Gut 1993; **34**: 531–536

Sex differences in colonic function: a randomised trial

J W Lampe, S B Fredstrom, J L Slavin, J D Potter

Abstract

There are sex differences in large bowel cancer rates and a variety of other gastrointestinal disorders possibly because of differences in gut biology. To determine whether men and women have different gastrointestinal responses when consuming identical intakes of dietary fibre, 16 women and 18 men consumed liquid formula diets and 'quick breads' with 0 g, and 10 g, and 30 g of fibre as wheat bran and vegetable fibre. The five test diets were consumed in random order, each treatment lasting 23 days. Mean transit time was faster ($p=0.02$), and stool weights (g/day) were greater ($p=0.0005$) for men than women. Neutral detergent fibre (NDF) excretion was greater in men ($p=0.01$), and women tended to digest more NDF ($p=0.06$). Men and women seemed to respond differently to wheat bran and vegetable fibre with regard to NDF excretion and digestibility. There were no gender differences in the faecal pH or moisture content. Concentrations and daily excretion of the secondary bile acids, lithocholic and deoxycholic acid, were greater for men than women ($p<0.05$). Gender differences in bowel function and bile acid excretion, observed when men and women consumed the same amounts of dietary fibre, may be relevant for understanding colonic disease aetiology and for undertaking future dietary intervention trials.

(*Gut* 1993; **34**: 531–536)

Department of Food Science and Nutrition, University of Minnesota, St Paul
J W Lampe
J L Slavin

Division of Epidemiology, School of Public Health, University of Minnesota, Minneapolis
J W Lampe
J D Potter

Division of Gastroenterology, Hepatology and Nutrition, University of Minnesota Hospital and Clinics, Minneapolis, Minnesota, USA
S B Fredstrom

Correspondence to:
Dr J D Potter, Division of Epidemiology, University of Minnesota, 1300 South Second Street, Minneapolis, MN 55454, USA.

Accepted for publication
31 August 1992

There is a male excess for most chronic diseases, and particularly cancer. Diseases of the biliary and intestinal systems, however, frequently show an excess in women. This is often even more noticeable before the age of menopause. Real sex differences in the physiological functioning of the biliary and intestinal organs may exist, differences that may be pertinent to the aetiology of colon cancer particularly, and are certainly pertinent to the gender differences in the age and subsite distribution of that cancer.[1] In Western societies, rates of colon cancer in premenopausal women are often similar[1] or exceed[2] the male rates at all ages. These women tend to experience their colon cancers somewhat younger and more proximally, while men present older with more distal cancers.[1 2]

There are data from epidemiological, clinical, and animal studies to show that gender, hormonal status, and reproductive events may influence variously, bile composition,[3-6] transit time,[7-9] faecal weight,[8 10 11] and faecal biochemistry.[8 12] Furthermore, in ecological studies, an increased risk for colon cancer has been associated with reduced stool bulk,[13] more alkaline faecal pH,[14] and increased faecal bile acid concentrations.[15] Typically, women have slower transit times and lower faecal bulk.[9 16 17] These gender differences, however, have not always been observed[18 19] and results are often confounded by differences in dietary intake, with the men consuming more dietary fibre than the women.

Few studies have examined gender differences in colonic function under tightly controlled dietary conditions. We report here the results of a randomised trial designed to compare transit time, faecal weight, faecal pH, faecal bile acid excretion, and fibre digestibility in healthy men and women. The hypothesis tested was that premenopausal women would have slower transit times, smaller faecal mass, higher total bile acid excretion, and more alkaline pH than a group of similarly aged men consuming the same defined diets.

Methods

SUBJECTS

Subjects were recruited from the University of Minnesota community. Healthy, non-smokers who had not used antibiotics within 6 months of the start of the study were screened for their ability to complete a rigorous schedule of defined diet ingestion and extensive biological sample collection. All subjects were healthy, had not been taking medication, and had no history of diabetes, heart disease, gastrointestinal malabsorption, or renal disease. The design of the study was approved by the Committee on Use of Human Subjects in Research at the University of Minnesota, and informed written consent was obtained from all subjects before the start of the study.

Forty six subjects were initially randomised into the study, but because of commitment required, nine people dropped out during the first week on the defined diet and three more dropped out after two diet periods. Thirty four subjects (16 women, 18 men) finished all aspects of the study. All the women were premenopausal and none were using oral contraceptives. The mean (SD) age, height, weight, and body mass index for the men and women were 25·9 (7·5) years, 1·79 (0·07) metres, 74·5 (9·1) kg, 23·3 (2·6) kg/m^2 and 26·7 (5·3) years, 1·69 (0·06) metres 63·4 (7·9) kg, 22·1 (1·9) kg/m^2, respectively.

