

## Dietary Fiber and Cancer Prevention

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Epidemiologic, laboratory, and clinical metabolic research suggest that cancer risk can be reduced by a high intake of fiber-containing foods. Although there have been numerous reviews on the association between dietary fiber and colon cancer,<sup>8, 36, 37, 90</sup> more recent studies have also suggested an association with other gastrointestinal cancers, as well as cancers of the breast, ovary, and endometrium. This review will focus on studies since 1980 for both colon and other cancers.

### DEFINITION OF FIBER

*Dietary fiber* is a group of endogenous components of plant materials in the diet that are resistant to human digestive enzymes.<sup>83</sup> Dietary fiber is not a single entity, but a heterogeneous mixture of polysaccharide polymers and lignin. Based on chemical structure, dietary fiber can be divided into seven major categories: cellulose, hemicelluloses, pectins, gums, mucilages, algal polysaccharides, and lignin.

Cellulose is the principal cell wall structural material and consists of a polymer of glucose linked by (1-4) beta glycosidic bonds. It is usually found as part of a complex plant cell wall matrix in combination with hemicelluloses, lignin, and pectins. There are more than 250 different hemicellulose polymers. These plant polysaccharides consist mostly of branched polymers of pentose and hexose sugars such as mannose, glucose, galactose, xylose, and arabinose. Pectins are a mixture of colloidal polysaccharides present in the cell wall matrix and bind adjacent cell walls. Citrus fruits, apples, and sugar beet pulp are rich sources of pectins. Gums are found as exudates at

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the sites of injury to plants and are water-soluble polysaccharides consisting primarily of galactose, glucose, and galacturonic acid. Seaweeds, oatmeal, and legumes are good sources of gums. Mucilages are a mixed group of complex polysaccharides that are not generally part of the cell wall and are often associated with the endosperm. Algal polysaccharides are derived from algae and seaweed. Lignin consists of polymers of aromatic alcohols such as sinapyl, coniferyl, and p-coumaryl alcohols and are therefore not polysaccharides. As the plant matures, the lignin content increases, which increases its rigidity.

Dietary fiber has also been classified according to its solubility in water. It has been suggested that the water solubility of fiber as measured *in vitro* corresponds roughly to the bacterial fermentability of fiber in the colon.<sup>19</sup> The structural fibers cellulose, lignin, and some hemicelluloses are generally insoluble in water and are nonfermentable, whereas the natural gel-forming fibers including pectins, gums, mucilages, and remaining hemicelluloses are water-soluble and more fermentable. Table 1 lists the soluble, insoluble, and total dietary fiber values for some commonly consumed foods. Although the proportion of soluble to insoluble fiber is somewhat dependent on the analytic method employed,<sup>20</sup> this table points out the much smaller proportion of soluble fiber in foods. It has been estimated that only 25 to 30% of the fiber is soluble in an average American diet.<sup>83</sup> Although some foods such as wheat products contain only insoluble fibers, there are no foods that contain only soluble fiber.

Because plant foods contain a variety of fiber fractions in varying proportions, American diets generally consist of mixtures of these fiber fractions. However, no national food tables currently include data on individual fiber fractions; the major United States government food tables still give fiber values for crude fiber.<sup>120</sup> The relationship between crude fiber and the dietary fiber content of a single food is quite variable, but is usually only a third or a quarter as high. In the last few years there has been a great deal of research on the analysis of fiber in foods, and provisional food tables with more accurate dietary fiber data are becoming available.<sup>4, 55</sup> Because data on the amount of individual fiber fractions as well as total dietary fiber are still limited, many epidemiologists have instead examined the relationship between cancer risk and food sources of fiber, such as fruits, vegetables, and cereal grains.

### PHYSIOLOGIC EFFECTS OF DIETARY FIBER

Dietary fiber exerts its influence along the entire alimentary tract from the time of ingestion to excretion.<sup>39</sup> It is well documented that fiber is necessary to maintain the normal function of the gastrointestinal tract.<sup>47, 104</sup> These effects are dependent on both the chemical and physical properties of the fiber.

Evidence indicates that it is the nonfermentable fraction of fiber, consisting of cellulose, some of the hemicelluloses, and the lignin, that modifies large bowel function by retaining water in the stool. Thus, fiber sources such as wheat bran, which are high in nonfermentable fibers,

Table 1. *Water-Soluble, Insoluble, and Total Dietary Fiber in Selected Foods*<sup>121, 122</sup>

|                       | TOTAL                      |           | DIETARY FIBER |
|-----------------------|----------------------------|-----------|---------------|
|                       | SOLUBLE                    | INSOLUBLE |               |
|                       | (GRAMS PER 100 GRAMS FOOD) |           |               |
| <i>Fruits</i>         |                            |           |               |
| Apple                 | 0.7                        | 1.1       | 1.8           |
| Banana                | 0.7                        | 1.0       | 1.7           |
| Grape                 | 0.7                        | 0.9       | 1.6           |
| Grapefruit            | 1.0                        | 0.9       | 1.9           |
| Orange                | 1.2                        | 1.2       | 2.4           |
| Peach                 | 0.8                        | 1.3       | 2.1           |
| Pear                  | 0.7                        | 2.1       | 2.8           |
| Plum                  | 0.7                        | 1.7       | 1.7           |
| Prune                 | 2.5                        | 6.2       | 8.7           |
| Raisin                | 3.5                        | 6.2       | 8.7           |
| Strawberry            | 0.9                        | 1.5       | 2.4           |
| <i>Vegetables</i>     |                            |           |               |
| Broccoli              | 0.9                        | 1.6       | 2.5           |
| Cabbage               | 0.9                        | 1.1       | 2.0           |
| Carrot                | 0.8                        | 2.4       | 2.4           |
| Cauliflower           | 0.7                        | 1.6       | 1.9           |
| Peas, fresh           | 0.5                        | 5.0       | 5.5           |
| Peas, frozen          | 0.3                        | 6.2       | 6.5           |
| Pepper, red sweet     | 0.9                        | 1.0       | 1.9           |
| Cucumber              | 0.4                        | 0.7       | 1.1           |
| Lettuce               | 0.4                        | 0.8       | 1.2           |
| Potato                | 0.4                        | 1.0       | 1.4           |
| Spinach               | 0.4                        | 0.9       | 1.3           |
| Tomato                | 0.6                        | 0.8       | 1.4           |
| Zucchini              | 0.6                        | 1.4       | 2.0           |
| <i>Grain Products</i> |                            |           |               |
| Corn flakes           | 0.4                        | 5.0       | 5.4           |
| Rice, puffed          | 0.5                        | 4.5       | 5.0           |
| Oats, puffed          | 0.7                        | 4.2       | 4.9           |
| Oats, rolled          | 1.1                        | 4.6       | 5.7           |
| Macaroni              | 1.0                        | 2.0       | 3.1           |
| Rice, polished        | 0.2                        | 2.1       | 2.3           |
| Rice, parboiled       | 0.6                        | 4.2       | 4.8           |
| Wheat bread           | 0.8                        | 2.7       | 3.5           |
| Wheat flour, whole    | 1.0                        | 8.9       | 9.9           |
| Wheat flour           | 0.9                        | 2.6       | 3.5           |
| Wheat bran            | 1.2                        | 36.3      | 37.5          |
| Wheat germ            | 1.3                        | 12.7      | 14.0          |

increase stool weight and defecation frequency and decrease gastrointestinal transit time.<sup>26, 52, 110, 112, 116</sup> Moreover, the same fiber sources are beneficial in the treatment of constipation.<sup>16, 26, 27, 113</sup> and diverticular disease.<sup>12, 80</sup>

