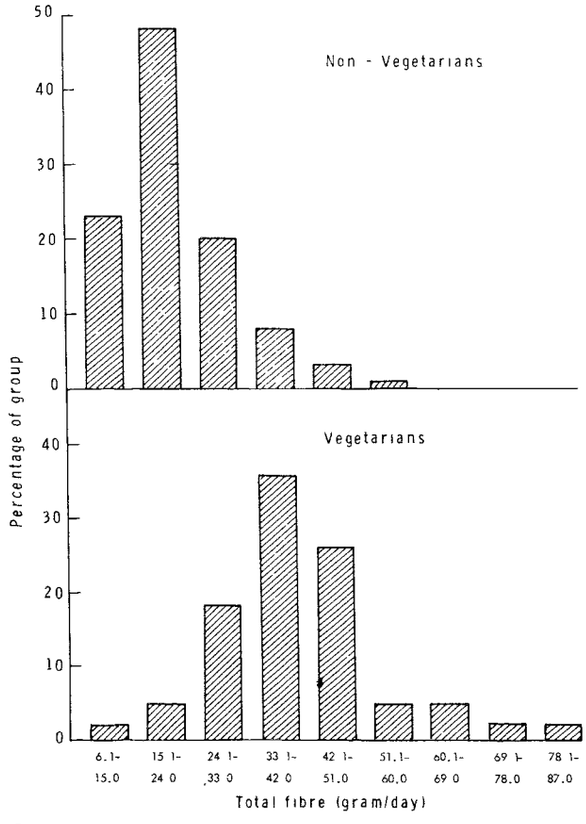

Fig. 2—Comparison of total fibre intake in the non-vegetarian and vegetarian groups.

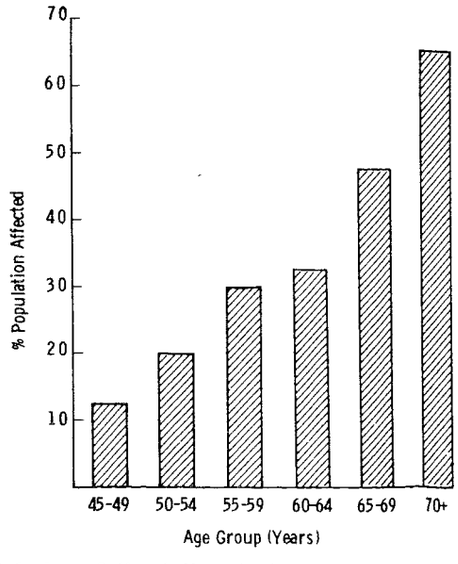

Fig. 3—Relation of distal diverticular disease to age in the non-vegetarian group.

TABLE IV—MEAN FIBRE CONSUMPTION OF 100 NON-VEGETARIANS AND 23 VEGETARIANS AGED 60 YEARS OR OVER WITH AND WITHOUT DIVERTICULAR DISEASE

Type of fibre	Non-vegetarians		Vegetarians	
	With diverticular disease (n=51)	Without diverticular disease (n=49)	With diverticular disease (n=5)	Without diverticular disease (n=18)
Total dietary fibre	19·5±6·6	22·7±8·6*	27·7±9·5	42·7±9·9‡
Cereal fibre	6·5±5·0	9·3±7·1†	10·9±7·2	18·0±6·3§
Vegetable fibre	9·7±3·8	9·4±5·3	7·8±4·4	13·9±4·7¶
Fruit fibre	2·3±1·7	2·7±2·1	8·7±2·8	9·2±4·0

Results given in g±S.D.
Difference between subjects with and without diverticular disease: *t=2·11, P=0·037; †t=2·31, P=0·023; ‡t=3·03, P=0·006; §t=2·16, P=0·042; ¶t=2·56, P=0·018.

ticular disease and age, the data were considered separately for younger and older subjects. Subjects >59 years old with diverticular disease had a significantly lower total mean fibre intake than those without in both the vegetarian and the non-vegetarian groups (table IV). This difference was chiefly accounted for by a difference in cereal fibre intake in both vegetarians and non-vegetarians; in addition, vegetable fibre intake tended to be lower in vegetarians with diverticular disease. Further subdivision of the data indicated that this difference in the older age-group was largely confined to women. Study of the younger age-group revealed one significant difference in the fibre intake of affected and unaffected individuals—non-vegetarians with diverticular disease consumed more vegetable fibre than those without.

Examination of data among individuals whose fibre intake was considered to be "stable" during adult life showed an overall difference in total and cereal fibre consumption between affected and non-affected subjects in both study groups. This difference was apparent in most of the subgroups, but small numbers precluded statistical analysis, and the data are therefore not presented here. The data were also re-examined according to different definitions of diverticular disease (e.g., the presence of three or more diverticula). The findings were essentially similar to those already described.

Discussion

There is little reliable information on the prevalence of symptomless diverticular disease. Most authors who have provided estimates have failed to define the disease under investigation, and only one study, done in Denmark, relates to a randomly selected population of which 52% agreed to take part.[8] The prevalence of symptomless diverticular disease in this Danish study was related to age, being 7% in those below the age of 50 years and 43% in those above that age.

