DIETARY FIBER AND DISEASE*

DAVID KRITCHEVSKY, PH.D.
Associate Director
Wistar Institute Of Anatomy and Biology
Philadelphia, Pennsylvania

Hippocrates commended the laxative properties of dietary fiber.[1] Early studies of the physiological effects of fiber by Cowgill et al.[2,3] and Williams and Olmstead[4] were concerned with its laxative properties. The modern fiber era had its genesis in the writing and research of Cleave,[5] who felt that modern diseases were related to the intake of refined carbohydrates; Burkitt,[6,7] who associated increased colon cancer with decreased fiber intake; and Trowell, [8,9] who correlated increased incidence of coronary heart disease with decreased fiber intake. Public notice of the fiber issue dates to the popular interpretations of a paper by Burkitt, Walker, and Painter,[10] which listed eight conditions prevalent in the United States but virtually nonexistent in Africa, and attributed the difference to our low intake of dietary fiber. The eight conditions cited were appendicitis, colon cancer, diverticular disease, gallstones, hemorrhoids, hiatus hernia, varicose veins, and ischemic heart disease. The public began to add fiber to its diet without regard to source, chemistry, or physiological effect.

The most widely accepted definition of fiber is that it is a substance of plant origin that cannot be digested by human endogenous enzymes. It should be pointed out that fiber is digested by bacterial enzymes in the colon with consequent production of hydrogen, carbon dioxide, methane, water, and short-chain fatty acids.

The chemical and physiological aspects of the common classes of dietary fiber are summarized in Tables I and II. The fiber content of foods has, until recently, been expressed as crude fiber, which is principally cellulose and lignin. Accurate fractionation of fiber has become possible only recently, and is due to the work of Van Soest[11] and Southgate.[12]

---

*Presented as part of a *Symposium on Assessing Therapeutic Dietary Claims* presented by the Section on Clinical Nutrition of the New York Academy of Medicine February 28, 1981.

This study was supported, in part, by a Career Research Award (HL00734) from the National Institute of Health and a grant-in-aid from the Commonwealth of Pennsylvania.

TABLE I
CLASSIFICATION OF FIBER BY STRUCTURE

Class	*Chemical components of main chain*
Cellulose	Linear glucose polymer
Hemicellulose	Xylose, mannose, glucose, galactose
Pectin	Galacturonic acid
Gums	Galacturonic acid — rhamnose or mannose
Mucilages	Galactose — mannose Galacturonic acid — rhamnose Arabinose — xylose
Algal Polysaccharides	Mannose, xylose, glucose, glucuronic acid
Lignin	Sinapyl, coniferyl, coumaryl alcohols

TABLE II
PHYSIOLOGICAL ACTIONS OF FIBER

Fiber class	*Possible functions in man*
Pectins, gums, and mucilages	Slow gastric emptying may bind bile acids May affect trace mineral excretion
Hemicellulose	Holds water; increases stool bulk May bind bile acids Reduces elevated colonic intraluminal pressure Reduces transit time
Cellulose	Holds water May reduce colonic intraluminal pressure May affect trace mineral excretion Reduces transit time
Lignin	Possible antioxidant Holds water May bind trace minerals Affects fecal steroids

LIPID METABOLISM

Ershoff and Wells[13-15] fed rats a fiber-free diet containing 1% cholesterol and observed a small increase in serum cholesterol and a five-fold increase in liver cholesterol. Addition of 10% pectin, carageenan, guar gum, or locust bean gum kept the increase in liver cholesterol down to 100%. Cellulose, alginic acid, or agar increase liver cholesterol levels when added to the basal diet.[13,16,17]

About 20 years ago it was reported [18,19] that rabbits fed saturated fat added to a semipurified diet developed atherosclerosis. A summary of the literature [20] showed that saturated fat did not exert a hypercholesterolemic or atherogenic effect when added to stock diet. Experiments [21,22] have confirmed the hypothesis that the fiber present in the diet mediates the influence of the saturated fat (Table III). Moore[23] fed rabbits a semipurified diet containing 20% butterfat and 19% wheat straw, cellulose, cellophane, or cellophane-peat (14:5). Average atheromatosis in the four groups was 13%, 21%, 38%, and 11%, respectively. Disposition of endogenous and exogenous cholesterol was studied in rabbits fed semisynthetic or stock diets.[24] Animals fed the semisynthetic diet retained more cholesterol in their serum, liver, and aorta and excreted less of this sterol (Table IV).

