Jpn. J. Cancer Res. 84, 13–19, January 1993

Relationship of Diet to Small and Large Adenomas of the Sigmoid Colon

Suminori Kono,[1,3] Koji Imanishi,[2] Koichi Shinchi[2] and Fumio Yanai[2]

[1]*Department of Public Health, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama 359 and* [2]*Self-Defense Forces Fukuoka Hospital, 173-2 Kokura, Kasuga, Fukuoka 816*

The relation of dietary factors to the risk of adenomas of the sigmoid colon was examined in men receiving a retirement health examination at the Self-Defense Forces Fukuoka Hospital between October 1986 and 1990. A total of 187 adenoma cases and 1557 controls with normal colonoscopy were identified in the series. Cases were further classified into small-adenoma (<5 mm, n=78) and large-adenoma (≥5 mm, n=67) groups. The consumptions of selected foods and beverages were ascertained before colonoscopy by means of a self-administered questionnaire. After adjustment for smoking, alcohol use, rank and body mass index, low rice consumption and high meat intake were independently associated with an increased risk of large adenomas. The risk of small adenomas was not related to either rice consumption or meat intake. Adjusted odds ratios of large adenomas for the low, intermediate and high consumption levels of rice were estimated to be 1.0 (referent), 0.83 and 0.43, respectively (trend $P=0.08$), and the corresponding figures for meat consumption were 1.0 (referent), 1.58 and 2.38, respectively (trend $P=0.02$). The findings suggest that low rice consumption and high meat intake may promote the growth of colon adenomas, thereby increasing the risk of colon cancer.

Key words: Diet — Colon polyp — Size of adenoma

The majority of colon cancers are known to arise from preexisting adenomas,[1-3] and recent genetic studies have further strengthened the evidence for an adenoma-carcinoma sequence.[4,5] It is hypothesized that different factors act in the multistage process from the initiation of adenoma to the transition to carcinoma and that dietary factors, especially intake of animal fat and meat, may be responsible for the growth of adenomas.[6] A few studies have examined the relation between dietary factors and colon or colorectal adenomas,[7-10] and in some, diets high in animal fat and low in fiber were found to be associated with an increased risk of adenomas,[7-9] being consistent with observations relating diet to colorectal cancer.[11,12] However, the size of adenoma was not taken into consideration in the previous studies, except in one small case-control study.[7]

In an earlier analysis of the on-going study of self-defense officials in Japan, we reported that rice consumption tended to be inversely related to the risk of adenomas of the sigmoid colon.[13] Using expanded data, we have now examined the relation between dietary factors and adenomas of the sigmoid colon, taking into account the size of adenoma.

MATERIALS AND METHODS

The study population comprised male self-defense officials who were admitted at the Self-Defense Forces Fukuoka Hospital for a retirement health examination between October 1986 and December 1990. Details of the health examination have been described elsewhere.[13-15] A routine colonoscopy necessarily examined the rectum and sigmoid colon, and more proximal sites were also examined if the subjects tolerated the physical discomfort. The length of intubation and the location and size of polyps were recorded. Histological diagnosis was referred to the pathology department of a university hospital.

The case subjects consisted of men having adenomas at a distance of 11–60 cm from the anus, which was defined as the sigmoid colon here, and control subjects were those who were examined at least up to 60 cm from the anus and who were free of pathological lesions. Of 2596 subjects undergoing colonoscopy in the series of 2756 men, 207 cases and 1644 controls were identified. For the present study, men having polyposis coli, colorectal adenocarcinoma or known colorectal polyps were excluded from the cases. Further exclusion criteria for both case and control groups were as follows: a history of colectomy, colorectal polypectomy, cancer, apoplexy or myocardial infarction; inflammatory bowel disease; newly diagnosed cancer; coronary heart disease on medication; and diabetes mellitus under dietary or drug treatment. A total of 187 cases and 1557 controls fulfilled the eligibility criteria; 107 cases were newly added to those used in the earlier analysis covering the period from October 1986 to December 1988.[13] Controls in the earlier study had a minimum intubation of 40 cm, and 787 of them conformed to the present definition. The distribution of adenoma size is shown in Table I, separately for the two

[3] To whom reprint requests should be sent.