We attempted to determine whether the non-vegetarians in our study were representative of all individuals over 45 years of age on the list of the participating practitioners, by investigating as many as possible of 100 randomly selected individuals; we had approached most of the subjects in the study only once, and participants were therefore largely self-selected. In the sample of 100, however, further letters were sent to those not responding to the initial approach. The prevalence of diverticular disease among those of the 100 subjects who responded to the initial request was 39% (13 affected out of 33, 2 films unsatisfactory), which was similar to the 31% (6 affected out of 16, 1 film unsatisfactory) among those who required further follow-up. However, altogether only 52 subjects were X-rayed. Of the remaining 48, 9 had moved and 39 refused to participate. The participation-rate in the intensively followed group was therefore 57% (52/91), and the prevalence-rates we have reported may not be representative. Nonetheless, the prevalence of diverticular disease in non-vegetarians in the present investigation is similar to that reported in the Danish study and a little higher than that reported from Oxford by Manousos and his colleagues in 1967.[9]

Our study confirms the association between dietary fibre and diverticular disease, but it also raises some questions. Asymptomatic diverticular disease occurred significantly less frequently amongst vegetarians than amongst non-vegetarians consuming significantly less cereal, vegetable, and fruit fibre. Vegetarians and non-vegetarians differ in ways other than in their dietary fibre intake; hence "within-group" comparisons are important. The differences in fibre intake between affected and non-affected individuals in both the vegetarian and the non-vegetarian groups were largely confined to older females, although in the vegetarian group as a whole there was a definite trend towards a higher consumption of total and cereal fibre amongst those individuals who did not have diverticular disease.

There are two possible explanations for the different effects in different age-groups. Firstly, diverticular disease is common and strongly related to age; accordingly, diverticula will eventually develop in many disease-free young individuals. Secondly, younger people may have a less stable eating pattern, which could mask any relation. Examination of data from only those individuals who reported a stable fibre intake during adult life showed an overall relation between diverticular disease and dietary fibre consumption. This relation, based on a small number of observations, was not statistically significant.

It is more difficult to explain why the difference in fibre consumption between those with and without diverticular disease was more striking amongst women. This was apparent in both vegetarians and non-vegetarians. We have also found a difference in bowel transit-time between men and women (to be published) and, considered together, these findings suggest that the sex difference not be due to chance.

This study has shown a relation between symptomless diverticular disease and consumption of dietary fibre. Furthermore, it appears that fibre of cereal origin is the most important component of dietary fibre for protection against diverticular disease. This finding is consistent with a number of other observations. Cereal fibre is poorly digested by colonic bacteria,[10] and it has a mamum effect on increasing stool-weight and reducing transit-time.[11] Cereal fibre used therapeutically in patients with diverticular disease produces improvement in symptoms and reduces the abnormally high intrasigmoid pressures.[12,13] It is concluded that an adequate intake of cereal fibre appears, in females at least, to protect the colon against the development of diverticular disease.

We thank the members of the Vegetarian Society and other volunteers for their participation, Dr G. M. Ardran, Dr G. Fowler, and Dr N. MacLennan for their help, staff of the Oxford University Press and W. Lucy and Co, Engineers, who participated in the pilot study, Dr K. McPherson and Dr D. Yates for statistical and computing assistance, Mrs A. Reeve and Miss V. Williams for secretarial help, and the Medical Research Council for financial support.

Requests for reprints should be addressed to J. I. M., Department of Social and Community Medicine, 8 Keble Road, Oxford OX1 3QN.

REFERENCES

1. Painter, N. S., Burkitt, D. P. *in* Refined Carbohydrate Foods and Disease (edited by D. P. Burkitt and H. C. Trowell); p. 99. London, 1975.
2. Mendeloff, A. I. *New Engl. J. Med.* 1977, **297**, 811.
3. Brodribb, A. J. M., Humphreys, D. M. *Br. med. J.* 1976, i, 421.
4. Burke, B. S. *J. Am. diet. Ass.* 1947, **23**, 1041.
5. McCance and Widdowson *in* The Composition of Foods (edited by A. A. Paul and D. A. T. Southgate). H. M. Stationery Office, 1978.
6. Ardran, G. M., Nolan, D. J., Gear, J. S. S., Fursdon, P. S., Brodribb, A. J. M. *Br. J. Radiol*, 1978, **51**, 472.
7. Irradiation of Human Subjects for Medical Research (based on a W.H.O. working document). *Br. Inst. Radiol. Bull.* 1975, **1**, 4.
8. Weinreich, J., Hougaard-Enevddsen, O., Dinesen, K. *Scand. J. Gastroent.* 1976, **11**, 86.
9. Manousos, O. N., Truelove, S. C., Lumsden, K. *Br. med. J.* 1967, iii, 760.
10. Van Soest, P. J., Robertson, J. B. *Nutr. Rev.* 1977, **35**, 12.
11. Cummings, J. H., Southgate, D. A. T., Branch, W., Houston, H., Jenkins, D. J. A., James, W. P. T. *Lancet*, 1978, i, 5.
12. Findlay, J. M., Smith, A. N., Mitchell, W. D., Anderson, A. J. B., Eastwood, M. A. *ibid.* 1974, i, 146.
13. Brodribb, A. J. M. *ibid.* 1977, i, 664.