STUDY DESIGN AND SAMPLE ANALYSIS

Before the start of the randomised fibre trial, baseline data were collected for 9 days while subjects ate their normal diet (self selected

diet). Radiopaque pellets (Portex Ltd, Hythe, England) were swallowed on days 1 and 7 to measure transit time, and all stools were individually collected and frozen at −20°C over the 9 day period. Five day diet records were analysed for nutrient and dietary fibre content using a computerised nutrient analysis program (Nutritionist III, N-Squared Computing, Silverton, OR, USA).

Five test diets, varying in absolute amounts and type of fibre, were consumed by all subjects in assigned random order: (1) 0 g added fibre; (2) 10 g total dietary fibre (TDF) as white wheat bran (American Association of Cereal Chemists, St Paul, MN, USA); (3) 30 g TDF as white wheat bran; (4) 10 g TDF as mixed vegetable fibre (VF); (5) 30 g TDF as VF. The vegetable fibre in the 10 g VF and 30 g VF breads was a mixture of pea hull fibre (Fiberich Technologies Inc, Minneapolis, MN, USA), soy polysaccharide (Protein Technologies International, St Louis, MO, USA) and citrus pectin (Hercules, Wilmington, DE, USA), added at levels of 62, 33, and 5% by weight of total fibre, respectively. A 'quick bread', prepared in our laboratory, was the vehicle to deliver the fibres, and a quick bread without added fibre was provided during the 0 g fibre diet. The quick breads formulations were based on the TDF content of the products as reported by the companies. TDF content was also determined in our laboratory by a modification of the current Association of Official Analytical Chemists method.[20]

The subjects consumed a fibre free enteral supplement (Resource, Sandoz Nutrition, Minneapolis, MN, USA), deionised water, and one loaf of quick bread daily. Subjects were instructed to eat all of the quick bread and consume enough liquid supplement daily (in addition to the quick bread) to maintain their usual weight. The quick breads were consumed plain, without spreads. To limit formation of Maillard products in the breads, subjects were instructed not to heat the breads in a conventional oven and instead warm them in a microwave oven.

Each test diet was consumed for 23 days. No adjustment was made for the phase of menstrual cycle. There was a washout period of at least 10 days between each diet period during which subjects resumed their habitual diets. Subjects consumed the test diets for 1 week before any samples were collected. Radiopaque pellets were swallowed on days 7, 13, and 19 of each period for transit time determinations, and all stools were individually collected and frozen from days 7–23.

Subjects recorded all quick bread and nutrition supplement intake and daily exercise for each feeding period. Any bread that was not eaten was returned by the subjects and the uneaten portions were weighed and subtracted from the average bread weight. To ensure greatest compliance by this 'outpatient' group, subjects reported daily to pick up food and drop off faecal samples and diet records. The importance of total faecal collections and adherence to the diet were stressed continuously with the subjects. Daily nutrient and fibre intakes for 6 days during the last week of each feeding period were calculated using the nutrient content of the liquid supplement as reported by the company and the nutrient content of the quick breads analysed in our laboratory as previously described.[21]

All faecal samples were weighed and mean stool weight and mean daily faecal weight were determined. The samples were *x* rayed for pellet content and the time needed to pass each pellet was averaged to calculate mean transit time (MTT).[22] The appearance of the first pellets swallowed on days 13 and 19 were used as the limit markers for faecal composites: starting with stools containing pellets swallowed on day 13, all stools up to the appearance of pellets swallowed on day 19 were included. Composites were homogenised with addition of deionized water and faecal pH was measured. Duplicate aliquots of the homogenates were freeze dried to determine faecal dry weight and faecal moisture content was calculated after correcting for the added water. Faecal acidic sterols were measured by gas chromatography as described previously.[23] Minor bile acids detected in small amounts, were summed and presented as 'miscellaneous bile acids'.

To determine the amount of fibre excreted and digested, the neutral detergent fibre (NDF) content of freeze dried faeces and food samples from the five test diets was analysed by the method of Robertson and Van Soest.[24] Heat stable α amylase (Sigma, St Louis, MO, USA) and sodium sulphite (Aldrich Chemical, Milwaukee, WI, USA) were added to improve the removal of starch and protein. Fibre digestibility was calculated as: (g faecal fibre − g fibre ingested)/g fibre ingested.