Table I. Distribution of Adenoma Cases by Size in the Two Periods, 1986–1988 and 1989–1990

Diameter[a]	1986–1988[b]	1989–1990
<5 mm	19	59
5–9 mm	26	22
≥10 mm	7	12
Unknown	28	14
Total	80	107

a) Diameter of the largest adenoma.
b) From October 1986.

Table II. Reproducibility of Dietary Assessment (n=93)

Food and beverage	Rank correlation coefficient
Rice (bowls/day)	0.47
Soy paste soup (bowls/day)[a]	0.72
Bread for breakfast[b]	0.78
Pickles[b]	0.66
Raw vegetables[b]	0.64
Fruits[b]	0.71
Fish[b]	0.70
Meats[b]	0.50
Milk (glasses/day)[a]	0.79
Coffee (cups/day)	0.77
Green tea (cups/day)	0.58

a) Values 0 and 0.5 were assigned to the categories of none or less than once per week and 1–5 times per week, respectively.
b) Weekly frequency was scored as follows: none or less than once per week=0; once per week=1; 2–3 times per week=2; 4–5 times per week=4; and almost daily=6.

periods. Small adenomas (<5 mm) were more frequently detected in the later period.

A self-administered questionnaire, inquiring about smoking habit, alcohol use, physical activity, dietary habits and other lifestyle characteristics, was distributed on the first day of admission and collected on the second day with a supplemental interview for unfilled answers. The questionnaire was revised in January 1989 as to alcohol use and physical activity. However, in the two questionnaires, never, past and current drinkers were defined in the same way, and current drinkers reported the consumption frequency and quantity of five alcoholic beverages (sake, shochu, beer, whiskey/brandy and wine). The estimated alcohol intake was closely associated with serum high-density-lipoprotein cholesterol and γ-glutamyltransferase activity equally in the two periods, i.e., before and after the revision.[15] Questions on physical activity were so much changed that analysis of the combined data could not be justified.

Dietary questions inquired about the consumption of selected foods and beverages on average in the past one year. Both consumption frequency and quantity consumed per day were ascertained for brewed coffee, instant coffee, green tea, milk, soy paste soup and rice. Weekly frequency was queried regarding the consumption of breakfast bread, pickles, raw vegetables, fruits, raw fish, soy sauce-cooked fish, broiled fish and meats, using precoded answers. Numbers of cups consumed per day of brewed and instant coffee were added to estimate total coffee consumption, and consumptions of the three fish dishes were also combined. As shown in Table II, dietary assessment was found to be fairly reproducible in a sample of the study subjects (n=93, response rate=86%) with whom the questionnaire was readministered by mail with an interval of 1–3 months.

Age range was 49–55 years in cases and 48–56 in controls, and men aged 52 years accounted for approximately three-quarters of each group. Thus, age was omitted in the analysis. Smoking, alcohol use, rank and body mass index (weight (kg)/height $(m)^2$) were *a priori* selected as potential confounding variables. Smoking was classified into 0, 1–399, 400–799 and ≥800 cigarette-years (cigarettes smoked per day multiplied by years of smoking), and alcohol consumption was categorized into five groups of never, past and current drinkers consuming <30, 30–59 or ≥60 ml of alcohol per day. The rank was classified into low, middle and high ranks, and categories of body mass index were <22.5, 22.5–24.9 and ≥25.0. The consumption of foods and beverages was categorized into three levels as used in the earlier analysis except for coffee and green tea,[13] for which the consumption was classified into four levels. Multiple logistic regression analysis was employed to control for the effects of confounding variables using indicator terms for their categories. Odds ratio (OR) and 95% confidence interval (CI) were derived from the regression coefficient and standard error for an indicator term which corresponded to a certain category of independent variable. The trend of the association was assessed by assigning ordinal scores (0, 1, 2 and so forth) to levels of the independent variable. Reported *P* values are always two-sided, and all computations were done by using the Statistical Analysis System.[16]