The fermentable fiber fraction also modifies bowel function,<sup>61, 105</sup> probably by stimulating microbial growth in the intestine; this has been shown for pectic substances and fiber from apple and carrot.<sup>114</sup> The increased fecal bacterial mass, which may comprise up to one half of the entire stool mass,<sup>115</sup> is correlated with a decreased transit time through the gut.<sup>18</sup> Water-soluble fibers such as viscous pectins and gums also have a hypoglycemic

effect<sup>16</sup> and have therefore been used to improve carbohydrate metabolism in diabetes mellitus.<sup>5, 6</sup> Some studies have shown that soluble fiber fractions, such as pectin, guar gum, and foods that contain soluble fractions, such as barley and oat bran, have a hypocholesteremic effect in humans if given in large amounts.<sup>3, 79, 83</sup>

### CANCER MECHANISMS

#### Colon

Numerous studies suggest that fat promotes colon cancer and that fiber may in turn neutralize this process. Fat is thought to promote colon cancer by increasing the amount of bile acids in the colon.<sup>51, 89</sup> Colonic bacteria may convert these bile acids to secondary bile acids, such as lithocholic acid. These secondary bile acids have been shown in rat models to alter the proliferative activity of the intestinal crypt cells<sup>84</sup> and to promote tumorigenesis.<sup>85</sup> Moreover, the amount of fat in the diet directly affects the concentration of free fatty acids in the bowel lumen,<sup>78</sup> and these free fatty acids have been shown to damage bowel mucosa.<sup>90</sup>

Fiber is postulated to reduce the adverse effect caused by fat through several mechanisms, including dilution of carcinogens, decreased transit time, reduction in fecal pH, chemical binding, and alteration in fecal bacteria metabolism.<sup>41, 44</sup> These metabolic changes have been demonstrated in numerous metabolic epidemiologic studies, as well as in animal models. Fibers that are not fermented by the anaerobic bacteria of the colon increase the fecal bulk by absorbing water, thereby diluting potential carcinogens.<sup>94</sup> This increased bulk also reduces transit time and contact with the colonic mucosa.<sup>90</sup>

Dietary fiber is fermented by the anaerobic bacteria in the large bowel, resulting in the production of short chain fatty acids (SCFA), consisting primarily of acetate, butyrate, and propionate.<sup>43</sup> Butyrate is the principal source of energy for the colonic epithelium.<sup>97</sup> Evidence also suggests that butyrate plays an important role in the normal maintenance and differentiation of the colonic mucosa *in vivo*<sup>21</sup> and inhibits tumorigenesis in cultured human intestinal epithelial cells.<sup>25</sup>

These SCFA also reduce the pH of the colon.<sup>21</sup> Studies indicate that the increased risk of colon cancer is correlated with higher fecal pH.<sup>89, 124</sup> At a higher pH, most of the bile acids and acidic lipids are in solution. As the pH is reduced, the acids are converted to their protonated state and bind with the calcium and other salts in the colon,<sup>14</sup> thus protecting the colonic mucosa from damage by the bile acids. However, the pH throughout the colon is not uniform. The pH of the cecum and proximal colon changes with the ingestion of the fermentable fiber, whereas the pH of the distal colon tends to remain unchanged.<sup>21, 63</sup>

#### Breast

The hypothesized role of reproductive hormones in the initiation and progression of breast cancer is well known.<sup>53</sup> Recent evidence suggests that

fiber may modify the biologic action of hormones, which in turn may reduce the risk of hormone-related cancers. The lower plasma prolactin and estradiol levels and higher fecal estrogen levels found in women consuming high-fiber diets could be due to the fiber-mediated change of the intestinal bacteria leading to decreased deconjugation of bound estrogens as a consequence of reduced beta-glucuronidase activity.<sup>32, 33</sup> An additional mechanism by which dietary fiber may exert its influence has been tested<sup>106</sup> *in vitro*, which showed that the unconjugated estrogens bind to fibers. It has been recently reported that, in women, dietary fiber intake is directly proportional to the excretion of urinary lignans.<sup>98</sup> These lignans can be formed by intestinal bacteria from diphenolic compounds found in grain and other fiber-rich foods. Lignans, not to be confused with the dietary fiber lignin, may influence estrogen metabolism<sup>1</sup> and thus explain the association of fiber-rich foods with various gynecologic cancers.

The mechanism by which fiber might be protective for cancers of the esophagus, oral cavity and pharynx, stomach, and rectum is not known. Over the last decade research has demonstrated that fiber is not merely an inert component of the diet, but one that elicits a variety of physiologic effects. In some studies it is not known whether the protection is due to fiber or other components present in the fiber-rich foods, such as carotenoids, vitamin C, and other micronutrients. In addition, because high-fat diets are also usually low in fiber, an indirect protective role for dietary fiber can be accordingly constructed for all cancers positively associated with high-fat foods.

### COLON CANCER

#### Animal Studies

Studies examining the role of dietary fiber as an inhibitor of colon cancer in animal models have provided conflicting results. This can be accounted for by differences in species, strain of animal, type and route of carcinogen administration, basal diet, and the type and amount of fiber fed in individual experiments. Moreover, dietary fiber used in animal studies generally contains supplements of concentrated forms of a single fiber source such as wheat or oat bran, or purified fibers such as cellulose, pectin, or carrageenan. The effect of such fiber supplements on the formation of intestinal cancer in animal models is variable. Animal experiments indicate that defined diets supplemented with fibers that are relatively insoluble and poorly fermentable, like cellulose, lignin, or wheat bran, tend to inhibit the development of tumors.<sup>45, 83</sup>

In recent years a few studies have investigated the interaction between the promoting and protective influence of fat and fiber on chemically induced carcinogenesis in rat models. Sinkeldam et al<sup>107</sup> reported that a high-fat, low-fiber diet resulted in an increased number of colon tumors in animals as compared to a high-fat, high-fiber diet. In another study, animals were fed four different diets: high-fat, high-fiber; low-fat, high-fiber; high-fat, low-fiber; and low-fat, low-fiber. The percentage of colon tumors in the

four groups was highest in the high-fat, low-fiber diet (63.7%), followed by the low-fat, low-fiber (21.8%), high-fat, high-fiber (10.9%) and low-fat, high-fiber diet (3.6%).<sup>31</sup> Results from these studies indicate that colon carcinogenesis in the rat depends on both the fat and the fiber content of the experimental diet.