STATISTICAL ANALYSIS

Bowel function parameters, bile acid excretion, and fibre digestibility in men and women were compared using repeated measures analysis of variance where gender was used as a group variable for subjects and the interaction of gender and diet was included in the model. Data are presented as means (SD) by gender.

Results

The effects of fibre type and dose on bowel function characteristics were published previously[25] and are not discussed here.

Mean transit times were consistently faster ($p=0{\cdot}02$) and faecal wet weights were consistently greater ($p=0{\cdot}0005$) for men than women on all diets (Fig 1), despite the same fibre intakes by men and women (Table I). Faecal dry weights, 35 (2) and 26 (3) g/day for men and women, respectively, followed an identical pattern to that of wet weights ($p<0{\cdot}0001$). The overall faecal moisture content (70·7 (1·8) and 70·5 (1·9)% for men and women, respectively) and the faecal pH (7·4 (0·1) and 7·4 (0·2) for men and women, respectively) were similar between the sexes.

The concentrations and daily excretion of faecal bile acids are presented in Figure 2 and Tables II and III. Both the concentrations and daily excretion of the secondary bile acids,

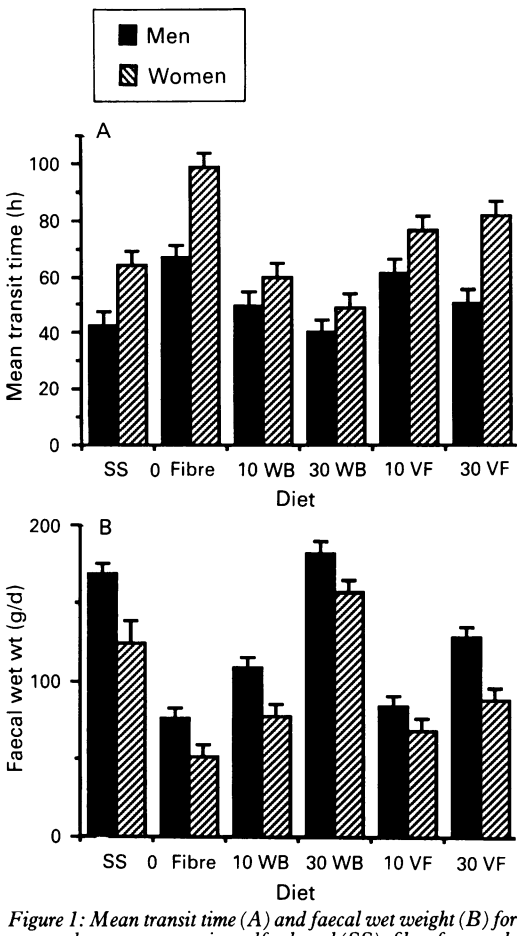

Figure 1: Mean transit time (A) and faecal wet weight (B) for men and women consuming self-selected (SS), fibre-free, and wheat bran (WB) and vegetable fibre (VF) test diets. (Values, mean (SD).)

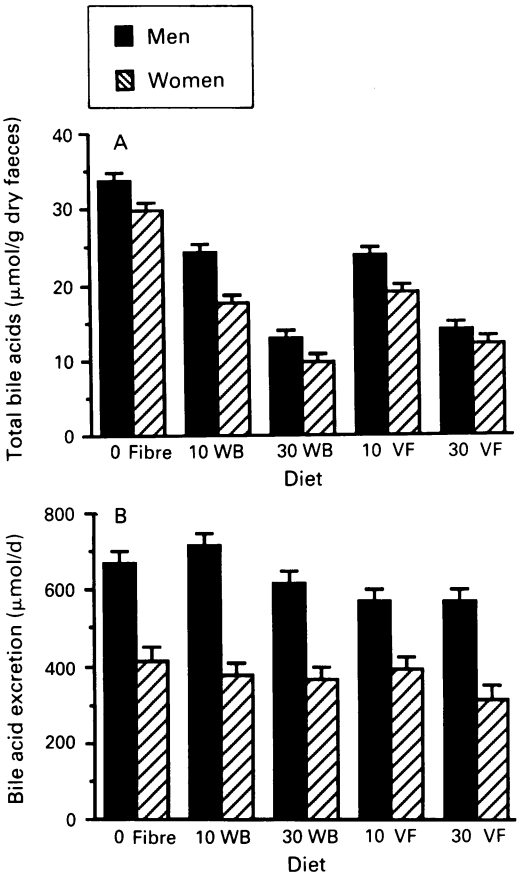

Figure 2: Mean total bile acids (A) and bile acid excretion (B) for men and women consuming fibre free and wheat bran (WB) and vegetable fibre (VF) test diets. (Values, mean (SD).)