RESULTS

Table III shows the relation between selected dietary factors and adenomas of all sizes combined after adjustment for smoking, alcohol use, rank and body mass index. None of the foods and beverages were appreciably associated with the overall risk of adenomas, although meat intake showed a tendency of positive association

Table III. Risk of Adenomas of the Sigmoid Colon according to Consumption of Selected Foods and Beverages[a)]

Food and beverage		Consumption level			*P* value for trend
		Low	Intermediate	High	
Rice[b)]	No.	37/295	121/972	29/290	
	OR (95% CI)	1.0	0.99 (0.67–1.47)	0.81 (0.48–1.36)	0.44
Soy paste soup[c)]	No.	49/392	100/818	38/347	
	OR (95% CI)	1.0	0.99 (0.68–1.42)	0.87 (0.55–1.37)	0.56
Breakfast bread[d)]	No.	107/774	44/518	36/265	
	OR (95% CI)	1.0	0.65 (0.44–0.94)	1.05 (0.69–1.59)	0.60
Pickles[e)]	No.	53/409	29/224	105/924	
	OR (95% CI)	1.0	0.96 (0.59–1.56)	0.85 (0.60–1.22)	0.36
Raw vegetables[e)]	No.	37/309	49/330	101/918	
	OR (95% CI)	1.0	1.26 (0.80–2.00)	0.94 (0.63–1.40)	0.49
Fruits[e)]	No.	88/682	43/334	56/541	
	OR (95% CI)	1.0	1.07 (0.72–1.59)	0.91 (0.63–1.31)	0.64
Fish[e)]	No.	51/468	55/538	81/551	
	OR (95% CI)	1.0	0.94 (0.62–1.40)	1.24 (0.85–1.82)	0.23
Meats[f)]	No.	52/524	103/815	32/218	
	OR (95% CI)	1.0	1.31 (0.92–1.87)	1.48 (0.92–2.37)	0.08
Milk[d)]	No.	32/273	85/672	70/612	
	OR (95% CI)	1.0	1.13 (0.73–1.75)	1.07 (0.68–1.68)	0.86

OR: odds ratio, CI: confidence interval.
Numbers are numbers of cases/controls.
a) Adjusted for smoking, alcohol use, rank and body mass index.
b) Consumption level: <3 (low), 3–4 (intermediate) and ≥ 5 (high) bowls per day.
c) Consumption level: <1 (low), 1 (intermediate) and ≥ 2 (high) bowls per day.
d) Consumption level: <once per week (low), 1–5 times per week (intermediate) and almost daily (high).
e) Consumption level: <4 times per week (low), 4–5 times per week (intermediate) and almost daily (high).
f) Consumption level: <2 (low), 2–3 (intermediate) and ≥ 4 (high) times per week.

with the risk. Adenoma cases were classified into two groups of small (<5 mm) and large (≥ 5 mm) adenomas. Results of the repeated analyses by size of adenoma are given in Table IV. While there was virtually no association between small adenomas and any of the dietary variables studied, the risk of large adenomas was decreased with increasing levels of rice consumption, and was positively associated with meat consumption.

When rice and meats were simultaneously examined in relation to the risk of large adenomas, associations of these two dietary factors with large adenomas were found: ORs for the intermediate and high consumption levels of rice were 0.83 (95% CI 0.45–1.51) and 0.43 (95% CI 0.17–1.07), respectively (trend $P=0.08$), and the corresponding figures for meats were 1.58 (95% CI 0.86–2.89) and 2.38 (95% CI 1.15–4.94), respectively (trend $P=0.02$).

