Dietary fibre and large bowel cancer

By JOHN H. CUMMINGS, *Dunn Clinical Nutrition Centre, Addenbrookes Hospital, Trumpington Street, Cambridge*

Dietary fibre, the non-starch polysaccharide component of the diet, is the most recent of a number of dietary components to be implicated in the aetiology of large bowel cancer. Other nutrients which are thought to be important are fat, animal protein and cholesterol. It is likely that cancer in the large bowel arises by two related processes; first, the induction of malignant potential in mucosal cells by carcinogenic substances and secondly, the promotion of tumour growth by other factors. At the present time no substance has been identified which is definitely carcinogenic for the human colon and most experimental work has concentrated on the mechanisms of tumour promotion. Dietary fat and protein are thought to be promoting agents in the gut. Fibre, however, is seen as being protective against bowel cancer (Burkitt, 1971) and therefore to act by neutralizing any promotional effects of fat and protein. A direct effect on the initiating carcinogen (or carcinogens) is also possible.

It should be realized that little, if anything, is known about the molecular events which produce cancer in the bowel and therefore any attempt to relate diet to this process must, of necessity, be somewhat speculative. Most of the evidence is circumstantial, particularly for fibre which, it has to be postulated, is protecting us from processes which have not actually been defined except by inference. What then is the evidence that fibre is involved in the development of large bowel cancer? Information can be derived from three main sources, epidemiological observations, case control studies and animal experiments.

Epidemiology

Table 1 lists eleven studies in which reference to fibre or fibre containing foods has been made in epidemiological investigations of large bowel cancer. It will be noted that all these papers have appeared in the past decade, much of the impetus to seek an association with fibre and this cancer coming after the publication of Burkitt's paper in 1971, although prior to this other workers in South Africa had discussed such a possible association.

Taken together, the studies in Table 1 do not show a consistent protective effect of fibre but their interpretation is confounded by two things. Firstly, the adequacy of the information on dietary fibre intakes in the populations concerned, and secondly, the statistical methods used. Three of the studies report a protective effect of cereals for large bowel cancer (3,5,6) whilst in two (4,9) such an effect was specifically looked for and not found. The inability to substantiate a protective effect is because of the intercorrelation observed amongst the consumption of the various dietary components, and the failure to use appropriate statistical

0029–6651/81/4013–4502 $01.00

Table 1. *Fibre and bowel cancer–epidemiology*

No.	Study	Food data	Country	Effect of fibre
1	Burkitt (1971)	Personal observations	Many—especially Africa	Protective
2	Drasar & Irving (1973)	FAO	Thirty-seven countries	No effect
3	Irving & Drasar (1973)	FAO	Thirty-seven countries	Cereals weakly protective
4	Armstrong & Doll (1975)	FAO and other sources	Thirty-two countries	No effect
5	Howell (1975)	FAO	Thirty-seven countries	Cereals and pulses protective
6	Schrauzer (1976)	OECD	Sixteen countries	Cereals protective
7	IARC (1977)	Diet record and food analyses	Denmark and Finland	Protective
8	Malhotra (1977)	Regional food patterns	India	Protective
9	Liu *et al.* (1979)	FAO	Twenty countries	No effect
10	Bingham *et al.* (1979)	NFS	UK	Pentose fraction of fibre protective
11	Hill *et al.* (1979)	Questionnaire	Hong Kong	More fibre-rich foods eaten in high risk group

FAO, Food and Agriculture Organization food balance sheets; OECD, Organization for Economic Co-operation and Development; NFS, UK National Food Survey.

techniques to overcome this. Armstrong & Doll (1975) noted a correlation of between −0·51 and −0·70 for colon cancer mortality with cereal consumption but cereal and animal protein intakes were also correlated (r −0·76). When first-order partial correlation coefficients for cereals were calculated, controlling for meat or animal protein the relationship with cereals was no longer significant (r −0·1 to −0·2). No association between bowel cancer and consumption of fruit, vegetables, pulses or potatoes was found in their study. Similarly, Liu *et al.* (1979) found a significant correlation between fibre (that is fibre containing foods as percentage energy intake) and cancer mortality (r −0·77) but when the partial correlation was calculated controlling for cholesterol intake the relationship was no longer significant (r 0·03), and cholesterol intake was judged to be the most important dietary variable. Studies where a protective effect of fibre has been shown are generally those where the intra-dietary associations have not been taken into account.