lithocholic and deoxycholic acid, were significantly greater ($p<0.05$) for men than women, as was daily excretion of chenodeoxycholic acid. As a result, the total bile acid concentration was greater for men than women on all diets ($p=0.02$) and, with the added effect of greater stool weights among men, daily total bile acid excretion was also greater for men ($p<0.0001$) (Fig 2). The only significant gender by diet interaction observed for the bile acid data was for daily lithocholic acid excretion ($p=0.04$), where men and women seemed to respond differently to the two doses of wheat bran and vegetable fibre. When the data were analysed for men and women separately, lithocholic acid excretion tended to decrease in men (350 (103) *v* 311 (95) μmol/day, $p=0.09$) but not women (168 (50) *v* 164 (49) μmol/day, $p=0.5$) with higher wheat bran (10 g *v* 30 g); it tended to decrease in women (169 (71) *v* 134 (89) μmol/day, $p=0.08$), but not men (256 (82) *v* 253 (67) μmol/day, $p=0.9$), with higher vegetable fibre (10 g *v* 30 g). There was no difference in the ratios of secondary to primary bile acids or of lithocholic acid to deoxycholic acid between the sexes.

Dietary fibre intakes during the test diet periods, calculated as TDF and NDF, are presented in Table IV. The amount of fibre as TDF and NDF were the same for the 0 g fibre bread and for the two wheat bran breads; NDF was 60% of the TDF value for the vegetable fibre breads. Faecal NDF excretion was greater in men than women ($p=0.01$) (Table IV) and the interaction of gender and diet was highly significant ($p<0.0001$). Men excreted more NDF than women with consumption of the 30 g fibre doses. Individual NDF digestibilities varied widely on all diets. However, digestibility tended to be greater in women than men (Table IV) ($p=0.06$). The interaction of gender and diet ($p=0.015$) seemed to be due primarily to greater digestion of the 10 g wheat bran and 30 g vegetable fibre diets in women.

Despite similar dietary fibre consumption by

TABLE I *Comparison of daily macronutrient and dietary fibre intakes for men and women during the self-selected diet period and the controlled feeding periods. (Values mean (SD))*

	Self-selected			*Controlled feeding*		
	Men	*Women*	p *value*	*Men*	*Women*	p *value*
Energy (MJ)	10·54 (1·98)	8·34 (1·76)	0·003	12·64 (2·3)*	8·62 (0·80)	0·0001
Protein (g)	86 (19)	67 (18)	0·007	109 (19)	75 (7)	0·0001
Fat (g)	105 (29)	78 (21)	0·005	120 (19)	85 (7)	0·0001
Total dietary fibre (g)	12·1 (5·6)	13·8 (8·3)	0·5	19·0 (0·8)	18·8 (0·5)	0·4

* Data for individuals were averaged across all test diets prior to calculation of gender mean.

TABLE II *Faecal bile acid concentrations (μmol/g dry faeces) for men (n=18) and women (n=16). (Values mean (SD))*

	Men	*Women*	p *value*
Lithocholic acid	10·09 (1·15)	7·66 (1·13)	0·005
Deoxycholic acid	9·47 (1·21)	7·56 (1·48)	0·049
Chenodeoxycholic acid	0·87 (0·16)	0·81 (0·15)	0·7
Cholic acid	0·20 (0·15)	0·15 (0·08)	0·6
Miscellaneous	1·07 (0·28)	1·39 (0·26)	0·12
Total*	21·69 (2·39)	17·58 (2·63)	0·024

* Summation of the individual and miscellaneous bile acids.

TABLE III *Daily faecal bile acid excretion (μmol/day) for men (n=18) and women (n=16). (Values mean (SD))*

	Men	*Women*	p *value*
Lithocholic acid	294 (24)	164 (26)	0·0001
Deoxycholic acid	272 (31)	158 (30)	0·0001
Chenodeoxycholic acid	25 (5)	17 (3)	0·02
Cholic acid	7 (6)	3 (2)	0·23
Miscellaneous	32 (7)	32 (4)	1·0

both sexes during the self selected and controlled feeding periods, energy and macronutrient intakes were greater for men and women (Table I). When energy intake was included as a covariate in the statistical model, bowel function differences between the sexes were no longer statistically significant. This suggests that the sex differences may be partly the result of differences in energy intake between men and women. In these subjects, sex and energy intake were so closely correlated as to exclude virtually any overlap in the male and female energy intake distributions. This ensured almost complete confounding between energy intake and sex. However, means adjusted for energy intake were similar to the unadjusted means. Unlike the bowel function parameters, faecal bile acid concentrations were still significantly higher in men than women even after adjusting for energy and fat intake.