Coffee and green tea showed a moderate positive correlation with the consumptions of meats and rice, respectively, and the former two were also negatively intercorrelated. In the 1557 controls, rank correlation coefficients were 0.14 between coffee (cups per day) and meats (times per week); 0.12 between green tea (cups per day) and rice (bowls per day); and -0.13 between coffee and green tea. Thus, the relation between these two beverages and adenomas was further examined with controlling for rice, meats and either coffee or green tea. As shown in Table V, the overall risk of adenomas was slightly less with higher intake of coffee and green tea, but the decrease was not statistically significant. When analyzed separately for small and large adenomas, the inverse relation tended to be confined to small adenomas. Again, however, the decreased risk of small adenomas was not substantiated statistically for either coffee or green tea.

DISCUSSION

As discussed previously,[13, 14] the present study had several methodological advantages in that almost all men

Table IV. Risk of Small (<5 mm) and Large (≥5 mm) Adenomas of the Sigmoid Colon according to Consumption of Selected Foods and Beverages[a)]

Food and beverage		Consumption level[b)]			P value for trend
		Low	Intermediate	High	
Small adenomas					
Rice	No.	14	51	13	
	OR (95% CI)	1.0	1.10 (0.60–2.04)	0.96 (0.44–2.10)	0.92
Soy paste soup	No.	24	39	15	
	OR (95% CI)	1.0	0.81 (0.48–1.38)	0.72 (0.37–1.40)	0.31
Breakfast bread	No.	42	19	17	
	OR (95% CI)	1.0	0.67 (0.38–1.17)	1.14 (0.63–2.09)	0.97
Pickles	No.	21	16	41	
	OR (95% CI)	1.0	1.33 (0.68–2.62)	0.85 (0.49–1.46)	0.43
Raw vegetables	No.	16	20	42	
	OR (95% CI)	1.0	1.21 (0.61–2.40)	0.90 (0.50–1.63)	0.56
Fruits	No.	36	19	23	
	OR (95% CI)	1.0	1.13 (0.64–2.02)	0.86 (0.50–1.50)	0.64
Fish	No.	23	20	35	
	OR (95% CI)	1.0	0.77 (0.42–1.43)	1.25 (0.72–2.18)	0.36
Meats	No.	24	40	14	
	OR (95% CI)	1.0	1.11 (0.66–1.87)	1.38 (0.70–2.74)	0.37
Milk	No.	14	33	31	
	OR (95% CI)	1.0	0.98 (0.51–1.87)	1.05 (0.55–2.03)	0.83
Large adenomas					
Rice	No.	16	44	7	
	OR (95% CI)	1.0	0.84 (0.46–1.52)	0.45 (0.18–1.13)	0.10
Soy paste soup	No.	17	39	11	
	OR (95% CI)	1.0	1.11 (0.62–2.00)	0.73 (0.33–1.59)	0.48
Breakfast bread	No.	40	15	12	
	OR (95% CI)	1.0	0.61 (0.33–1.12)	0.96 (0.48–1.89)	0.52
Pickles	No.	17	6	44	
	OR (95% CI)	1.0	0.62 (0.24–1.60)	1.15 (0.64–2.05)	0.49
Raw vegetables	No.	13	18	36	
	OR (95% CI)	1.0	1.32 (0.63–2.75)	0.97 (0.50–1.86)	0.72
Fruits	No.	36	11	20	
	OR (95% CI)	1.0	0.67 (0.34–1.35)	0.80 (0.45–1.42)	0.39
Fish	No.	18	23	26	
	OR (95% CI)	1.0	1.13 (0.60–2.13)	1.10 (0.59–2.06)	0.79
Meats	No.	16	36	15	
	OR (95% CI)	1.0	1.53 (0.84–2.80)	2.28 (1.10–4.71)	0.03
Milk	No.	12	30	25	
	OR (95% CI)	1.0	1.08 (0.54–2.15)	1.01 (0.50–2.07)	0.98

OR: odds ratio, CI: confidence interval.
Numbers are numbers of cases.
a) Adjusted for smoking, alcohol use, rank and body mass index.
b) Same as used in Table III.