In man, cellulose exerts little or no hypocholesteremic effect.[25] In 1976 Truswell and Kay[26] summarized findings from 10 studies in which an average of 14 subjects were fed 14 to 100 g. of bran daily (average 37g.) for periods ranging from three to 19 weeks. Of the 10 studies, only one showed a serum cholesterol lowering of 7%. Pectin[25,27-31] (6 to 50g./day) and guar gum[32,33] (6 to 39 g./day) exert a hypercholesterolemic effect. Stasse-Wolthuis et al.[34] compared the effects of bran, pectin, and vegetables and fruits on serum and fecal lipids (Table V). After 5 weeks pectin had lowered serum cholesterol significantly but bran had raised it. Excretion of fecal steroids was increased in men but was variable in women.

Fiber exerts an effect on bile acid metabolism in rats[35,36] and primates.[37,38] Different types of fiber show variable effects in binding bile acids and bile salts.[39-41] Fiber can also bind cholesterol and phospholipids.[42,43]

Diabetes Mellitus

Cleave and Campbell[44] were the first to suggest that fiber-depleted foods might result in increased incidence of diabetes mellitus. Anderson et al. [45-47] showed that diabetic subjects fed a diet high in complex carbohydrate (hence high in fiber) have reduced serum cholesterol and glucose levels and reduced insulin requirements (Table VI). These effects have been confirmed by others.[48-52] While bran is hypoglycemic, wood cellulose and bagasse are hyperglycemic.[53]

Gallstones

Dam[54] found that a diet containing 74% sucrose and 20% casein was lithogenic for hamsters. Replacing 5% of the carbohydrate with pectin

TABLE III
INFLUENCE OF SPECIAL DIETS ON ATHEROSCLEROSIS IN RABBITS*

*Group***	*Fiber (%)*	*Fat (%)*	*Serum cholesterol (mg./dl. ±SEM)*	*Atherosclerosis (graded visually 0-4)*
A	Cellulose (15)	HCNO (14)†	207 ± 36	1.7
B	Cellulose (15)	HCNO (12) Stock (2)‡	249 ± 41	1.8
C	Stock (85)§	HCNO (14)	64 ± 9	0.8
D	Stock (86)‖	HCNO (12) Stock (2)	35 ± 2	0.5
E	Stock (98)‖	Stock (2)	40 ± 9	0.3

* After references 21, 22
** Diets A and B contain 40% dextrose, 25% casein.
† Hydrogenated coconut oil
‡ Fat extracted from stock diet
§ Residue from fat extraction
‖ Unextracted stock diet

TABLE IV
CHOLESTEROL DISPOSITION IN RABBITS FED STOCK OR SEMIPURIFIED DIETS*

	Group	
	Stock	*Semipurified*
Radioactivity		
[^{3}H] dpm./total serum x 10^5	0.38 ± 0.11	4.03 ± 0.36
[^{14}C]dpm./total serum	Undetected	2757
[^{3}H] dpm./liver x 10^6	1.34 ± 0.44	4.41 ± 0.52
[^{14}C] dpm./liver x 10^4	1.05 ± 0.28	3.99 ± 0.59
[^{3}H] dpm./aorta pool	920	2160
Free/ester	6.67	8.00
[^{14}C] dpm./aorta pool	88	198
Free/ester	0.33	1.25
Feces		
Weight (g.) (3 day collection)	98 ± 18	23 ± 9
[^{3}H] dpm. × 10^6	18.96 ± 11	4.70 ± 1.5
Neutral/acidic	121	4
[^{14}C] dpm. × 10^3	11.75 ± 4.3	8.86 ± 3.0
Neutral/acidic	31	1.4

* After Kritchevsky et al.[24]
Semipurified diet = 25% casein, 20% starch, 20% sucrose, 14% hydrogenated coconut oil
[1,2-^{3}H]cholesterol (10 μCi) and [2-^{14}C] mevalonic acid (0.5 μCi) injected intraperitoneally 72 hrs. before autopsy.
dpm. = disintegrations per minute