Regression analysis of the data undertaken for men and women separately does not show a clear diet dependent association between energy intake and faecal output: there was no association between daily energy intake and daily faecal wet weights on the self selected diet (men: r= 0·18, p=0·5; women: r=0·4, p=0·2) and 30 g levels of wheat bran (men: r=0·34, p=0·2; women: r=0·0, p=0·9) and vegetable fibre (men: r=0·06, p=0·8; women: r=0·2, p=0·5); the association was significant for men, but not women, when the subjects consumed 10 g doses of wheat bran (men: r=0·53; p=0·03; women: r=0·4, p=0·14) and vegetable fibre (men: r= 0·6, p=0·01; women: r=0·09, p=0·7); for the 0 g fibre diet, there was a positive association for both men and women (men: r=0·51, p=0·03; women: r=0·7, p=0·001). Similar results were observed when energy intake and faecal dry weight were analysed.

Discussion

We have previously postulated an important role for sex differences in gut function in explaining differences in the risk of colon cancer[2 3] and other gastrointestinal disorders.[3] In the present study, we observed significant gender differences in bowel function parameters, faecal bile acid excretion, and faecal NDF excretion, even though men and women consumed the same absolute amount of fibre on each test diet.

Gastrointestinal transit times were shorter and faecal output greater for men than women. Similar results have been reported previously when men and women consumed their habitual diets[9 10 16 17] and when fed controlled fibre diets.[7 11] Using a single film technique for assessment of segmental colon transit, Metcalf *et al*[9] showed that the sex difference in transit time was most apparent in the right colon, with a smaller difference in the left colon, and no difference in the rectosigmoid. Ecological studies show higher stool weights in those populations with lower colon cancer risks,[26 27] but to date no studies have shown an association between colon cancer risk and transit time. The findings of Metcalf *et al*[9] provide additional detail on the sex difference we report here and are especially interesting in light of the epidemiological data that show that women have an excess of proximal cancers compared with men throughout life.[2]

Faecal moisture content was the same for men and women. Thus, the significant sex difference in faecal wet weight was a function of difference in faecal dry matter. By administering drugs which change colonic motility, Stephen *et al*[28] showed that changing transit time altered microbial growth. Greater faecal bulk as a function of faster transit time was due to an increase in faecal bacterial mass and in excretion of non-starch polysaccharides.[28] Stephen *et al* attributed the efficiency of anaerobic microbial growth not only to substrate availability but also to the rate of passage of material through the lumen: somewhat counter intuitively, microbial growth is greater and a greater mass of bacteria is produced with faster transit.[28] The pattern of faster gastrointestinal transit and greater faecal weight and NDF excretion in men compared with women in our study suggests that men have greater faecal bacterial mass than women despite a tendency to ferment less fibre. This suggests either that more non-fibre substrate is available in male colons (consistent with their higher energy intake and the possible influence of energy intake on stool weight) or that male and female colonic flora differ substantially. One possible explanation for the positive relationship between faster transit time and greater stool mass is that a more rapid transit time may reduce the likelihood of build up of 'toxic'/'antibiotic' metabolites in the colonic microenvironment (for example compounds which may inhibit bacterial growth). It does suggest that, for whatever reason, there are male/female differences in the capacity to support the colonic microflora.

It has been reported previously that faecal output is positively correlated and gastrointestinal transit is negatively correlated with energy intake and total food consumption.[16 29] Thus, reported sex differences in bowel function may be the result of energy intake differences between men and women. Unfortunately, in our study, the complete confounding of energy intake and gender made it difficult to resolve this issue. Men and women had similar fibre intakes

TABLE IV *Total dietary fibre (TDF) intake and neutral detergent fibre (NDF) intake, excretion, and digestibility with consumption of wheat bran (WB) and vegetable fibre (VF) breads by 18 men and 16 women. (Values mean (SD))*

