Risks Associated with Source of Fiber and Fiber Components in Cancer of the Colon and Rectum

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ABSTRACT

In this case-control study, we examined the food sources of fiber and fiber solubility to determine whether particular components of dietary fiber were differentially associated with risk of colon and rectal cancer. In Western New York, cases with pathologically confirmed, single, primary cancers of the colon and rectum as well as age-, sex- and neighborhood-matched controls were interviewed from 1976–1986. The sample included 428 colon case-control pairs (229 females, 205 males) and 422 rectal case-control pairs (145 females, 277 males). Subjects were interviewed regarding usual quantity and frequency of consumption of foods. For the colon, risk decreased with intake of grain fiber for both females and males and with intake of fruit/vegetable fiber for males only. Insoluble grain fiber was more strongly associated with risk than soluble grain fiber. For the rectum, fruit/vegetable fiber was associated with decreased risk, whereas grain fiber was not. There was no difference in risk for soluble and insoluble fiber components for the rectum. Analysis of risk associated with fiber by food source and by components of the fiber may provide insight into possible mechanisms of a fiber effect on cancer of the colon and rectum.

INTRODUCTION

Since Burkitt (1) first hypothesized a protective role for fiber in the etiology of cancer of the large bowel, there has been considerable interest in examination of the role of fiber. However, dietary fiber is not a single entity. Its composition varies among plants, and the components of dietary fiber differ widely both in their physical properties (2) and in their effects in the large intestine (3). The tremendous variability in the rate and degree of fermentation of different types of fiber has important consequences for the intestinal microflora (4). By-products of fiber fermentation by the microflora, as well as certain of the fiber components themselves, have been shown to affect carcinogenesis and cell proliferation in the large bowel (5, 6). There is some evidence from case-control studies that a protective effect of fiber is more strongly related to fruit and vegetable intake or to fruit and vegetable fiber intake rather than to grain or grain fiber intake (7–11). Fruit and vegetable fiber tends to be more fermentable and to contribute less to fecal bulk than the highly lignified grain fiber. We have previously published data indicating that fiber adjusted for fat intake may be protective in cancer of the colon and rectum (12, 13). We examine here associations with dietary fiber by food source of the fiber, by fiber solubility, and by fiber component to determine whether risk was more strongly related to fiber of one type.

MATERIALS AND METHODS

This study of cancer of the colon and rectum has been described in detail elsewhere (12, 13). Briefly, incident, single, pathologically confirmed cases of colon and rectal cancer in Erie, Niagara, and Monroe counties in Western New York were identified by nurse interviewers. Colon cases were those identified during 1975-1984; cases of rectal cancer were adenomatous cancers of the rectum identified in 1978-1986. Cases of cancer of the rectosigmoid and the anus were not included in this series because of insufficient numbers for analysis. All subjects were Caucasians.

Cases were identified from hospital pathology records and their physicians were then contacted for permission to interview the cases. Only relatively alert, healthy subjects could tolerate the 2.5-h interview. We were able to interview 65% of colon cases and 54% of rectal cases.

Controls were matched to cases for age (±5 years), sex, and neighborhood. The intention of using neighborhood controls was to control for both socioeconomic status and ethnicity in order to focus the inquiry on dietary differences. There were no significant differences between cases and controls in either age or education. Controls were selected by a standardized protocol requiring interviewers to approach systematically those residences closest to the home of the case, first on one side of the house, then the other, and then across the street. Interview attempts were made at different times of the day, including evenings, and on different days of the week, including weekends. If there was anyone at home, a census of the household was taken to determine whether there was a match resident in that home. When a match was identified, that person was pursued vigorously to obtain an interview. If the potential control refused to participate, the interviewer went on to the next house designated by the protocol. We interviewed 53% of eligible controls. This study cannot be considered population based but should rather be viewed as a case series consisting simply of persons selected from the major hospitals in the three counties who were successfully interviewed and their matched controls who we were able to interview.