In fairness to the dietary fibre hypothesis, however, it must be said that in only two of the studies listed in Table 1 (7,10) have the authors actually obtained measurements of fibre intakes in the relevant populations. This is because food tables containing dietary fibre information are available in only one or two countries of the world at present, largely because of difficulties in the analysis of fibre. In those studies where fibre has been measured, then a clear protective effect against bowel cancer has been observed. In the work reported by the IARC (1977) dietary intake was measured in a randomly selected group of thirty middle-aged

men in Copenhagen (Denmark) and Kuopio (Finland). The age-adjusted incidence of colon cancer was four times higher in the appropriate Danish than in the Finnish population. Food consumption was measured by asking the subjects to keep a diary of all food eaten over 4 d and on the fourth day, duplicate samples of the diet were collected for analysis. No difference in fat intake was noted between the two populations and total protein intake was in fact lower in the Danes. The biggest difference was in fibre intake which was 17·2±5·1 (SD) g/d in the Danes and 30·9±11·3 (SD) g/d ($P<0·001$) in the Finns. Further work by this same group of investigators covering more groups of the Scandinavian population have confirmed this inverse association with fibre.

In another study, Bingham *et al.* (1979) calculated food intakes for nine regions of the UK (excluding Northern Ireland) from British National Food Survey results. Food intakes were then related to regional large bowel cancer mortality. Food composition, including dietary fibre intakes were obtained from food tables and other sources. Appropriate statistical techniques were used and with these no association between colon cancer mortality and intakes of fat, animal protein nor total dietary fibre was found. However, average intakes of the pentose fraction of dietary fibre were significantly correlated with mortality rates (r −0·96) as were intakes of vegetables (other than potatoes) (r −0·94), suggesting a protective effect for fibre. It is worth noting in this context that physiological studies of the effect of fibre on large bowel function have shown the pentose fraction of dietary fibre to be the most important in determining changes (Cummings *et al.* 1978).

Over all, therefore, epidemiological studies of fibre and large bowel cancer are not conclusive. The recently described studies, however, in which appropriate methodology has been used indicate that this line of enquiry should be pursued.

Case control studies

An alternative approach to the epidemiology of diet and cancer is to look at the food intake of patients with cancer and compare this with suitable control subjects. Differences between the two groups are then ascribed an aetiological role in the development of the tumour.

Table 2 summarizes the results of eight case control studies of large bowel cancer patients in which fibre or fibre-containing foods are mentioned. At first glance they appear to support a protective role for fibre more consistently than do population studies. There are, however, major problems with methodology and interpretation. In none has dietary fibre intake been quantitated, not even as crude fibre. Of course, neither appropriate food tables nor analytical facilities were available to any of the authors. A more fundamental problem is that of quantitating dietary intake in these subjects at all. Food intakes have been assessed by use of either a food frequency questionnaire or structured interview. The defects of such methods and lack of validation studies have been reviewed by Graham & Mettlin (1979). Moreover, most investigations have included an assessment of food intake at anything from 1–10 years prior to the time of interview, a so-called retrospective dietary history. The precision of information acquired in this way has never been

Table 2. *Fibre and bowel cancer (case controls)*

Study	Dietary method	Number of Cases	Number of Controls	Findings re fibre
Higginson (1966)	Interview	340	1020	No differences
Wynder & Shigematsu (1967)	Interview	791	791	No differences
Haenszel *et al.* (1973)	Questionnaire	179	357	Legumes increase risk
Bjelke (1974)	Questionnaire	651	3091	Lower intakes of vegetables, cereals and crude fibre in cases
Modan *et al.* (1975)	Interview	198	396	Lower intakes of high fibre foods in cases
Phillips (1975)	Interview	41	123	Green leafy vegetables weakly protective
Graham *et al.* (1978)	Interview	470	1348	Vegetables protective
Dales *et al.* (1978)	Interview	99	280	Less frequent use of high fibre foods in cases

substantiated and given the vagueness of memory it is surprising that any associations are found at all.

Phillips (1975) also points out that whilst, in his study, a decreased relative risk for cancer was seen with consumption of green leafy vegetables, the strong correlation (in Seventh Day Adventist subjects) between the fat and fibre content of most foods, makes any association with low fibre intakes likely to be secondary to a relationship with fat intake.

The need to assess dietary intake retrospectively in case control studies arises for two reasons. Firstly, the promotional effects of diet on tumour growth are said to occur long before the growth becomes clinically manifest. The interval is thought to be 10 or even 20 years and is based on in vitro studies of cancer. The exact length of that interval has, however, not been measured in man. It could be as short as one year and may well vary considerably between individuals. Implicit in the need to go back in time with dietary evaluation is the assumption that people change their diet from year to year. This is not known with certainty but should be amenable to study. If diet does not change then this component of the need for retrospective analysis becomes invalid.