TABLE V
INFLUENCES OF DIETARY FIBER ON SERUM AND FECAL LIPIDS IN MAN*

	Group			
	Control	*Vegetables and fruit*	*Citrus pectin*	*Bran*
Number	16	15	15	16
Serum cholesterol, mg./dl.				
Before experiment	168	162	171	166
After control period	182	176	185	180
After five weeks	178	169	172	193
HDL-Cholesterol				
Before experiment	58	55	62	58
After control period	58	56	64	59
After five weeks	59	57	65	62
Transit time (% change)	+25	−20	+0.7	−28
Fecal steroids (% change)				
Males Neutral	−3	+50	+18	−5
Males Acidic	+18	+3	+51	−23
Females Neutral	+52	−16	−24	+33
Females Acidic	+2	−31	+53	+41

*After Stasse-Wolthuis et al.[34]

TABLE VI
EFFECT OF HIGH FIBER DIETS IN DIABETICS* (10 SUBJECTS)

	Control	*High fiber***
Glucose, mg./dl.	182 ± 12	163 ± 12
Cholesterol, mg./dl.	209 ± 16	142 ± 7
Triglycerides, mg./dl.	135 ± 24	132 ± 25
Insulin, U/day	27 ± 3	12 ± 4

*After Anderson et al.[46]
**Simple/complex carbohydrate: control diet, 0.98; high fiber diet, 0.33
Plant fiber, g./day: control diet, 20; high fiber diet, 64

reduces the incidence of gallstones by 50% and 5% lignin eliminates gallstone formation in rabbits fed a diet containing 30% casein and 15% beef tallow.[55,56] Gallstone formation in man is associated with a diminished bile acid pool.[57] Addition of fiber to the diet of rats,[58] monkeys,[59] or man[60] expands the bile acid pool, which may explain its effects on gallstone formation.

COLON CANCER

Whereas Burkitt[7] has interpreted international epidemiological data to show that incidence of colon cancer is related to low levels of dietary fiber, Drasar and Irving[61] found virtually no correlation between cancer of the colon or breast and fiber intake. Modan et al.[62] compared the diets of confirmed colon cancer patients with those of neighborhood or surgical controls and found significant differences in fiber intake. Most other data implicating lack of dietary fiber in the development of colon cancer are indirect. For example, Glober et al.[63] found that Hawaiian-born Japanese had an incidence of colon cancer like that of their Caucasian neighbors despite exhibiting shorter intestinal transit time and greater fecal bulk. Their transit time and fecal weight resembled those of their immigrant fathers, but their cancer incidence was five times higher.

Bile acids have been implicated in the etiology of colon cancer as promoters.[64] Because bile acids are promoters, it is reasonable to suppose that substances which bind them would affect experimental colon carcinogenesis. Bran[65] and cellulose,[66] substances that have very low binding capacities, inhibit dimethylhydrazine (DMH)-induced colon cancer in rats whereas cholestyramine, a potent bile acid-binding resin, enhances colon cancer induced by dimethylhydrazine, azoxymethane, or methylnitrosourea.[67]

Azoxymethane or methylnitrosoura were used to induce colon tumors in rats fed 15% alfalfa, bran, or pectin.[68] The former compound, which was administered by injection, was significantly less carcinogenic in rats fed bran or pectin; the latter, instilled intrarectally, was significantly more carcinogenic in rats fed alfalfa (Table VII). We have shown that substances which bind bile acids disrupt the morphology of the intestine,[69] and this may explain the results obtained by Nigro et al.[67] and Watanabe et al.[68]

In man, fecal steroids have been analyzed in subjects with colon cancer or prone to it: Mower et al.[70] analyzed fecal bile acids in Hawaiian Japanese and in residents of Akita, Japan. The Hawaiians have a five times greater incidence of colon cancer, but the two groups have identical ratios of fecal primary to secondary bile acids, indicating similar metabolism. Reddy et al.[71] analyzed fecal steroids in colon cancer patients and controls, but no consistent patterns emerged (Table VIII). Residents of Kuopio, Finland, have a much lower incidence of colon cancer than do New Yorkers. The two groups excrete the same amount of bile acid, but the concentration of fecal bile acids in New York residents is twice that seen in the Finns.[71] This

TABLE VII
INFLUENCE OF FIBER (15%) ON COLON TUMORS IN RATS*

	*Treatment***			
	Azoxymethane (AOM)		*Methylnitrosourea (MNU)*	
Dietary fiber	*Incidence (%)*	*Tumors/rat*	*Incidence (%)*	*Tumors/rat*
Control	57	0.8	69	1.0
Alfalfa	53	0.7	83	2.3
Bran	33	0.4	60	0.8
Pectin	10	0.1	59	1.0