An exhaustive dietary interview was developed after initial pilot testing. Reliability and validity of the questionnaire was tested (14, 15) and was found to be similar for cases and controls. Most of the interview focused on usual food intake. For cases, the period 1 y prior to the onset of symptoms was assessed and for controls the year prior to the interview was used as the time referent. (Median onset of symptoms was 2 months before diagnosis.) Questions included information on frequency of intake (from 12 possible categories), seasonality of intake, whether each food was eaten raw or cooked, and, if cooked, if the food was fresh, canned, or frozen. Portion size was quantified as multiples of the portion in a pictured example. From this information, an index of 14 nutrients and energy intake was determined using United States Department of Agriculture and other published food composition data (16-18).

Total dietary fiber was calculated from the tables of Paul and Southgate (17) and those of Lanza and Butrum (19). Intake of cellulose, hemicellulose, lignin, and total insoluble fiber, determined by the detergent method of Van Soest (20, 21), was calculated using values compiled by Horvath and Robertson (22). Insoluble fiber values, equivalent to neutral detergent fiber or neutral detergent residue, are obtained by extraction through a neutral detergent procedure. The three subfractions, hemicellulose, cellulose, and lignin, are computed by difference. Hemicellulose is the difference between neutral detergent fiber and acid detergent fiber, cellulose is the weight loss upon treatment with 72%...
Because the number of cases of rectal cancer was smaller than that of colon cancer,
for males and for males for colon cancer and for males for rectal cancer were operative, control for fat would be important. Analyses were conducted both with and without fat as a covariate.

Matched analysis of the case-control pairs was computed by conditional logistic regression. Subjects were ordered by the relative magnitude of their intake of fiber and classified into categories. Analysis was by quartiles for females and males for colon cancer and for males for rectal cancer. Because the number of cases of rectal cancer was smaller for females (145 cases), analysis was by tertiles for this group. Cutoff points for categories were based on an even distribution of controls to each category within sex and site groups.

RESULTS

Mean intake of total dietary fiber, fruit/vegetable fiber and fiber from grains is shown in Table 1. Mean intakes were similar for controls of the same sex for colon and rectal cancer. Mean intake of cases was not significantly different from that of controls with the exception of males with rectal cancer whose intake of fruit/vegetable fiber for males, while for females, such an association was not apparent. For grain fiber, risk decreased as intake increased, especially for males. The upper quartile odds ratio was 0.30 for males and 0.80 for females. For both males and females, there was a significant linear trend of decreased risk of colon cancer associated with increased intake of grain fiber.

For rectal cancer, after adjustment for fat, risk was decreased in the upper quartile of total fiber intake for males and the upper tertile for females. Unlike the colon, this protective effect was more strongly associated with the fruit/vegetable, rather than the grain, component of total dietary fiber. For males there was an odds ratio of 0.26 associated with upper quartile intake of fruit/vegetable fiber as well as a significant linear trend; the risk associated with upper quartile intake of grain fiber was 1.20. For females there was also a greater drop in risk associated with fruit/vegetable than with grain fiber intake; neither odds ratio was significantly different from 1.0, nor was the test for linear trend significant.

These analyses were repeated for fruit/vegetable fiber controlling for grain fiber and fat, and results were of similar magnitude to those without control for grain fiber. Similarly, associations between risk and intake of grain fiber did not change after control for fruit/vegetable fiber (data not shown).

Fiber Solubility. Next, we considered the soluble and insoluble fractions of grain and fruit/vegetable fiber to determine whether there was an effect more particularly associated with one fraction than with another (Table 3). For colon cancer, insoluble grain fiber was associated with a significant decrease for rectal cancer which was significantly lower for cases than for controls (not shown). For fruit/vegetable and for grain fiber, insoluble fiber constituted about 60% of the total.

Total Fiber and Fiber Source. In Table 2, risks associated with increased intake of total fiber, fruit/vegetable fiber, and grain fiber are shown. All of these analyses were adjusted for fat as a continuous variable. In analysis without adjustment for fat (data not shown), results were in the same direction but closer to unity. The exception was for grain fiber; there was a significant positive association of grain fiber with risk of rectal cancer in males before adjustment for fat. The fourth quartile odds ratio was 1.62.

For colon cancer, after adjustment for fat, there was no significant association between intake of total fiber and risk for either males or females, although there was some evidence of a trend toward decreased risk with increased intake. There was a significant linear trend for decreased risk associated with increased intake of fruit/vegetable fiber for males, while for females, such an association was not apparent. For grain fiber, risk decreased as intake increased, especially for males. The upper quartile odds ratio was 0.30 for males and 0.80 for females. For both males and females, there was a significant linear trend of decreased risk of colon cancer associated with increased intake of grain fiber.