### Epidemiologic Studies

**Observational Studies.** Table 2 lists the observational epidemiologic studies reported since 1980. These studies, categorized as international, within country, metabolic, and time trend, are briefly summarized subsequently.

Only one international correlation study examined the relationship between colon cancer and total dietary fiber.<sup>72</sup> This study found a stronger association for total dietary fiber than for crude fiber values. This association was strongest for cereal fiber and remained significant after adjustment for availability of total fat and animal fat.

Six of seven within-country or national correlation studies conducted in diverse populations have in general found a protective effect from fiber or fiber-containing foods.<sup>56</sup> Protective associations were found in various countries such as Israel,<sup>101</sup> South Africa,<sup>67</sup> Sweden,<sup>48, 100</sup> the United Kingdom,<sup>9</sup> and the United States.<sup>28</sup> In a recently reported study of cancer mortality rate ratios from 1968 to 1978 in 24 countries throughout Sweden, cereal fiber showed a strong protective effect for colorectal cancer for both men and women. This association was not altered by controlling for fat intake.<sup>100</sup> One epidemiologic study analyzed individual fiber fractions for

Table 2. Summary of Observational Epidemiologic Studies Examining Dietary Fiber and Colon Cancer (Since 1980)

| AUTHORS (REF NO)                          | YEAR | FIBER | CEREALS | VEGETABLES |
|---|------|-------|---------|------------|
| <i>International Correlation Studies</i>  |      |       |         |            |
| McKeown-Eyssen & Bright-See (72)          | 1985 | -     | -       | -          |
| <i>Within Country Correlation Studies</i> |      |       |         |            |
| Enstrom (28)                              | 1980 | -     | -       | -          |
| Rozen et al (101)                         | 1981 | -     | -       | -          |
| Maisio & Bremner (67)                     | 1981 | -     | -       | -          |
| Jensen et al (49)                         | 1982 | -     | -       | -          |
| Bingham et al (9)                         | 1985 | -     | -       | -          |
| Smith et al (111)                         | 1985 | +     | -       | -          |
| Rosen et al (100)                         | 1988 | -     | -       | -          |
| <i>Metabolic Correlation Studies</i>      |      |       |         |            |
| Reddy et al (93)                          | 1980 | -     | -       | -          |
| Jensen et al (48)                         | 1983 | -     | -       | -          |
| Reddy et al (91)                          | 1984 | -     | -       | -          |
| Nair et al (77)                           | 1984 | 0     | -       | -          |
| Walker et al (124)                        | 1986 | -     | -       | -          |
| <i>Time Trend Correlation Studies</i>     |      |       |         |            |
| Helms et al (41)                          | 1982 | -     | -       | -          |
| Powles et al (87)                         | 1984 | -     | -       | -          |

Key: - Inverse association (protective effect)

+ Direct association

0 No association

specific foods eaten in each of nine regions in Great Britain and correlated these data to mortality data for large bowel cancer.<sup>9</sup> The study found a protective association for both cellulose and the uronic acid-containing fibers.

Several metabolic epidemiologic studies support an association for fiber and colon cancer. In this relatively new type of study, metabolic parameters and thought to be associated with a disease are examined in study subjects and then correlated with incidence or mortality data of that disease in the general population. Of five epidemiologic studies since 1980, four showed an inverse association with dietary fiber or fiber-containing foods. A study on large bowel cancer and diet was undertaken in Finland and Denmark by the International Agency for Research in Cancer (IARC). This study compared diet and large bowel cancer in four populations: urban and rural Finland, and urban and rural Denmark.<sup>49</sup> A significant negative correlation was found for the nonstarch polysaccharides (NSP), which consists of cellulose, hemicellulose, pectins, gums, and mucilages. In this study, more than 60% of the NSP in the diets was derived from cereals.

Another type of correlational study listed in Table 2 is the time trend analysis. Helms et al<sup>41</sup> found that the consumption of nonstarch polysaccharide has decreased in Denmark in the last 50 years, and this is inversely correlated to the prevalence of colon cancer. Moreover, a drop in the colon cancer incidence was observed in England, Wales, Ireland, and Switzerland after World War II. This was attributed to the compulsory increase in the percentage of bran left in the flour after milling during the war time.<sup>87</sup>

**Analytic Studies.** Since 1980, 17 case-control studies have assessed the role of fiber or fiber-containing foods in relation to colon cancer (Table 3). Among these studies, 12 showed an inverse association, 3 noted no association, and 2 revealed a positive association. All but one of these case-control studies also showed an excess risk with fats, meats, or energy. The protective effect of fiber was enhanced when adjusting for fat or calories (five studies), or not changed (three studies), or not performed (in the remainder of the studies), which suggests that the protective association of fiber must represent more than confounding.

Unlike earlier studies, which looked at food groups or derived fiber food indices, many of the newer case-control studies have looked at the effects of a quantitative measure of dietary fiber. Since 1980 eight studies have utilized both a quantitative food frequency questionnaire, in order to quantitate the amount of food consumed, and a quantitative measure of fiber intake. Six of these studies<sup>11, 34, 54, 64, 66, 109</sup> found a significant protective association with fiber and only two<sup>46, 86</sup> found no association.

It has been suggested that the case-control study findings for protection from vegetables are more compelling than those showing protection from fiber.<sup>16, 85</sup> A recent meta-analysis of these studies found the strength of these associations to be nearly equal. The estimated combined odds ratio (OR) was 0.58 for fiber and 0.48 for vegetable consumption.<sup>118</sup> Because vegetables constitute a major portion of dietary fiber in western diets, the available evidence does not permit discrimination between possible protective effects of vegetables related to their fiber content, other nutrients, or phytochemicals.