The second reason why retrospective analysis of dietary intake is attempted by investigators stems from the effect of the disease itself on food intake. Patients with cancer, particularly bowel cancer, are likely to change their diet once the tumour has developed. The two commonest presenting symptoms in colon cancer are abdominal pain and a change in bowel habit (Jones & Sleisenger, 1978). Both of these symptoms are likely to make patients change their diet in order to try and overcome or ameliorate them. Unfortunately, the foods which cancer subjects are most likely to omit from their diet are vegetables and cereals which are known to stimulate colonic activity and are widely believed, perhaps not correctly, to aggrevate bowel symptoms. The case-control study for bowel cancer particularly is vulnerable to criticism on this count.

To overcome these and other problems a prospective study is needed. This should incorporate a valid means of assessing dietary intake and the measurement would need to be repeated with time to check on long-term changes in food intake. The incidence of bowel cancer in the population is relatively low (only 20–40 cases/100 000 people per annum even in high risk areas) so a large number of subjects would need to be studied. The information on diet would, however, be useful in relation to other diseases. Meanwhile the apparent consistency of findings in case-control studies must be viewed with some scepticism.

Animal experiments

The relative infrequency with which man gets bowel cancer has led to the development of animal models to study the effect of diet on this tumour. The model currently most popular is the rat, dosed with dimethylhydrazine (DMH). This model is thought to be a valid one by some investigators (Reddy *et al.* 1975; LaMont & O'Gorman, 1978) but has been criticized (Newcombe, 1979; Crofts, 1979) mainly on the grounds that parenterally administered carcinogen is not appropriate for this organ. Since the Burkitt hypothesis (1971) requires that the tumorigenic process is essentially an intraluminal one, the value of the DMH model is limited. The model can also be questioned because the incidence of tumours in treated animals is very high (70–100%) and many of them (at least 33%) are benign adenomas or plaque-like lesions unlike those found in man. In addition, the sequence of progression of adenoma to carcinoma believed to be an essential part of the tumour process in man (Morson, 1976) is not seen in animals.

It is perhaps not surprising therefore that considerable dispute remains as to whether the model can be used to test the effect of fibre in bowel cancer. Table 3 lists the results of ten studies, half of which suggest fibre is protective. Of these, Wilson *et al.* (1977) were able to show protection against the development of only benign tumours. The study of Fleiszer *et al.* (1978) has been criticized because the

Table 3. *Fibre and bowel cancer—animal studies*

Study	Fibre source and dose (% of diet)	Species	Protective effect of fibre: Decrease in no. of rats with tumour (%)	Protective effect of fibre: Decrease in no. of tumours/rat
Ward *et al.* (1973)	Cellulose (20 or 40)	Rat	No	No
Freeman *et al.* (1978)	Cellulose (4·5)	Rat	Yes	Yes
Wilson *et al.* (1977)	Bran (20)	Rat	Yes	No
Barbolt & Abraham (1978)	Bran (20)	Rat	No	Yes
Chen *et al.* (1978)	Bran (40)	Mouse	No	No
Cruse *et al.* (1978)	Bran (20)	Rat	No	—
Fleiszer *et al.* (1978)	Bran–Chow	Rat	Yes	—
Asp *et al.* (1978)	Bran (20)	Rat	No	No
	Carrot (20)	Rat	No	No
	Pectin (7)	Rat	No	No
Castleden (1977)	Various gums (1)	Rat	No	
Carachi *et al.* (1977)	Unknown	Rat	Yes	

https://doi.org/10.1079/PNS19810002 Published online by Cambridge University Press

levels of fat and protein in their diets changed in addition to fibre intakes, because the growth rates of the different groups of rats varied and on its use of statistics. In the paper of Barbolt & Abraham (1978) it is not clear whether the reduction in number of tumours/rat with bran referred to benign or malignant growths. In only the study of Freeman *et al.* (1978) can a clearly protective effect for fibre (cellulose) be said to have occurred, and even here there could be criticism of the design of the study (Peto, 1974). The study of Carachi *et al.* (1977) has been reported in only preliminary form to date.

Whilst those studies which have shown an apparent protective effect of fibre can be criticized so also can those which have not. Problems include unnecessarily high doses of DMH (Cruse *et al.* 1978; Thorne, 1979) and of study design, histological classification, and problems with DMH toxicity. The rat iself may not be a very suitable species since it handles fibre in a different way from the human. The rat is a poor digester of fibre whilst man digests most types (bran being the exception) almost completely (Cummings, 1981). It is difficult, therefore, to see how much useful evidence for the role of fibre can be obtained from this particular model.