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Fiber Solubility. Next, we considered the soluble and insoluble fractions of grain and fruit/vegetable fiber to determine whether there was an effect more particularly associated with one fraction than with another (Table 3). For colon cancer, insoluble grain fiber was associated with a significant decrease

<table>
<thead>
<tr>
<th>Colon</th>
<th>Total dietary fiber</th>
<th>Fruit/vegetable fiber</th>
<th>Grain fiber</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>No.</td>
<td>223</td>
<td>20.3 ± 9.3*</td>
</tr>
<tr>
<td>Cases</td>
<td>223</td>
<td>20.9 ± 9.7</td>
<td>14.8 ± 8.7</td>
</tr>
<tr>
<td>Controls</td>
<td>205</td>
<td>24.1 ± 9.5</td>
<td>16.3 ± 7.8</td>
</tr>
<tr>
<td>Males</td>
<td>205</td>
<td>24.8 ± 11.1</td>
<td>17.2 ± 9.1</td>
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<tr>
<td>Recess</td>
<td>Females</td>
<td>145</td>
<td>19.3 ± 9.8</td>
</tr>
<tr>
<td>Cases</td>
<td>145</td>
<td>20.1 ± 9.4</td>
<td>15.0 ± 8.5</td>
</tr>
<tr>
<td>Controls</td>
<td>277</td>
<td>24.3 ± 10.7</td>
<td>16.6 ± 8.2</td>
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<tr>
<td>Males</td>
<td>277</td>
<td>24.9 ± 11.1</td>
<td>18.1 ± 10.1</td>
</tr>
<tr>
<td>* Mean ± SD.</td>
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<tr>
<td>$t$ test for case-control difference, $P &lt; 0.01$.</td>
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</table>
in risk. There was no apparent association between soluble grain fiber and risk. For rectal cancer, the effect on risk for both colon and rectal cancer was not different for soluble and insoluble fruit/vegetable fiber. The pattern of a protective effect associated with both soluble and insoluble components was similar to that for total fruit/vegetable fiber for both males and females.

Risks associated with fruit/vegetable hemicellulose, cellulose, and lignin are described in Table 4. Risk of colon cancer associated with upper quartile intake of fruit and vegetable lignin was significantly decreased for males; risks associated with hemicellulose and cellulose were of similar magnitude. For rectal cancer, there was a decreased risk for males and females associated with all three components of insoluble fruit/vegetable fiber.

Of the components of insoluble grain fiber, there was a significant decrease in risk of colon cancer for both males and females associated with upper quartile intake of hemicellulose; there was a similar trend toward a decrease in risk with increased cellulose and lignin intake (Table 5). For rectal cancer, there was no significant increase in risk for any of the components of grain fiber.

**DISCUSSION**

Fiber cannot be examined as a single entity. Rapidly fermented undigested starch and bean oligosaccharides, more slowly fermented fruit and vegetable fiber, and extremely slowly fermented grain fiber can each be expected to differ in their effects on cell growth and function of the large intestine. We...
found that colon cancer risk decreased with increased intakes of grain fiber for both males and females and to a lesser extent with fruit and vegetable fiber for males. Insoluble more than soluble grain fiber was associated with this decrease in risk. Rectal cancer risk decreased with fruit/vegetable but not grain fiber intake. Soluble and insoluble fruit/vegetable fibers were associated with effects of similar magnitude for rectal cancer. Risks for both colon and rectal cancer associated with hemicellulose, cellulose, and lignin were generally similar in magnitude.

In ecological studies, a protective association with total fiber (23) and fiber from cereals (23–25) but not fruits and vegetables (25) has been found. However, unlike our own findings, in most other case-control and cohort studies, grain intake and grain fiber have not been shown to be protective with regard to risk of colon and rectal cancer (7–11, 26, 27), although in one study, some protective effect for colorectal cancer associated with grain fiber intake was found (28). Because grain fiber intake is generally lower than fruit and vegetable fiber intake, an effect may possibly be obscured. In concordance with the findings of our study, fruit and vegetable intake and fruit and vegetable fiber have been generally associated with a protective effect (7–11, 28–32). In a few studies no fruit and vegetable effect was found (27, 33, 34).