	Fibre intake from quick breads (g/d)		*Faecal NDF excretion (g NDF/d)*		*NDF digestibility (%)*	
Diet	*TDF*	*NDF*	*Men*	*Women*	*Men*	*Women*
0 g fibre	2·2 (0·1)	3·2 (0·1)	1·1 (0·6)	1·1 (0·6)	64 (21)	66 (21)
10 g WB	11·2 (0·8)	11·5 (1·1)	7·5 (1·7)	6·3 (1·4)	34 (15)	42 (17)
30 g WB	28·9 (2·0)	30·4 (1·4)	19·2 (2·4)	17·2 (4·2)	37 (8)	43 (13)
10 g VF	14·7 (0·8)	10·2 (0·5)	6·7 (1·9)	6·5 (2·4)	33 (20)	33 (26)
30 g VF	36·8 (1·8)	26·6 (1·2)	19·0 (4·4)	13·0 (5·9)	29 (17)	51 (22)

during the self selected diet period despite significant differences in intakes of other macronutrients (Table I). Interestingly, no association between energy intake and faecal output was observed when the subjects consumed the self selected diet or 30 g fibre doses. The strongest association was observed on the 0 g fibre diet. This suggests that when fibre availability in the colonic lumen is low (that is, no or low fibre) the volume of other macronutrients entering the colonic lumen may become more important in determining faecal output. In our study, men and women consumed the same amount of starch and dietary fibre since both ate one loaf of quick bread/day. The only difference in carbohydrate intake between the sexes was as maltodextrin and sugar from the liquid formula. Refined sugars,[30] in addition to starch,[31] are known to influence gut function and the composition of bowel contents. Thus, these other aspects of diet must be considered. Additional controlled studies are needed to address this problem.

The colonic pH is largely determined by fermentation and the production of short chain fatty acids (SCFA).[32] In humans, fibre fermentation occurs predominantly in the caecum and proximal colon, and SCFA concentrations are highest and the pH is lowest in these areas.[33] SCFA are rapidly absorbed and the pH rises as the contents proceed distally.[33] Stephen *et al*[8] found the faecal pH, corrected for stool weight, to be indeed lower in men than women. In a study in the US and China, faecal pH, not corrected for fibre intake differences, was also observed to be lower in men (6·4) than women (6·9) when study subjects consumed their habitual diets.[4] In men, if less fibre is fermented in the caecum and proximal colon, continued fermentation and SCFA production the length of the colon and in the rectosigmoid may contribute to the output of more acidic stools. In women, slower transit and greater fermentation in the proximal colon with concomitant absorption of SCFA may reduce the substrate available for fermentation in the rectosigmoid and result in more alkaline stools. In our study, however, where fibre intakes were the same for men and women, faecal pH was not significantly different between the sexes. It is not clear what explains the failure to observe the gender differences in faecal pH that others have reported. One important difference is that subjects in our study consumed a highly controlled liquid diet, rather than a diet of regular food.

Based on the epidemiological research which suggests: (1) that female rates of colon cancer at premenopausal ages may exceed male rates[2] and (2) that concentrations of faecal bile acids are higher in populations at high risk for the development of colon cancer,[13 26 27 34] we hypothesised that women would have higher bile acid excretion than men. However, our results indicate that secondary bile acid concentrations and daily bile acid excretion were actually greater in men than women.

There are few studies of faecal bile acid excretion in men and women with which to compare our results, and the results of these studies are conflicting. No significant sex difference in faecal bile acid excretion was detected in a group of 25 subjects habitually consuming low fibre diets,[35] or in men and women with mean daily fibre intakes of 15·4 and 11·9 g, respectively.[19] Likewise, Reddy *et al*[36] found no sex difference in faecal bile acid excretion when men and women ate their usual diets and diets supplemented with wheat and rye flour. More recently, Yeung *et al*[4] reported significantly higher concentrations of bile acids in women than men consuming their habitual diets in Sha Giao, People's Republic of China and in San Francisco County, United States. In a controlled fibre feeding study, Stasse-Wolthuis *et al*[11] observed that when men and women consumed test diets containing various dietary fibres, men and women seemed to respond differently to the fibre containing diets. Bile acid excretion was greater for male subjects consuming citrus pectin or fruits and vegetables compared with women on the same diets, while excretion was reduced for men on the bran diet and was enhanced for women consuming bran. None of the studies, including ours, controlled for women's menstrual cycles. Despite this lack of control, significant, albeit disparate, differences in bile acid excretion have been observed. Since female hormones are known to alter bile acid secretion,[37] controlled, long term studies taking into account the subjects' hormone status are warranted.