Table 3. Survey of the Case-Control Studies Examining Dietary Fiber and Colon Cancer (Since 1980)

| AUTHORS<br>(REF NO)          | YEAR | FIBER | CEREALS | VEGETABLES | EXCESS RISK WITH |        |
|------------------------------|------|-------|---------|------------|------------------|--------|
|                              |      |       |         |            | FATS, MEAT, OR   | ENERGY |
| Haenszel et al (38)          | 1980 | 0     | -       | -          | No               |        |
| Jain et al (46)              | 1980 | 0     | -       | -          | Yes              |        |
| Martinez et al (71)          | 1981 | +     | +       | -          | Yes              |        |
| Mannous et al (69)           | 1983 |       |         | -          | Yes              |        |
| Pickle et al (82)            | 1984 | 0     |         |            | Yes              |        |
| Bristol et al (11)           | 1985 |       |         |            | Yes              |        |
| Potter & McMichael<br>(86)   | 1986 | +     | +       |            | Yes              |        |
| Maquart-Moulin<br>et al (66) | 1986 | -     |         | -          | Yes              |        |
| Kune et al (54)              | 1987 | -     | -       | -          | Yes              |        |
| Lyon et al (64)              | 1987 |       |         | -          | Yes              |        |
| Vlajinic (123)               | 1987 | 0     |         |            | Yes              |        |
| Graham et al (34)            | 1988 | -     |         |            | Yes              |        |
| La Vecchia et al (60)        | 1988 |       |         | -          | Yes              |        |
| Slattery et al (109)         | 1988 | -     |         |            | Yes              |        |
| Tuyns et al (119)            | 1988 |       |         | -          | Yes              |        |
| Young & Wolf (126)           | 1988 |       |         | -          | Yes              |        |
| Peters et al (81)            | 1989 |       |         | -          | Yes              |        |

Key: - Inverse association (protective effect)

+ Direct association

0 No association

There have been two recent cohort studies that have examined the association between colon cancer and fiber intake. Willett et al<sup>25</sup> found no association for total dietary fiber and colon cancer in women, but a protective effect for crude fiber from fruits. Heilburn et al<sup>10</sup> found a significant negative association of dietary fiber and colon cancer risk among those men consuming low-fat diets, again suggesting that the imbalance between fat and fiber intake may be the more relevant determinant of colon cancer risk.

**Intervention Studies.** Although it is generally agreed that a randomized controlled dietary intervention trial would provide the most definitive data in demonstrating a causal relationship between fiber and colon cancer, the cost and time involved when cancer is the endpoint is enormous. Bruce<sup>14</sup> has estimated that such a clinical trial would require 100,000 subjects and take from 5 to 10 years. Thus, fiber intervention studies to date have employed only protocols using different hypothesized precursor lesions as endpoints. Often referred to as "intermediate endpoints," these can be divided into two distinct categories: those general changes in the internal large bowel or colon such as fecal bile acids, fecal mutagens, and pH; and changes that involve a specific alteration at the organ, tissue, cell, or molecular level, such as cell proliferation and adenomatous polyps.<sup>108</sup> Reddy et al<sup>12</sup> found changes in both the concentration of fecal secondary bile acids and fecal mutagen activity when feeding cellulose and wheat bran, but not with the more fermentable fiber such as oat bran. Two recent studies have examined the effect of wheat bran supplementation on cell proliferation rates in rectal mucosal biopsies. In one study no change in cell proliferation

as assayed by thymidine labeling was found in normal healthy volunteers after supplementing their diet for 2 weeks with 30 grams per day of wheat bran fiber.<sup>117</sup> The other study found a significant decrease in thymidine labeling in 13 subjects who had previous resected colon cancer after 8 weeks with 13.5 grams per day of wheat bran fiber.<sup>2</sup>

It is commonly accepted that most large bowel cancers arise in adenomatous polyps, especially those that are large. These often have a villous growth pattern or show severe dysplasia.<sup>76</sup> There are currently three studies examining the effects of fiber on the recurrence of adenomatous polyps. A Canadian study comprising 200 participants on a low-fat, high-cereal fiber supplement is being completed.<sup>10</sup> In an Australian study, the effects of reduced fat intake, wheat bran fiber supplement, and a beta-carotene supplement are being examined in a 2 × 2 × 2 randomized factorial design involving 424 participants.<sup>65</sup> This study should be completed in 1990. The third polyp study is just beginning and will involve 2000 subjects from 12 different regions of the United States. This National Cancer Institute trial will randomize participants to either a low-fat, high-fiber, fruit and vegetable-enriched eating plan or their usual diet. The change in dietary fiber does not involve a supplement but is rather implemented through a change in dietary pattern from the traditional western diet to one that is considered to be of less risk for colon cancer.<sup>102</sup> Results from this study will not be available until 1997. Familial adenomatous polyposis, a premalignant autosomal disorder, is characterized by a multitude of adenomatous polyps and progression to cancer in almost 100% of patients, if not treated.<sup>7</sup> In a wheat bran intervention trial of 58 polyposis patients, a limited degree of polyp regression was observed after 6 months in the high-fiber group.<sup>23</sup> The mean daily intake of fiber for the treatment group was 22.4 grams per day.

### OTHER CANCERS

Table 4 lists the case-control studies that have assessed the association between dietary fiber and other cancers. Although the role of dietary fiber in cancers of the mouth, pharynx, esophagus, breast, stomach, ovary, and endometrium has not been studied as extensively as in the large bowel, the recent findings for associations with these other cancers are intriguing.

#### Breast Cancer

Of the seven case-control studies that have assessed the relationship between breast cancer and fiber or fiber-rich foods, six studies have demonstrated an inverse association (see Table 4). Lubin et al<sup>22</sup> evaluated both the separate and combined effects of fat, protein, and fiber on the risk of developing breast cancer. They found an increased risk associated with a diet high in fat and protein, and low in fiber. Subjects on a high-fat, low-fiber diet were at twice the risk for breast cancer compared to those on a low-fat, high-fiber diet. In case-control studies in both Australia<sup>88</sup> and Argentina,<sup>42</sup> weak protection was noted for fiber, even though there was no association with fat intake. One case-control study attempted to assess

**Table 4. An Overview of Case-Control Studies in Relation to Dietary Fiber and Various Cancers**

| AUTHORS<br>(REF NO)       | YEAR | LOCATION  | SITE OF<br>MALIGNANCY | FIBER | CEREALS | VEGETABLES<br>AND FRUITS |
|---------------------------|------|-----------|-----------------------|-------|---------|--------------------------|
| Graham et al (35)         | 1982 | US        | Breast                | NA    |         | 0                        |
| Katsouyanni et al<br>(50) | 1986 | Greece    | Breast                |       |         |                          |
| Lubin et al (62)          | 1986 | Israel    | Breast                |       |         |                          |
| La Vecchia et al (58)     | 1987 | Italy     | Breast                |       |         |                          |
| Rohan et al (98)          | 1988 | Australia | Breast                |       |         |                          |
| Pryor et al (88)          | 1989 | US        | Breast                |       |         |                          |
| Iscovich et al (42)       | 1989 | Argentina | Breast                |       |         |                          |
| De Carli et al (22)       | 1987 | Italy     | Esophagus             |       |         |                          |
| McLaughlin et al<br>(73)  | 1988 | US        | Oral Pharyngeal       |       |         |                          |
| Modan et al (75)          | 1974 | Israel    | Stomach               |       |         |                          |
| Risch et al (96)          | 1985 | Canada    | Stomach               |       |         |                          |
| Freudenheim et al<br>(29) | 1990 | US        | Rectum                |       |         |                          |
| La Vecchia et al (57)     | 1986 | Italy     | Endometrium           |       |         |                          |
| Byers et al (15)          | 1983 | US        | Ovarian               |       |         |                          |
| La Vecchia et al (59)     | 1987 | Italy     | Ovarian               |       |         |                          |
| Slattery et al (108)      | 1989 | US        | Ovarian               | 0     |         | 0                        |

Key: - Inverse association (protective effect)  
+ Direct association  
0 No association

the relationship between adolescent diet and breast cancer risk.<sup>88</sup> In postmenopausal women, high-crude fiber intake produced elevated odds ratios. This elevated risk was associated with fiber from fruits and vegetables, whereas fiber from grains resulted in decreased risk in both postmenopausal and premenopausal women. The increased risk from fiber from fruits and vegetables is contrary to two other studies, which found a protective association for breast cancer with high vegetable intake.<sup>50, 58</sup> The latter study found that women in the lowest quintile of vegetable intake had about 10 times the risk of breast cancer risk as compared to the highest quintile. In five of these seven studies, the association with fiber and/or vegetables was stronger than the association with dietary fat.