Other studies

If fibre protects against the development of large bowel cancer, then it should be possible to construct an hypothesis as to how this protection occurs, and to test it. Burkitt in 1971 put forward just such an hypothesis. Acknowledging that there might be multiple factors in large bowel cancer aetiology, he suggested that fibre exerted its protective effect by increasing stool weight and shortening transit time through the gut. He thought that these changes might result in altered bacterial metabolism particularly in relation to bile acids.

As an alternative strategy for the investigation of the aetiology of large bowel cancer, several investigators have taken up this hypothesis and designed studies to test it. The proposed protective effect of an increased stool weight has been tested epidemiologically, admittedly in only limited numbers so far, by measuring faecal output in populations with high and low cancer risk (IARC 1977; Reddy *et al.* 1978). These studies show the highest stool weights in those populations with the lower cancer risks. Similarly, in both animal studies (Wilson *et al.* 1977; Barbolt & Abraham, 1978; Freeman *et al.* 1978) and in man (Cummings *et al.* 1978) feeding dietary fibre leads to an increase in stool output.

An increase in stool output as such is unlikely to be a major factor in large bowel cancer prevention. More likely it is indicative of other changes in colonic function which bear more directly on the cancerous process. The most obvious associated change is in the concentration of substances in the colon. The increased volume of gut contents due to fibre is likely to dilute any noxious substance. Such a dilution effect has been shown for inert material in the gut (Cummings *et al.* 1976) but when the effect of fibre on the concentration of soluble substances is examined, then the story becomes more complex. When bran is added to the controlled diets of subjects there is no change in faecal sodium, short chain fatty acid or ammonia concentration despite an almost threefold increase in stool weight (Cummings

et al. 1979). These results are not surprising if the colonic metabolism of these substances is examined. Were the molecular nature of the carcinogenic process to be better defined, then this physiological approach could be more fruitful.

Much less evidence has been published to support the suggestion that shorter transit time is important in protecting against large bowel cancer. Hill (1974) has argued strongly against it being involved and indeed in two epidemiological studies where transit has been measured in populations with widely differing large bowel cancer risks, no differences in transit time have been found (Glober *et al.* 1977; IARC, 1977). It is probably unwise, however, to dismiss transit as being unimportant. The role transit is likely to play is in controlling metabolic events in the colon and experimental evidence indicates that transit may indeed be a determining factor in some colonic events (Cummings, 1978; Stephen, 1980). Moreover, there is considerable evidence from studies of ruminant metabolism that time is crucial to the process of microbial carbohydrate digestion and metabolism (Isaacson *et al.* 1975) and in man similar relationships hold (Stephen, 1980).

Conclusions

The role of dietary fibre in the aetiology of large bowel cancer has been investigated using epidemiology, animal models, case-control studies and experiments in human physiology. From none of these sources is there conclusive evidence that fibre will prevent large bowel cancer, although neither is there evidence that fibre is not involved. Of the problems which face the investigator the most inhibiting is lack of knowledge of the substance, or substances, involved in the cellular and intraluminal events which lead to tumour production. Without such information the evidence for associating large bowel cancer and fibre (or any other dietary component) will remain circumstantial. It is, however, possible that the carcinogens involved and possibly even the promotional agents (at the molecular level) will never be identified with certainty. In which case, further detailed dietary epidemiology, using adequate methods for assessing food intake, metabolic epidemiology and physiological studies of the colon are likely, together, to prove valuable in establishing the hypothesis for the role of fibre in this cancer.

At the present time the evidence relating fibre to large bowel cancer is inadequate, but fibre cannot be dismissed since appropriate studies have not been done.

REFERENCES

Armstrong, B. & Doll, R. (1975). *Int. J. Cancer* **15**, 617.
Asp, N. G., Bauer, H., Dahlquist, A., Fredlund, P. & Öste, R. (1978). *Naringsforsk.* **22**, (Suppl. 16), 64.
Barbolt, T. A. & Abraham, R. (1978). *Proc. Soc. exp. Biol. Med.* **157**, 656.
Bingham, S., Williams, D. R. R., Cole, T. J. & James, W. P. T. (1979). *Br. J. Cancer* **40**, 456.
Bjelke, E. (1974). *Scand. J. Gastroent.* **9**, (Suppl. 31), 1.
Burkitt, D. P. (1971). *Cancer* **28**, 3.
Carachi, R., Busuttil, A. & Joffe, S. N. (1977). *Gut* **17**, A410.
Castleden, W. M. (1977). *Br. J. Cancer* **35**, 491.
Chen, W. F., Patchefsky, A. S. & Goldsmith, H. S. (1978). *Surgery Gynec. Obstet.* **147**, 503.