AUTOLOGOUS BONE-MARROW TRANSPLANTATION IN RELAPSED ADULT ACUTE LEUKÆMIA

K. A. DICKE, G. SPITZER, L. PETERS, K. B. MCCREDIE, A. ZANDER, D. S. VERMA, L. VELLEKOOP, J. HESTER

Departments of Developmental Therapeutics and Radiotherapy, University of Texas System Cancer Center, M. D. Anderson Hospital, and Tumor Institute, 6723 Bertner, Houston, Texas 77030, U.S.A.

Summary 24 cases of adult acute leukæmia, of which 21 were evaluable, were treated in irreversible relapse with high-dose piperazinedione and supralethal total-body irradiation (T.B.I.) in conjunction with autologous marrow transplantation (A.B.M.T.). The grafted marrow cells had been collected and stored in liquid nitrogen at the time of remission. In 12 patients the marrow cells were fractionated on discontinuous albumin gradients in an attempt to separate normal cells from residual leukæmic cells. 11 patients achieved complete remission (C.R.); 7 other patients had signs of engraftment but died before C.R. The median remission duration was 4 months (2–14). 6 of 9 acute myeloblastic leukæmia patients, in whom bone-marrow transplantation was the first treatment of relapse, achieved C.R. 4 of 5 patients with acute lymphoblastic leukæmia, whose bone-marrow cells were collected during first remission, reached C.R. Autologous bone-marrow transplantation is a valuable first treatment for acute myeloblastic leukæmia in relapse and acute lymphoblastic leukæmia in second relapse.

Introduction

RECENT advances in the treatment of adult acute leukæmia have improved rates of complete remission and lengthened survival.[1,2] However, despite this progress the majority of adult acute leukæmia patients die of recurrence of leukæmia within 2 years of disease onset.

The prognosis of adult acute myeloblastic leukæmia (A.M.L.) after the first relapse is dismal. Only 30% achieve a second remission, which is of short duration, and overall survival is only 18 weeks.[3] The survival of patients with acute lymphoblastic leukæmia (A.L.L.) and undifferentiated leukæmia (A.U.L.) in their second relapse equals that of patients with A.M.L. in their first relapse.[4] The resistance of relapsed leukæmia could be overcome with high-dose chemotherapy plus total body irradiation (T.B.I.) followed by allogeneic bone-marrow transplantation from HLA-identical, mixed-lymphocyte-culture-negative donors. However, allogeneic bone-marrow transplantation is limited by the scarcity of suitable donors: only 30% of our leukæmia patients have HLA-identical donors. There is a large early mortality, up to 75%, within 3 months of transplantation because of infectious complications, interstitial pneumonia, and graft-versus-host disease resulting from histoincompatibility. Only up to 17% of the transplanted patients survive 2 years after transplantation in complete remission (C.R.).[5,6] Patients treated by the Seattle group with syngeneic bone-marrow transplantation—i.e., transplantation of marrow from identical twins—showed longer term survival because they had no fatal graft-versus-host disease and a lower incidence of interstitial pneumonia.[7] Syngeneic bone-marrow transplantation, however, is limited by the very low incidence of identical twins.

As an alternative to syngeneic and allogeneic bone-marrow transplantation, we have transplanted the leukæmic patient's own cryopreserved remission bone-marrow after high-dose chemotherapy and irradiation.[8] In some cases we attempted to reduce possible leukæmic-cell contamination of the marrow-cell suspension collected during remission by discontinuous albumin density gradient centrifugation of the cells.

Patients

14 patients had A.M.L., 8 had A.L.L., and 2 had A.U.L. The median age was 28 (18-48). All except 5 bone-marrows (patients 1, 7, 10, 12, 15) were aspirated during first remission. Patients with A.L.L. and A.U.L. entered the transplantation programme in second, third, or fourth relapse; patients with A.M.L. in first and second relapse. All patients had received extensive induction, consolidation, maintenance, and late intensification therapy.[1] 15 patients had received second-line chemotherapy, 2 even investigational chemotherapy, and were considered failures. 9 patients (8, 11, 13, 14, 16, 18–21) were grafted without receiving second-line chemotherapy. 3 patients 2 A.M.L., 1 A.L.L.) could not be evaluated because they died within 5 days of transplantation of pre-existing conditions such as fungæmia, liver failure, and *Pseudomonas* septicæmia.

12 of the 24 patients, 10 of the 21 evaluable cases, received fractionated marrow. The decision to perform marrow fractionation before storage depended on the work load of the laboratory, namely, on the number of other marrows simultaneously being frozen, an important determinant in quality control of freezing and thawing procedures.