#### Oral and Pharyngeal Cancer

An inverse relationship between fruit and vegetable intake and risk of esophageal cancer,<sup>22</sup> and between fruit intake and oral and pharyngeal cancer<sup>73</sup> has been reported.

#### Gastrointestinal Cancer

Two case-control studies reported a protective effect of fiber-rich foods against gastric cancer.<sup>75, 98</sup> The study conducted by Risch et al<sup>98</sup> in Canada found a protective association for total dietary fiber as well as high-fiber foods. The protective effect from fiber was even greater than that from high vegetable intake, an association frequently noted for reduced stomach cancer risk. This study also reported a reduced risk from bran cereal, and an increased risk from starch and total grain intake. A recent case-control

study examining the relationship of diet to rectal cancer<sup>29</sup> suggests that dietary fiber from vegetables but not from grains is inversely associated with cancer risk. Although many of the studies previously mentioned under Colon Cancer included colorectal cancer, this was one of the few studies that examined a separate association for rectal cancer.

#### Gynecologic Cancers

Among other cancers, endometrial cancer was associated with less frequent intake of vegetables, fruits, and whole grain food.<sup>57</sup> A potential role of dietary fiber in the etiology of ovarian cancer has been examined in three case-control studies.<sup>15, 59, 108</sup> Two of the three studies suggest a protective effect against ovarian cancer from fiber-rich foods.<sup>15, 59</sup> Significantly increased risk was associated with diets low in fiber, fruits, and vegetables rich in beta-carotene. Again, it is not known if the protection is due to fiber per se, to other components in fiber-rich foods, or to the fact that diets high in fiber-rich foods (plant foods) are usually lower in fats and calories.

#### CONCLUSIONS

There are several unresolved issues related to dietary fiber and cancer prevention. The roles of specific types of fiber have not been delineated. Other phytochemicals present in foods, such as carotenoids, indoles, and flavonoids, might also be contributing to the observed protective association for certain cancers. Although the specific roles of the numerous potentially protective substances in plant foods are not yet understood, populations with diets high in fiber-rich foods, such as vegetables, fruits, beans, peas, and whole grain products, experience many health advantages, including lower rates of diet-sensitive cancers.

The increase in fiber-rich foods should be gradual, over a 4- to 6-week period, to minimize potential complications such as flatulence, diarrhea, bloating, and diffuse abdominal pain.<sup>64</sup> In addition, fluid intake should be increased simultaneously with increased fiber intake, especially in individuals consuming a single concentrated source of dietary fiber, in order to avoid the development of intestinal obstruction.<sup>74</sup> Because the epidemiologic studies reviewed in this article focus on dietary patterns in which fiber-rich foods usually occur as a complex mixture with other foods and food components, the emphasis for dietary recommendation should be on a dietary pattern rather than on a single dietary variable. Thus, any recommendation for increasing dietary fiber for cancer prevention should be made in the context of the total diet, as suggested by the National Cancer Institute in their interim dietary guidelines for cancer prevention (Table 5).

#### SUMMARY

A large body of literature suggests that eating a variety of foods containing high fiber has a protective effect against colon cancer. Evidence

Table 5. National Cancer Institute Dietary Guidelines

|   |
|---|
| Reduce fat intake to 30% or less of calories                      |
| Increase fiber intake to 20 to 30 g/day                           |
| Eat a variety of vegetables and fruits daily                      |
| Avoid obesity   |
| Consume alcoholic beverages in moderation, if at all              |
| Minimize consumption of salt-cured, salt-pickled, or smoked foods |

also indicates that a high fiber-containing diet may be protective against breast, ovary, endometrial, and gastrointestinal cancer. The focus of this review is the epidemiologic data for an inverse association between a high-fiber diet and risk for the previously mentioned cancers. Epidemiologic studies are categorized as international, within country, metabolic, time trend, case control, and cohort. Since 1980, 32 studies have assessed the role of fiber-containing foods in relation to colon cancer. Among these studies, 25 showed an inverse association. Of the seven case-control studies, which evaluated the relationship between the fiber-rich diet and breast cancer, six demonstrated an inverse association. For cancers of the esophagus, mouth, pharynx, stomach, rectum, endometrium, and ovary, there are only a limited number of studies, most showing a protective effect from eating a diet high in fiber-containing foods. The epidemiologic studies reviewed previously focus on dietary patterns in which fiber-rich foods usually occur as a complex mixture with other foods and food components, thus making it difficult to assess at this time if the protection is clearly from fiber per se or some other dietary component, such as low fat. For cancer prevention, the emphasis for dietary recommendation should be on a dietary pattern rather than on an isolated dietary fiber supplement.