In conclusion, there were significant differences in transit time, faecal bulk, and bile acid excretion between men and women consuming the same absolute amounts of fibre. Furthermore, faecal fibre excretion was greater in men than women; correspondingly, women tended to digest more fibre than men. The findings are consistent with a lower degree of colonic fermentation in men than women and provide additional evidence for important sex differences in bowel function between men and women.

This study was supported by NCI Grant CA46618 and the Minnesota Agricultural Experiment Station (18–64). JWL currently receives support from NCI (5T32 CA09607).

Presented in part at the American Association for Cancer Research meeting, Washington DC, May 1990.

The authors thank Dr W C Duane, GI Section, Veterans Administration Medical Center, Minneapolis, MN for faecal bile acid determination, and Dr W O Thompson, Office of Research Computing and Statistics, Medical College of Georgia, Augusta, GA, for advice and assistance with statistical analyses. The authors are also grateful to Mrs E A Melcher and Mrs K S Baglien for their assistance during the study. Resource® was provided by Sandoz Nutrition Inc.

1 Faivre J, Bedenne L, Boutron MC, Milan C, Collonges R, Arveux P. Epidemiological evidence for distinguishing subsites of colorectal cancer. *J Epidemiol Community Health* 1989; **43**: 356–61.

2 McMichael AJ, Potter JD. Reproduction, endogenous and exogenous sex hormones, and colon cancer: a review and hypothesis. *J Natl Cancer Inst* 1980; **65**: 1201–7.

3 McMichael AJ, Potter JD. Do intrinsic sex differences in lower alimentary tract physiology influence the sex-specific risks for bowel cancer and other biliary and intestinal diseases? *Am J Epidemiol* 1983; **118**: 620–7.

4 Yeung KS, McKeown-Eyssen GE, Li GF, Glazer E, Hay K, Child P, *et al*. Comparisons of diet and biochemical characteristics of stool and urine between Chinese populations with low and high colorectal cancer rates. *J Natl Cancer Inst* 1991; **83**: 46–50.

5 Weisberg HF. Pathogenesis of gallstones. *Ann Clin Lab Sci* 1984; **14**: 243–51.

6 Fisher MM, Yousef IM. Sex differences in the bile composition of human bile: studies in patients with and without gallstones. *CMA Journal* 1973; **109**: 190–3.

7 Gear JSS, Brodribb AJM, Ware A, Mann JI. Fibre and bowel transit times. *Br J Nutr* 1981; **45**: 77–82.

8 Stephen AM, Wiggins HS, Englyst HN, Cole TJ, Wayman BJ, Cummings JH. The effect of age, sex and level of intake of dietary fibre from wheat on large bowel function in thirty healthy subjects. *Br J Nutr* 1986; **56**: 349–61.

9 Metcalf AM, Phillips SF, Zinsmeister AR, MacCarty RL, Beart RW, Wolff BG. Simplified assessment of segmental colonic transit. *Gastroenterology* 1987; **92:** 40–7.

10 Davies GJ, Crowder M, Reid B, Dickerson JWT. Bowel function measurements of individuals with different eating patterns. *Gut* 1986; **27:** 164–9.

11 Stasse-Wolthuis M, Albers HFF, van Jeveren JGC, Wil de Jong J, Hautvast JGAJ, Hermus RJJ, *et al.* Influence of dietary fiber from vegetables and fruits, bran or citrus pectin on serum lipids, fecal lipids, and colonic function. *Am J Clin Nutr* 1980; **33:** 1745–56.

12 Storer GB, Illman RJ, Trimble RP, Snoswell AM, Topping DL. Plasma and caecal volatile fatty acids in male and female rats: effects of dietary gum arabic and cellulose. *Nutr Res* 1984; **4:** 701–7.

13 Jensen OM, MacLennan R, Wahrendorf J. Diet, bowel function, fecal charcteristics, and large bowel cancer in Denmark and Finland. *Nutr Cancer* 1982; **4:** 5–19.

14 Thorton JR. High colonic pH promotes colorectal cancer. *Lancet* 1981; i: 1081–2.

15 Reddy BS, Wynder EL. Metabolic aspects of colon cancer: fecal bile acid and neutral sterols in colon cancer patients and patients with adenomatous polyps. *Cancer* 1977; **39:** 2533–9.

16 Kelsay JL, Clark WM. Fiber intakes, stool frequency, and stool weights of subjects consuming self-selected diets. *Am J Clin Nutr* 1984; **40:** 1357–60.