Table V. Risk of All Adenomas Combined, Small Adenomas (<5 mm) and Large Adenomas (≥5 mm) of the Sigmoid Colon according to Consumption of Coffee and Green Tea[a)]

Cups per day	No. of controls	All adenomas		Small adenomas		Large adenomas	
		No.	OR (95% CI)	No.	OR (95% CI)	No.	OR (95% CI)
Coffee							
0	567	72	1.00	24	1.00	27	1.00
1–2	432	55	0.95 (0.64–1.40)	31	1.55 (0.88–2.74)	14	0.62 (0.32–1.24)
3–4	397	46	0.80 (0.53–1.21)	18	0.87 (0.45–1.67)	19	0.89 (0.47–1.68)
≥5	161	14	0.61 (0.33–1.14)	5	0.55 (0.20–1.53)	7	0.94 (0.38–2.31)
			Trend P=0.10		Trend P=0.24		Trend P=0.84
Green tea							
0–2	384	49	1.00	23	1.00	14	1.00
3–4	563	73	1.00 (0.68–1.48)	32	0.91 (0.52–1.59)	28	1.43 (0.74–2.78)
5–6	438	47	0.79 (0.51–1.21)	16	0.57 (0.29–1.11)	17	1.07 (0.51–2.23)
≥7	172	18	0.77 (0.43–1.37)	7	0.65 (0.27–1.58)	8	1.19 (0.48–2.96)
			Trend P=0.20		Trend P=0.10		Trend P=0.92

OR: odds ratio, CI: confidence interval.
a) Adjusted for smoking, alcohol use, rank, body mass index, rice, meats and either of the listed variables.

in a defined population underwent colonoscopy and that dietary habits as well as other lifestyles were ascertained prior to colonoscopy. These features made the study free of selection and recall bias. A weakness was the use of a rather simple dietary analysis method which was unable to assess nutrient intake, although responses to each of the dietary questions were fairly reproducible.

The present study first demonstrated that low consumption of rice and high intake of meats were independently related to an increased risk of large adenomas, but not of small ones, of the sigmoid colon. It is thus considered that these dietary factors may be involved in the progression of colon adenomas rather than in the initiation. Interestingly, the findings are in agreement with a prospective observation in Japan that mortality from cancer of the sigmoid colon was associated inversely with rice and wheat consumption and positively with meat intake.[17)]

Our observation on meat consumption is consistent with previous studies of colorectal adenomas in Norway,[7)] France[8)] and the United States,[9)] but not with a study in Japan.[10)] The last study, based on cases of colorectal adenomas diagnosed at a cancer hospital and controls recruited from general population by means of telephone directories, reported that the frequency of meat consumption was inversely associated with adenomas of the distal colon; a similar pattern was also noted for adenomas of the proximal colon and rectum separately.[10)]

Since the overall risk of adenomas did not show a clear relation to either meat intake or rice consumption, it would be relevant to consider the size of adenomas in other studies. In a small case-control study of screened subjects in Norway,[7)] adenomas of 5 mm or larger were separated from smaller polyps. Adenomas smaller than 10 mm accounted for roughly 70% in the French case-control study[8)] and in the prospective study in the United States[9)]; the mean size was 9 mm in the latter and was not reported in the former. Another study in Japan did not mention the size of adenomas.[10)] In our study, the mean diameter in the whole series of adenomas was 5 mm, and that of the large adenomas was 7 mm. Adenomas studied in Western countries seem to correspond to the large adenomas in our study or even larger ones.

Epidemiological studies of colon cancer have almost invariably shown intake of vegetables and fruits to be protective,[11, 12)] but evidence is weak as to the protective effect of cereals or carbohydrates against colon cancer.[11)] Intake of starchy foods such as pasta and rice was associated with an increased risk of colorectal cancer in some case-control studies.[18–20)] On the contrary, previous studies of colorectal adenomas have consistently found an inverse association with grain fiber or carbohydrates as well as with vegetables and fruits,[7–9)] except for a study in Japan.[10)] A possible protective effect of starch against colon cancer has drawn less attention than that of fiber, but it has been suggested that indigestible starch reaching the large bowel may exert the same protective effect as has been proposed for dietary fiber.[21)] We failed to find an association between the consumption of raw vegetables and fruits and adenoma risk. Possibly, our dietary questions may have been inadequate to determine the overall consumption of vegetables and fruits.