## REFERENCES

- Adlercreutz H, Fotsis T, Bannwart C, et al: Determination of urinary lignans and phytoestrogen metabolites: potential antiestrogens and anticarcinogens, in urine of women on various habitual diets. *J Steroid Biochem* 25:791-797, 1986
- Alberts D, Buller W, Einspahr J, et al: Dietary wheat bran fiber supplementation significantly reduces [<sup>3</sup>H]-thymidine crypt organ labeling index in rectal mucosal biopsies from patients with resected colorectal cancer. *Proc Am Assoc Cancer Res* 30:258, 1989
- American Heart Association: Dietary guidelines for healthy Americans: A statement for physicians and health professionals by the nutrition committee. *Arteriosclerosis* 8:218A-221A, 1988
- Anderson JW, Bridges SR, Tietjen J, et al: Dietary content of simulated American diet and selected research diet. *Am J Clin Nutr* 49:353-357, 1989
- Anderson JW, Bryant CA: Dietary fiber, diabetes and obesity. *Am J Gastroenterol* 81:898-906, 1986
- Anderson JW: Dietary fiber in the nutrition management of diabetes. In Vahouny GV, Kritchevsky D (eds): *Dietary Fiber: Basic and Clinical Aspects*. New York, Plenum Press, 1986, pp 342-360
- Beart R: Colon, rectum, and anus. *Cancer* 33:684-688, 1990
- Bingham SA: Epidemiology of dietary fiber and colorectal cancer: Current status of the hypothesis. In Vahouny GV, Kritchevsky D (eds): *Dietary Fiber: Basic and Clinical Aspects*. New York, Plenum Press, 1986, pp 523-542
- Bingham SA, Williams DRR, Cummings JH: Dietary fibre consumption in Britain: New estimates and their relation to large bowel cancer mortality. *Br J Cancer* 52:399-402, 1985
- Bright-See E, McKeown-Eyssen G, Jacobson EA, et al: Dietary fiber and cancer: A supplement for intervention studies. *Nutr Cancer* 4:211-220, 1985
- Bristol JB, Emmett PM, Heaton KW, et al: Sugar, fat, and the risk of colorectal cancer. *Br Med J* 251:1467-1470, 1985
- Brodthb AJM, Humphreys DM: Diverticular disease: Three studies: Relation to other disorders and fibre intake; treatment with bran; metabolic effect of bran in patients with diverticular disease. *Br Med J* 1:424-430, 1976
- Bruce WR, McKeown-Eyssen G, Ciampi A, et al: Strategies for dietary intervention studies in colon cancer. *Cancer* 47:1121-1127, 1981
- Bruce WR: Recent hypotheses for the origin of colon cancer. *Cancer Res* 47:4237-4242, 1987
- Byers T, Marshall J, Graham S, et al: A case-control study of dietary and nondietary factors in ovarian cancer. *J Natl Cancer Inst* 71:681-686, 1983
- Committee on Diet and Health, Commission on Life Sciences National Research Council, National Academy of Sciences, Washington DC, National Academy Press, 1989
- Council on Scientific Report: Dietary fiber and health. *JAMA* 262:542-546, 1989
- Cranston D, McWhinnie D, Collin J: Dietary fiber and gastrointestinal disease. *Br J Surg* 75:508-512, 1988
- Cummings JH: Consequences of the metabolism of fiber in the large intestine. In Vahouny GV, Kritchevsky D (eds): *Dietary Fiber in Health and Disease*. New York, Plenum Press, 1982, pp 9-22
- Cummings JH: Fermentation in the large intestine: Evidence and implication for health. *Lancet* 1:1206-1209, 1983
- Cummings JH: Short chain fatty acids in the human colon. *Gut* 22:763-779, 1981
- Decarli A, Liati P, Negri E, et al: Vitamin A and other dietary factors in the etiology of esophageal cancer. *Nutr Cancer* 10:29-37, 1987
- DeCosse JJ, Miller H, Lesser M: Effect of wheat fiber and vitamins C and E on rectal polyps in patients with familial adenomatous polyposis. *J Natl Cancer Inst* 81:1290-1297, 1989
- Deschner EE, Cohen BI, Raitch HF: Acute and chronic effect of dietary cholic acid on colonic epithelial cell proliferation. *Digestion* 21:290-296, 1981
- Dexter DL, Lev R, Mckendall GR, et al: Sodium butyrate-induced alteration of growth properties and glycogen levels in cultured human colon carcinoma cells. *Histochem J* 16:137-149, 1984
- Eastwood MA, Brydon WB, Tadese K: Effect of Fiber on Colon Function. New York, Plenum Press, 1980, pp 1-26
- Edwards CA: Fiber and constipation. *Br J Clin Pract* 42:26-30, 1988
- Enstrom JE: Health and dietary practices and cancer mortality among California Mormons. In Cairns J, Lyon JL, Skolnick M (eds): *Banbury Report for Cancer Incidence in Defined Populations*. Cold Spring Harbor, NY, Cold Spring Harbor Laboratory, 1980, pp 69-92
- Freudenheim JL, Graham S, Marshall JR, et al: A case-control study of diet and rectal cancer in western New York. *Am J Epidemiol* 131:612-624, 1990
- Gagnella TS, Chadwick VS, Debonigne JC, et al: Perfusion of rabbit colon with ricinoleic acid: Dose-related mucosal injury, fluid secretion, and increased permeability. *Gastroenterology* 73:95-101, 1977
- Galloway DJ, Owen RW, Jarrett F, et al: Experimental colorectal cancer: The relationship of diet and fecal bile acid concentration to tumor induction. *Br J Surg* 73:233-237, 1986
- Goldin BR, Adlercreutz H, Dwyer J, et al: Effect of diet on excretion of estrogens in pre- and postmenopausal women. *Cancer Res* 41:3771-3773, 1981
- Goldin BR, Adlercreutz H, Gotbach SL, et al: Estrogen excretion patterns and plasma levels in vegetarian and omnivorous women. *N Engl J Med* 307:1542-1547, 1982
- Graham S, Marshall J, Haughey B, et al: Dietary epidemiology of cancer of the colon in western New York. *Am J Epidemiol* 128:490-503, 1988
- Graham S, Marshall J, Methin C, et al: Diet in the epidemiology of breast cancer. *Am J Epidemiol* 116:68-75, 1982