17 Rao SSC, Read NW, Brown C, Bruce C, Holdsworth CD. Studies on the mechanism of bowel disturbance in ulcerative colitis. *Gastroenterology* 1987; **93:** 934–40.

18 Wyman JB, Heaton KW, Manning AP, Wicks ACB. Variability of colonic function in healthy subjects. *Gut* 1978; **19:** 146–50.

19 Eastwood MA, Brydon WG, Baird JD, Elton RA, Helliwell D, Smith JH *et al.* Fecal weight and composition, serum lipids, and diet among subjects aged 18 to 80 years not seeking health care. *Am J Clin Nutr* 1984; **40:** 628–34.

20 Prosky L, Asp NG, Furda I, De Vries J, Schweizer TF, Harland B. Determination of insoluble, soluble, and total dietary fiber in foods and food products: interlaboratory study. *J Assoc Off Anal Chem* 1988; **71:** 1017–23.

21 Lampe JW, Slavin JL, Baglien KS, Thompson WO, Duane WC, Zavoral JH. Serum lipid and fecal bile acid changes with cereal, vegetable, and sugar-beet fiber feeding. *Am J Clin Nutr* 1991; **53:** 1235–41.

22 Cummings JH, Jenkins DJA, Wiggins HS. Measurement of the mean transit time of dietary residue through the human gut. *Gut* 1976; **17:** 210–8.

23 Subbiah MT. Hyocholic acid as internal standard for quantitation of human fecal bile acids. *J Lipid Res* 1973; **14:** 692–4.

24 Robertson JB, Van Soest PJ. Dietary fiber estimation in concentrate feed stuffs. *J Animal Sci* 1977; **45** (suppl 1): 254–5.

25 Lampe JW, Slavin JL, Melcher EA, Potter JD. Effects of cereal and vegetable fiber feedings on potential risk factors for colon cancer. *Cancer, Epidemiology, Biomarkers and Prevention* 1992; **1:** 207–11.

26 IARC Intestinal Microecology Group. Dietary fibre, transit-time, faecal bacteria, steroids, and colon cancer in two Scandinavian populations. *Lancet* 1977; ii: 207–11.

27 Reddy BS, Hedges AR, Laakso K, Wynder EL. Metabolic epidemiology of large bowel cancer: fecal bulk and constituents of high-risk North American and low-risk Finnish population. *Cancer* 1978; **42:** 2832–8.

28 Stephen AM, Wiggins HS, Cummings JH. Effect of changing transit time on colonic microbial metabolism in man. *Gut* 1987; **28:** 601–9.

29 Wrick KL, Robertson JB, Van Soest PJ, Lewis BA, Rivers JM, Roe DA, *et al.* The influence of dietary fiber source on human intestinal transit and stool output. *J Nutr* 1983; **113:** 1464–79.

30 Kruis W, Forstmaier G, Scheurlen C, Stellaard F. Effect of diets low and high in refined sugars on gut transit, bile acid metabolism, and bacterial fermentation. *Gut* 1991; **32:** 367–71.

31 Stephen AM. Starch and dietary fibre: their physiological and epidemiological interrelationships. *Can J Physiol Pharmacol* 1991; **69:** 116–20.

32 Rubenstein R, Howard AV, Wrong OM. *In vivo* dialysis of faeces as a method of stool analysis. IV. The organic anion component. *Clin Sci* 1969; **37:** 549–64.

33 Cummings JH, Pomare EW, Branch WJ, Naylor CPE, MacFarlane GT. Short chain fatty acids in human large intestine, portal hepatic and venous blood. *Gut* 1987; **28:** 1221–7.

34 Crowther JS, Drasar BS, Hill MJ, MacLennan R, Magnin D, Peach S, *et al.* Faecal steroids and bacteria and large bowel cancer in Hong Kong by socio-economic groups. *Br J Cancer* 1976; **34:** 191–8.

35 Ghoos Y, Rutgeerts P, Vantrappen G, Hiele M, Schurmans P. The effect of long-term fibre and starch intake by man on faecal bile acid excretion. *European J Clin Invest* 1988; **18:** 128–32.

36 Reddy BS, Sharma C, Simi B, Engle A, Laakso K, Puska P, *et al.* Metabolic epidemiology of colon cancer: effect of dietary fiber on fecal mutagens and bile acids in healthy subjects. *Cancer Res* 1987; **47:** 644–8.

37 Lynn J, Williams L, O'Brien J, Wittenberg J, Egdahl RH. Effects of estrogen upon bile: implications with respect to gallstone formation. *Ann Surg* 1973; **178:** 514–24.