Because some, but not all, epidemiological studies have reported a decreased risk of colon cancer in relation to

coffee drinking,[22,23] and because experimental evidence has suggested that green tea may inhibit colon carcinogenesis,[24] we made a close inspection of the relation between the consumption of coffee and green tea and adenoma risk. There was only a non-significant tendency of inverse association regarding both coffee and green tea. It seems puzzling that drinking coffee and green tea tended to be associated with a reduced risk of small adenomas rather than large adenomas. Factors linked with the occurrence or initiation of adenomas would be similarly associated with adenomas at a later stage if a proportion of initiated adenomas increase in size regardless of initiating factors. We have no clear explanation for the apparent lack of association with large adenomas, but an inverse association between drinking coffee and green tea and adenomas, whether overall or small, remains to be substantiated.

Based on the same data, but not allowing for dietary factors, we recently observed that alcohol intake, especially the consumption of sake, beer and whiskey, was positively associated with large adenomas but not with small adenomas.[15] It was confirmed that the reported association of alcohol and large adenomas was independent of the consumption of rice and meats (data not shown). We cannot totally rule out the possibility of a chance phenomenon due to subgroup analysis in the observed association between the consumption of rice and meats as well as of specific alcoholic beverages and the risk of large adenomas. Further study taking into account the size of adenoma is needed to corroborate our findings in this unique study population.

ACKNOWLEDGMENTS

This study was supported in part by a Grant-in-Aid for Cancer Research (2-3) from the Ministry of Health and Welfare, Japan. The authors thank the staff of the second ward at the Self-Defense Forces Fukuoka Hospital for their cooperation and Ms. Miyako Kono for her assistance.

(Received August 24, 1992/Accepted October 12, 1992)