36. Greenwald P, Lanza E, Eddy GA: Dietary fiber in the reduction of colon cancer risk. *J Am Diet Assoc* 87:1178-1188, 1987
37. Greenwald P, Lanza E: Role of dietary fiber in the prevention of cancer. *In* DeVita VT, Hellman S, Rosenberg SA (eds): *Important Advances in Oncology*. Philadelphia, JB Lippincott, 1986
38. Haenszel W, Locke F, Segi M: A case-control study of large bowel cancer in Japan. *J Natl Cancer Inst* 64:17-22, 1980
39. Heaton K: Dietary fiber in perspective. *Human Nutr Clin Nutr* 37C:151-170, 1980
40. Heilburn LK, Nomura A, Hankin JH, et al: Diet and colorectal cancer with special reference to fiber intake. *Int J Cancer* 44:1-6, 1989
41. Helms P, Jorgensen IM, Paerregaard A, et al: Dietary patterns in Them and Copenhagen, Denmark. *Nutr Cancer* 4:34-40, 1982
42. Iscovich JM, Iscovich RB, Howe G, et al: A case-control study of diet and breast cancer in Argentina. *Int J Cancer* 44:770-776, 1989
43. Jacobs LR: Effect of dietary fiber on colonic cell proliferation and its relationship to colon carcinogenesis. *Prev Med* 16:566-571, 1987
44. Jacobs LR: Fiber and colon cancer. *Gastroenterol Clin North Am* 17:747-760, 1988
45. Jacobs LR, Lupton JR: Relationship between colonic luminal pH, cell proliferation, and colon carcinogenesis in 1,2-dimethylhydrazine treated rats fed high fiber diets. *Cancer Res* 46:1727-1734, 1986
46. Jain M, Cook GM, Davis FC, et al: A case-control study of diet and colorectal cancer. *Int J Cancer* 26:757-768, 1980
47. Jenkins DJA: Carbohydrate. *In* Shills ME, Young VR (eds): *Dietary Fiber and Modern Nutrition in Health and Disease*. Philadelphia, Lea & Febiger, 1988, pp 52-71
48. Jensen OM: Cancer risk among Danish male Seventh-Day Adventists and other temperance society members. *J Natl Cancer Inst* 70:1011-1014, 1983
49. Jensen OM, MacLennan R, Wahrendorf J: Diet, bowel function, fecal characteristics, and large bowel cancer in Denmark and Finland. *Nutr Cancer* 4:5-19, 1982
50. Katsouyanni K, Trichopoulos D, Boyle P, et al: Diet and breast cancer: Case-control study in Greece. *Int J Cancer* 38:815-820, 1986
51. Kay R: Effects of diet on the fecal excretion and bacterial modification of acidic and neutral steroids, and implications for colon carcinogenesis. *Cancer Res* 41:3774-3777, 1981
52. Kelsey JL: A review of research on effects of fiber intake on man. *Am J Clin Nutr* 31:142-159, 1978
53. Korenman SG: Endocrinology of breast cancer. 48:874-878, 1980
54. Kune S, Kune GA, Watson LF: Case-control study of dietary etiological factors: The Melbourne colorectal cancer study. *Nutr Cancer* 9:21-42, 1987
55. Lanza E, Butrum R: A critical review of food fiber analysis and data. *J Am Diet Assoc* 86:732-743, 1986
56. Lanza E, Greenwald P: The role of dietary fiber in cancer prevention. *Cancer Prev* 1-9, Sept 1989
57. La Vecchia CL, Decarli A, Fasoli M, et al: Nutrition and diet in the etiology of endometrial cancer. *Cancer* 57:1248-1253, 1986
58. La Vecchia CL, Decarli A, Franceschi S, et al: Dietary factors and the risk of breast cancer. *Nutr Cancer* 10:205-214, 1987
59. La Vecchia CL, Decarli A, Negri E, et al: Dietary factors and the risk of epithelial ovarian cancer. *J Natl Cancer Inst* 79:663-669, 1987
60. La Vecchia CL, Negri E, Decarli A, et al: A case-control study of diet and colorectal cancer in Northern Italy. *Int J Cancer* 41:492-498, 1988
61. Leeds AR: Modification of intestinal absorption by dietary fiber and fiber components. *In* Vahouny GV, Kritchevsky D (eds): *Dietary Fiber in Health and Disease*. New York, Plenum Press, 1982, pp 53-71
62. Lubin F, Wax Y, Modan B: Role of fat, animal protein, and dietary fiber in breast cancer etiology: A case-control study. *J Natl Cancer Inst* 77:605-612, 1986
63. Lupton JR, Coder DM, Jacobs LR: Long-term effects of fermentable fibers on rat colonic pH and epithelial cell cycle. *J Nutr* 118:840-845, 1988
64. Lyon JL, Mahoney AW, West DW, et al: Energy intake: Its relationship to colon cancer risk. *J Natl Cancer Inst* 78:853-861, 1987
65. MacLennan R: Rationale for intervention trials of dietary fiber and adenomatous polyps. *In* Kritchevsky D, Bonfield C, Anderson JW (eds): *Dietary Fiber: Chemistry, Physiology, and Health Effects*. New York, Plenum Press, 1990, pp 481-488
66. Macquart-Moulin G, Riboli E, Cornée J, et al: Case-control study on colorectal cancer and diet in Marseilles. *Int J Cancer* 38:183-191, 1986
67. Maitto OE, Bremner CG: Cancer of the colon and rectum in the coloured population of Johannesburg. *South Afr Med J* 60:571, 1981
68. Malhotra SL: Fecal urobilinogen levels and pH of stools in population groups with different incidence of cancer of the colon, and their possible role in etiology. *J R Soc Med* 75:709-714, 1982
69. Manosus O, Day NE, Trichopoulos D, et al: Diet and colorectal cancer: A case-control study in Greece. *Int J Cancer* 32:1-5, 1983
70. Martlette JA, Chesters JG, Longacre MJ, et al: Recovery of soluble dietary fiber is dependent on the method of analysis. *Am J Clin Nutr* 50:479-485, 1989
71. Martinez I, Torres R, Friaiz Z, et al: Factors associated with adenocarcinomas of the large bowel in Puerto Rico. *Revista Latinoamericana De Oncologia Clinica* 13:45, 1981
72. McKeown-Eyssen GE, Bright-See E: Dietary factors in colon cancer: International relationships. An update. *Nutr Cancer* 7:251-253, 1985
73. McLaughlin JK, Gridley G, Block G, et al: Dietary factors in oral and pharyngeal cancer. *J Natl Cancer Inst* 80:1237-1243, 1988
74. Miller DL, Miller PF, Dekker J: Small-bowel obstruction from the bran cereal. *JAMA* 263:813-814, 1990
75. Modan B, Lubin F, Barel BA, et al: The role of starches in the etiology of gastric cancer. *Cancer* 34:2087-2092, 1974
76. Morrison BC: The poly-p-cancer sequence in the large bowel. *Proc R Soc Med* 67:451-457, 1974
77. Nair PP, Turjuman N, Goodman GT, et al: Diet, nutrition intake, and metabolism in populations at high and low risk for colon cancer. *Am J Clin Nutr* 40:931-936, 1984
78. Newmark HL, Wargovich MJ, Bruce WR: Colon cancer and dietary fat, phosphate, and calcium: A hypothesis. *J Natl Cancer Inst* 72:1323-1325, 1984
79. Nuovo J: Use of dietary fiber to lower cholesterol. *Am Fam Phys* 38:137-140, 1989
80. Painter NS, Almeida AZ, Colebourne KW: Unprocessed bran in treatment of diverticular disease of the colon. *Br Med J* 2:137-140, 1972
81. Peters RK, Garabrant DH, Yu MC, et al: A case-control study of occupational and dietary factors in colorectal cancer in young men by subtype. *Cancer Res* 49:5459-5468, 1989
82. Pickle LW, Greene MH, Ziegler RG, et al: Colorectal cancer in rural Nebraska. *Cancer Res* 44:363-369, 1984
83. Plich SM: Physiological Effects and Health Consequences of Dietary Fiber. Washington DC, Life Science Research Office, FASEB, 1987
84. Pichumoni GS, Hearlan HI, Yerra N: Current status of dietary fiber. *Tropical Gastroenterology* 3:113-122, 1988
85. Potter JD: Dietary fiber, vegetables, and cancer. *J Nutr* 118:1591-1592, 1988
86. Potter JD, McMichael AJ: Diet and cancer of the colon and rectum: A case-control study. *J Natl Cancer Inst* 76:557-569, 1986
87. Powles JW, Williams DRH: Trends in bowel cancer in selected countries in relation to wartime changes in flour milling. *Nutr Cancer* 6:40-48, 1984
88. Pryor M, Slattery ML, Robinson LM, et al: Adolescent diet and breast cancer in Utah. *Cancer Res* 49:2161-2167, 1989
89. Reddy BS: Diet and excretion of bile acids. *Cancer Res* 41:3766-3768, 1981
90. Reddy BS: Dietary fiber and colon carcinogenesis: A critical review. *In* Vahouny GV, Kritchevsky D (eds): *Dietary Fiber in Health and Disease*. New York, Plenum Press, 1982, pp 265-285
91. Reddy BS, Ekelund G, Bohe M, et al: Metabolic epidemiology of colon cancer: Dietary pattern and fecal sterol concentrations of three populations. *Nutr Cancer* 5:34-40, 1983
92. Reddy BS, Engle A, Katsifis S, et al: Biochemical epidemiology of colon cancer: Effect of types of dietary fiber on fecal mutagens, acid, and neutral steroids in healthy subjects. *Cancer Res* 49:4629-4635, 1989
93. Reddy BS, Sharma C, Darby L, et al: Metabolic epidemiology of large bowel cancer:

- Fecal mutagens in high and low-risk populations for colon cancer. *Mutat Res* 72:511-522, 1980
94. Reddy BS, Sharma C, Simi B, et al: Metabolic epidemiology of colon cancer: Effect of dietary fiber on fecal mutagens and bile acids in healthy subjects. *Cancer Res* 47:644-648, 1987
95. Reddy BS, Watanabe K, Weisburger JH, et al: Promoting effect of bile acids in colon carcinogenesis in germ-free and conventional F344 rats. *Cancer Res* 37:3238-3242, 1977
96. Risch HA, Jain M, Choi NW, et al: Dietary factors and the incidence of cancer of the stomach. *Am J Epidemiol* 122:947-959, 1985
97. Roediger WEV: Utilization of nutrients by isolated epithelial cells of rat colon. *Gastroenterology* 83:424-429, 1982
98. Rohan TE, McMichael AJ, Baghurst PA: A population-based case-control study of diet and breast cancer in Australia. *Am J Epidemiol* 128:478-489, 1988
99. Rose DP: Dietary fiber and breast cancer. *Nutr Cancer* 13:1-8, 1990
100. Rosen M, Nystrom L, Wall S: Diet and cancer mortality in the counties of Sweden. *Am J Epidemiol* 127:42-49, 1988
101. Rozen P, Hellerstein SM, Horvitz C: The low incidence of colorectal cancer in a "high-risk" population. *Cancer* 48:2692-2695, 1981
102. Schatzkin A, Lanza E, Ballard-Barbash R: The case for a dietary intervention study of large bowel polyps. *Cancer Prev*, in press
103. Schatzkin A, Schiffman M, Lanza E: Research priorities in large bowel cancer prevention. *Semin Oncol*, in press
104. Schneeman BO: Dietary fiber and gastrointestinal function. *Nutr Rev* 45:129-132, 1987
105. Schneeman BO: Pancreatic and digestive function. In Vahouny GV, Kritchevsky D (eds): *Dietary Fiber in Health and Disease*. New York, Plenum Press, 1982, pp 73-83
106. Shultz TD, Howie BJ: In vitro binding of steroid hormones by natural and purified fibers. *Nutr Cancer* 8:141-147, 1986
107. Sinkeldam EJ, Kuper CF, Bosland MC, et al: Interactive effects of dietary wheat bran and lard on n-methyl-n'-nitro-n-nitrosoguanidine-induced colon carcinogenesis in rats. *Cancer Res* 50:1092-1096, 1990
108. Slattery ML, Schuman KL, West DW: Nutrient intake and ovarian cancer. *Am J Epidemiol* 130:497-502, 1989
109. Slattery ML, Sorensen AW, Mahoney AW, et al: Diet and colon cancer: Assessment of risk by fiber type and food source. *J Natl Cancer Inst* 80:1474-1480, 1988
110. Slavin JL, Marlett JA: Influence of refined cellulose on human bowel function and calcium and magnesium balance. *Am J Clin Nutr* 33:142-159, 1980
111. Smith AH, Pearce NE, Joseph JG: Major colorectal cancer aetiological hypotheses do not explain mortality trends among Maori and non-Maori New Zealanders. *Int J Epidemiol* 14:79-85, 1985
112. Smith AN, Eastwood MA: The measurement of intestinal transit time. In Spiller GA, Kay RM (eds): *Medical Aspects of Dietary Fiber*. New York, Plenum Medical Book Co, 1980, pp 27-42
113. Spiller GA, Shipley EA, Chernoff MC, et al: Bulk laxative efficacy of psyllium seed hydrocolloid and a mixture of cellulose and pectin. *J Clin Phar* 19:313-320, 1975
114. Stephen AM, Cummings JH: Mechanism of action of dietary fiber in the human colon. *Nature* 284:283-284, 1980
115. Stephen AM, Cummings JH: The microbial contribution to human fecal mass. *J Med Microbiol* 13:45-46, 1980
116. Stephen AM, Cummings JH: Water-holding by dietary fiber in vitro in relation to fecal output in man. *Gut* 20:722-729, 1979
117. Stem HS, Gregorie RC, Young KS, et al: A randomized controlled trial of sodium sulfate and dietary fiber on fecal pH and mucosal risk factors for colon cancer. *Proc Annu Meeting Am Assoc Cancer Res* 30:A924, 1989
118. Trook B, Lanza E, Greenwald P: Dietary fiber, vegetables, and colon cancer: Critical review and meta-analysis of the epidemiological evidence. *J Natl Cancer Inst* 82:650-661, 1990
119. Tynys AJ, Kaaks R, Haertlerman M: Colorectal cancer and the consumption of foods: A case-control study in Belgium. *Nutr Cancer* 11:189-204, 1988

120. United States Department of Agriculture: *Composition of Foods. Agriculture Hand Book # 8-11*. Washington DC, United States Government Printing Office, 1984
121. Varo P, Laine R, Veitalainen K, et al: Dietary fibre and available carbohydrates in Finnish cereal products. *Journal of Agricultural Science in Finland* 56:39-48, 1984
122. Varo P, Laine R, Veitalainen K, et al: Dietary fibre and available carbohydrates in Finnish vegetables and fruits. *Journal of Agricultural Science in Finland* 56:49-59, 1984
123. Vlainac H, Adanja B, Jarebinski M: Case-control study of the relationship of diet and colon cancer. *Arch Geschwulstforsch* 57:493-498, 1987
124. Walker ARP, Walker BF, Walker AJ: Faecal pH, dietary fiber intake and proneness to colon cancer in four South African populations. *Br J Cancer* 49:321-324, 1986
125. Willett WC, Stampfer MJ, Colditz GA, et al: A prospective study of diet and colon cancer in women (abstract). *Am J Epidemiol* 130:820, 1989
126. Young TB, Wolf DA: Case-control study of proximal and distal colon cancer and diet in Wisconsin. *Int J Cancer* 42:167-175, 1988

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