In our study, the magnitude of the negative associations between fiber and risk was larger after controlling for fat intake. For rectal cancer, grain fiber was significantly associated with reduced risk after adjustment for fat intake (27, 33, 34). In controlled laboratory experiments, cellulose and wheat bran have generally been found to be protective (35–39), while soluble fibers have been found to increase tumor development (36). We found a stronger protective effect for insoluble than

Table 4  Risk of colon and rectal cancer associated with ingestion of fruit/vegetable hemicellulose, cellulose, and lignin, adjusted for fat intake, Western New York Diet Study, 1975–1986

<table>
<thead>
<tr>
<th></th>
<th>Colon</th>
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<tr>
<td></td>
<td>Females</td>
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<td></td>
<td>Males</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 (Low)</td>
<td>2</td>
<td>3</td>
<td>4 (High)</td>
<td>1 (Low)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Hemicellulose</td>
<td>1.00*</td>
<td>1.15</td>
<td>(0.67, 1.97)*</td>
<td>1.03</td>
<td>1.00</td>
<td>(0.42, 1.25)</td>
<td>1.10</td>
</tr>
<tr>
<td>Cellulose</td>
<td>1.00</td>
<td>1.40</td>
<td>0.83</td>
<td>0.92</td>
<td>1.00</td>
<td>0.87</td>
<td>0.84</td>
</tr>
<tr>
<td>Lignin</td>
<td>1.00</td>
<td>1.03</td>
<td>0.77</td>
<td>0.80</td>
<td>1.00</td>
<td>0.59</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Table 5  Risk of colon and rectal cancer associated with ingestion of grain hemicellulose, cellulose, and lignin, adjusted for fat intake, Western New York Diet Study, 1975–1986

<table>
<thead>
<tr>
<th></th>
<th>Colon</th>
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<tbody>
<tr>
<td></td>
<td>Females</td>
<td></td>
<td></td>
<td>Males</td>
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<tr>
<td></td>
<td>1 (Low)</td>
<td>2</td>
<td>3 (High)</td>
<td>4 (High)</td>
<td>1 (Low)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Hemicellulose</td>
<td>1.00</td>
<td>0.80</td>
<td>0.44</td>
<td>1.00</td>
<td>1.17</td>
<td>0.66</td>
<td>0.51*</td>
</tr>
<tr>
<td>Cellulose</td>
<td>1.00</td>
<td>0.43, 1.48</td>
<td>0.22, 0.87</td>
<td>1.00</td>
<td>0.70, 1.95</td>
<td>0.39, 1.10</td>
<td>0.30, 0.88</td>
</tr>
<tr>
<td>Lignin</td>
<td>1.00</td>
<td>0.91</td>
<td>0.58</td>
<td>1.00</td>
<td>0.59</td>
<td>0.60</td>
<td>0.42*</td>
</tr>
</tbody>
</table>

* Odds ratio.
* 95% confidence interval.
* *For linear trend, P < 0.05.

FIBER SOURCE AND COMPONENTS
for soluble grain fiber. However, total intake and variability of soluble grain fiber was low in this study, which may have limited our ability to detect an effect. Risk was not different for soluble and insoluble fruit/vegetable fiber. Fiber solubility correlates with fiber fermentation by gut microorganisms. Fermentation can vary among individuals (40) and can vary depending on the way food is cooked (41) and how coarse or finely divided the fiber is (42). These factors could not be controlled for with the data available to us.

In interpreting findings of studies using animals fed relatively large quantities of fiber, it should be noted that high fiber diets may cause an important dilution of the caloric concentration in food and reduce animals' caloric intake. Reduced tumor incidence may be a result of decreased caloric intake, decreased weight gain, or decreased availability of nutrients rather than a direct result of fiber intake (43). Similarly, for humans, a high fiber diet may differ from a low fiber diet in the amount and types of food, the caloric density, and the amount of fiber. It may be that, in spite of these associations with fiber, the true etiological agent is another food component or another environmental component correlated with fiber (44).