REFERENCES

1) Correa, P. and Haenszel, W. The epidemiology of large-bowel cancer. *Adv. Cancer Res.*, **26**, 1–141 (1978).
2) Muto, T., Bussey, H. J. R. and Morson, B. C. The evolution of cancer of the colon and rectum. *Cancer*, **36**, 2251–2270 (1975).
3) O'Brien, M. J., Winawer, S. J., Zauber, A. G., Gottlieb, L. S., Sternberg, S. S., Diaz, B., Dickersin, G. R., Ewing, S., Geller, S., Kasimian, D., Komorowski, R., Szporn, A. and the National Polyp Study Workgroup. The National Polyp Study: patients and polyp characteristics associated with high-grade dysplasia in colorectal adenomas. *Gastroenterology*, **98**, 371–379 (1990).
4) Vogelstein, B., Fearon, E. R., Hamilton, S. R., Kern, S. E., Preisinger, A. C., Leppert, M., Nakamura, Y., White, R., Smits, A. M. M. and Bos, J. L. Genetic alterations during colorectal-tumor development. *N. Engl. J. Med.*, **319**, 525–532 (1988).
5) Editorial. Colorectal cancer: new evidence for the adenoma/carcinoma sequence. *Lancet*, **340**, 210–211 (1992).
6) Hill, M. J., Morson, B. C. and Bussey, H. J. R. Aetiology of adenoma-carcinoma sequence in large bowel. *Lancet*, **i**, 245–247 (1978).
7) Hoff, G., Moen, I. E., Trygg, K., Frøhlich, W., Sauar, J., Vatn, M., Gjone, E. and Larsen, S. Epidemiology of polyps in the rectum and sigmoid colon: evaluation of nutritional factors. *Scand. J. Gastroenterol.*, **21**, 199–204 (1986).
8) Macquart-Moulin, G., Riboli, E., Cornée, J., Kaaks, R. and Berthezène, P. Colorectal polyps and diet: a case-control study in Marseilles. *Int. J. Cancer*, **40**, 179–188 (1987).
9) Giovannucci, E., Stampfer, M. J., Colditz, G., Rimm, E. B. and Willett, W. C. Relationship of diet to risk of colorectal adenoma in men. *J. Natl. Cancer Inst.*, **84**, 91–98 (1992).
10) Kato, I., Tominaga, S., Matsuura, A., Yoshii, Y., Shirai, M. and Kobayashi, S. A comparative case-control study of colorectal cancer and adenoma. *Jpn. J. Cancer Res.*, **81**, 1101–1108 (1990).
11) Willett, W. The search for the causes of breast and colon cancer. *Nature*, **338**, 389–394 (1989).
12) Trock, B., Lanza, E. and Greenwald, P. Dietary fiber, vegetables, and colon cancer: critical review and meta-analyses of the epidemiologic evidence. *J. Natl. Cancer Inst.*, **82**, 650–661 (1990).
13) Kono, S., Shinchi, K., Ikeda, N., Yanai, F. and Imanishi, K. Physical activity, dietary habits and adenomatous polyps of the sigmoid colon: a study of self-defense officials in Japan. *J. Clin. Epidemiol.*, **44**, 1255–1261 (1991).
14) Kono, S., Ikeda, N., Yanai, F., Shinchi, K. and Imanishi, K. Alcoholic beverages and adenomatous polyps of the sigmoid colon: a study of male self-defence officials in Japan. *Int. J. Epidemiol.*, **19**, 848–852 (1990).
15) Honjo, S., Kono, S., Shinchi, K., Imanishi, K. and Hirohata, T. Cigarette smoking, alcohol use and adenomatous polyps of the sigmoid colon. *Jpn. J. Cancer Res.*, **83**, 806–811 (1992).
16) Harrell, F. E., Jr. The LOGIST procedure. *In* "SUGI Supplementary Library User's Guide, 1983 Edition," ed. S. P. Joyner, pp. 181–202 (1983). SAS Institute Inc., Cary, North Carolina.
17) Hirayama, T. Association between alcohol consumption

and cancer of the sigmoid colon: observations from a Japanese cohort study. *Lancet,* **ii,** 725–727 (1989).

18) Haenszel, W., Locke, F. B. and Segi, M. A case-control study of large bowel cancer in Japan. *J. Natl. Cancer Inst.,* **64,** 17–22 (1980).

19) Macquart-Moulin, G., Riboli, E., Cornée, J., Charnay, B., Berthezène, P. and Day, N. Case-control study on colo-rectal cancer and diet in Marseilles. *Int. J. Cancer,* **38,** 183–191 (1986).

20) La Vecchia, C., Negri, E., Decarli, A., D'Avanzo, B., Gallotti, L., Gentile, A. and Franceschi, S. A case-control study of diet and colo-rectal cancer in northern Italy. *Int. J. Cancer,* **41,** 492–498 (1988).

21) Cummings, J. H. and Bingham, S. A. Dietary fibre, fermentation and large bowel cancer. *Cancer Surv.,* **6,** 601–621 (1987).

22) Rosenberg, L. Coffee and tea consumption in relation to the risk of large bowel cancer: a review of epidemiologic studies. *Cancer Lett.,* **52,** 163–171 (1990).

23) Jacobsen, B. K., Kvåle, G. and Heuch, I. Coffee drinking and the risk of colon cancer: unfinished business. *Epidemiology,* **2,** 77–78 (1991).

24) Yamane, T., Hagiwara, N., Tateishi, M., Akachi, S., Kim, M., Okuzumi, J., Kitao, Y., Inagake, M., Kuwata, K. and Takahashi, T. Inhibition of azoxymethane-induced colon carcinogenesis in rat by green tea polyphenol fraction. *Jpn. J. Cancer Res.,* **82,** 1336–1339 (1991).