Crofts, T. J. (1979). *Lancet* i, 108.
Cruse, J. P., Lewin, M. R. & Clark, C. G. (1978). *Lancet* ii, 1278.
Cummings, J. H. (1978). *J. Plant Fds* **3**, 83.
Cummings, J. H. (1981). *Br. Med. Bull.* (In the Press).
Cummings, J. H., Hill, M. J., Bone, E. S., Branch, W. J. & Jenkins, D. J. A. (1979). *Am. J. clin. Nutr.* **32**, 2094.
Cummings, J. H., Hill, M. J., Jenkins, D. J. A., Pearson, J. R. & Wiggins, H. S. (1976). *Am. J. clin. Nutr.* **29**, 1468.
Cummings, J. H., Southgate, D. A. T., Branch, W. P. T., Houston, H., Jenkins, D. J. A. & James, W. P. T. (1978). *Lancet* i, 5.
Dales, L. G., Friedman, G. D., Ury, H. K., Grossman, S. & Williams, S. R. (1978). *Am. J. Epidemiol.* **109**, 132.
Drasar, B. S. & Irving, D. (1973). *Br. J. Cancer* **27**, 167.
Fleiszer, D., Murray, D., MacFarlane, J. & Brown, R. A. (1978). *Lancet* ii, 552.
Freeman, H. J., Spiller, G. A. & Kim, Y. S. (1978). *Cancer Res.* **38**, 2912.
Glober, G. A., Nomura, A., Kamiyama, S., Shimada, A. & Abba, B. C. (1977). *Lancet* ii, 110.
Graham, S., Dayal, H., Swanson, M., Mittelman, A. & Wilkinson, G. (1978). *J. natn. Cancer Inst.* **61**, 709.
Graham, S. & Mettlin, C. (1979). *Am. J. Epidemiol.* **109**, 1.
Haenszel, W., Berg, J. W., Segi, M., Kurihara, M. & Locke, F. B. (1973). *J. natn. Cancer Inst.* **51**, 1765.
Higginson, J. (1966). *J. natn. Cancer Inst.* **37**, 527.
Hill, M. J. (1974). *Digestion* **11**, 289.
Hill, M. J., MacLennan, R. & Newcombe, K. (1979). *Lancet* i, 436.
Howell, M. A. (1975). *J. chron. Dis.* **28**, 67.
IARC Intestinal Microecology Group (1977). *Lancet* ii, 207.
Irving, D. & Drasar, B. S. (1973). *Br. J. Cancer* **28**, 462.
Isaacson, H. R., Hinds, F. C., Bryant, M. P. & Owens, F. N. (1975). *J. Dairy Sci.* **58**, 1645.
Jones, R. S. & Sleisenger, M. H. (1978). In *Gastrointestinal Disease,* p. 1784 [M. H. Sleisenger and J. S. Fordtran, editors]. Philadelphia.
LaMont, J. T. & O'Gorman, T. A. (1978). *Gastroenterology* **75**, 1157.
Liu, K., Stamler, J., Moss, D., Garside, D., Persky, V. & Soltero, I. (1979). *Lancet* ii, 782.
Malhotra, S. L. (1977). *Med. Hypotheses* **3**, 122.
Modan, B., Barell, V., Lubin, F., Modan, M., Greenberg, R. A. & Graham, S. (1975). *J. natn. Cancer Inst.* **55**, 15.
Morson, B. (1976). In *Clinics in Gastroenterology,* p. 505 [P. Sherlock and N. Zamcheck, editors]. London: W. B. Saunders Ltd.
Newcombe, R. G. (1979). *Lancet* i, 108.
Peto, R. (1974). *Br. J. Cancer* **29**, 101.
Phillips, R. L. (1975). *Cancer Res.* **35**, 3513.
Reddy, B. S., Hedges, A., Laakso, K. & Wynder, E. L. (1978). *Cancer Letters* **4**, 217.
Reddy, B. S., Narisawa, T., Maronpot, R., Weisberger, J. H. & Wynder, E. L. (1975). *Cancer Res.* **35**, 3421.
Schrauzer, G. N. (1976). *Med. Hypotheses* **2**, 39.
Stephen, A. M. (1980). PhD Thesis, University of Cambridge.
Thorne, M. C. (1979). *Lancet* i, 108.
Ward, J. M., Yamamoto, R. S. & Weisburger, J. H. (1973). *J. natn. Cancer Inst.* **51**, 713.
Wilson, R. B., Hutcheson, D. P. & Wideman, L. (1977). *Am. J. clin. Nutr.* **30**, 176.
Wynder, E. L. & Shigematsu, T. (1967). *Cancer* **20**, 1520.

Printed in Great Britain