For colon and rectal cancer, we found a difference in effect associated with fiber. For colon cancer, grain fiber was somewhat more strongly associated with risk. Grain fiber is associated with an effect on fecal bulk and the modification of cell proliferation; it may be that these mechanisms are more important for the etiology of colon cancer. For rectal cancer, fruit and vegetable fiber was associated with decreased risk, especially for males. Fermentation, possibly the production of short chain fatty acids, and the maintenance of a stable microbial population which appear to be the effects associated with fruit/vegetable fiber may serve as the mechanism for the protective effect of fiber in the distal bowel. There was some difference in effects of fiber for men and women. Dietary exposure may differ in the two groups. Total intakes were, of course, higher for males than females. In these subjects, intake of vegetables was higher for females than males (45). Also, for rectal cancer, there were fewer female cases so that associations may have been obscured because of a lack of power.

There are important sources of error in the actual measurement of fiber and fiber components. Values for neutral detergent fiber as a measurement of insoluble fiber have high repeatability and a large data base of food values. The detergent method for determining hemicellulose and cellulose has been shown to divide the insoluble fiber component into physiologically different fractions based on fermentability (46). However, because these components are measured by difference, error in their measurement may reduce the likelihood of identifying associations. Direct measurement of soluble fiber can vary depending on the technique used; the values in this paper were determined by difference using neutral detergent fiber and total dietary fiber values obtained from different techniques. The greater measurement error in the soluble fiber values may explain, at least in part, the weaker associations of soluble grain fiber with colon cancer risk. Measurement techniques for the physiologically relevant soluble and insoluble fractions continue to be refined (47). In addition to error in measurement of fiber, there can also be tremendous variability in the actual fiber content of foods called by the same name such as "wheat bread" (48). Fiber components, especially cellulose and lignin, are highly correlated with one another which makes it difficult to separate the effect of these components. The interaction of components within a food is also of significance. Highly lignified cellulose in grains is less fermentable than cellulose in vegetables. Analysis of effects by food source corrects, to some extent, for this type of interaction.

There are also important potential sources of error in dietary intake data of the kind we used. Nondifferential error in subjects' estimates of their own usual intake is to be expected. Participants gave information on recent usual intake; it may be that intake at an earlier period is the more important exposure. Error could also be introduced through the use of a limited list of foods. Although the list in this study was relatively extensive, true total intake would not be estimated. However, a food frequency questionnaire of this complexity should be adequate for estimation of rank ordering of subjects (49). Mean fiber intakes were similar to those reported by Potter and McMichael (27) and about 10 g/day lower than median intakes reported by Slattery et al. (9), both studies using food frequency questionnaires. Fiber intake values for the participants in this study were higher than those reported for a representative sample of the United States based on a 24-h recall (50). The food frequency questionnaire typically overestimates intake, while the 24-h recall may underestimate intake (49).

Given that the hypothesis of a protective effect of fiber is relatively well known, one might question whether the recall of intake of grains by cases was influenced by knowledge of their disease status. However, there is no reason to believe that recall bias would be different for cancer of the colon and rectum. The difference in the results for these two sites suggests that the case-control difference is not just the result of recall bias. Other possible sources of bias and loss of power in this study have been addressed in some detail elsewhere (12, 13). Briefly, there is the possibility of selection bias because of our inability to interview a large number of eligible cases and controls. It may be that cases with more advanced disease were not included and that these cases do not apply to more severe cancers or those which develop more rapidly. In selecting controls, there is some possibility that the controls who agreed to participate had consistently different dietary intakes from those who did not. The use of neighborhood controls should eliminate this bias, at least in part. There was no significant difference between cases' and controls' education level. In any case, these results need to be corroborated in other populations and in animal studies to determine whether these sources of bias are important. In general, our findings on other, better studied, dietary factors have been in concordance with those of other epidemiological studies (12, 13).

Replication of studies of fiber intake in colon and rectal cancer, further analysis of the effect of food source and individual fiber components, and improved food composition analysis will be required before any definitive conclusions can be drawn regarding fiber intake and risk. However, the accumulating human and animal data do suggest that the effect of grain fiber on risk differs from that of fruit and vegetable fiber and that the effect of each is different in the colon and rectum. The efficacy of grain fiber in reducing risk of colon and rectal cancer remains in question. While our results indicate some protective effect for the colon for grain fiber, most other studies do not find a grain effect. Fruit and vegetable fiber does seem to be related to an important protective effect. For recommendations regarding fiber intake, the source of the fiber should be taken into account.

REFERENCES


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