* After Watanabe et al.[68]
** AOM given intramuscularly; MNU intrarectally

TABLE VIII
FECAL STEROIDS IN SELECTED POPULATIONS*

Group	*No.*	*Primary/secondary bile acids*
Study I		
Colon cancer cases	35	0.074
Adenomatous polyps	15	0.061
Control	40	0.088
Study II		
U.S.-high fat	17	0.043
U.S.-vegetarian	12	0.127
U.S.-Seventh Day Adventists	11	0.025
Japanese	17	0.079
Chinese	11	0.071

*After Reddy[71]

aspect of diet and colon carcinogenesis merits further investigation. Fiber is not without its drawbacks. Dietary fiber has been shown to reduce bioavailability of calcium,[72,73] iron,[74] zinc,[74,75] and magnesium[76] and it may also contain inhibitors of proteolytic enzymes.[77]

In summary, dietary fiber seems to exert a definitely beneficial effect in diabetes mellitus in man, but a directly positive influence on lipid metabolism and colon cancer is not as apparent. More work remains to be done in relating fiber structure to specific physiological effects.

Questions and Answers

DR. MAURICE SHILS: Dr. Kritchevsky, Anderson talks about soluble fiber. What does he mean by that?
DR. KRITCHEVSKY: I think he means things like pectin which are water soluble and some of the gums which are gel-forming but water soluble.
DR. SHILS: He seems to put greater emphasis on the value of the soluble.
DR. KRITCHEVSKY: Jenkins finds the same thing. They both think that this gel-forming material can somehow form a matrix in the gut. If one wants to put it simply, the sugar can't get out. Anderson is not the first, but he has done studies to see how much fiber is broken down. Except for lignin, very few types of fiber pass through the gut completely unaffected. In fact, data show that if one feeds pectin to patients they excrete no pectin—it is all chewed up by the intestinal flora.
QUESTION: If one, for example, is going to use whole grain flour, is there any connection between the fineness of the grinding of the flour and its action?
DR. KRITCHEVSKY: One experiment in rats suggests that the more finely ground the bran, the more it inhibits absorption so that might be a positive thing. On the other hand, the same people showed that if the bran is too finely ground, one gets persorption, where little particles go into the blood stream. I would say that with something like flour, one probably wouldn't have any worries. One must remember that a lot of these studies are done for a very specific reason by a very specific modality and cannot always be related to human conditions.
QUESTION: I had occasion to speak to Dr. Anderson a couple of years ago. He has been doing some experimental work with oat bran and he finds oat bran does lower cholesterol, unlike wheat bran and rice bran. I wonder if you could comment about the use of oat bran?
DR. KRITCHEVSKY: Most people who use bran use wheat bran. Wheat bran has been used a lot because the American Association for Cereal Chemists had a special batch of it made so that everybody could use the same starting material. And wheat bran, except for bran made from hard red spring wheat, has no effect on serum cholesterol levels. Oat bran certainly has an effect as Anderson and people before him found. I know of nobody to date who has done structural studies to see

what the difference between those brans is. Malinow did studies in monkeys using corn bran, rice bran, and wheat bran and none of them affected serum lipids or lipid metabolism.

QUESTION: I noticed that you left psyllium out of the earlier part of your lecture on the structure and relationships of fiber to cholesterol levels and heart disease. Could you comment on that please?

DR. KRITCHEVSKY: Psyllium is just another form of gel-forming fiber. Most of the mucilaginous forms of fibers act more like pectin than anything else and their effect seems to be more like pectin than anything else.

REFERENCES

1. McCance, R. A. and Widdowson, E. M.: Old thoughts and new work on breads, white and brown. *Lancet 2:*205–10, 1955.
2. Cowgill, G. R. and Anderson, W. E.: Laxative effect of wheat bran and washed bran in healthy man. *J.A.M.A. 98:*1866–75, 1932.
3. Cowgill, G. R. and Sullivan, A. J.: Further studies on the use of wheat bran as a laxative. *J.A.M.A. 100:*795–802, 1933.
4. Williams, R. D. and Olmstead W. H.: The manner in which food controls the bulk of feces. *Ann. Intern. Med 10:*717, 1936.
5. Cleave, T. L.: The neglect of natural principles in current medical practice. *J. Royal Naval Med. Serv. 42:*55–82, 1956.
6. Burkitt, D. P: Related disease—related cause. *Lancet 2:*1229–31, 1969.
7. Burkitt, D. P.: Epidemiology of large bowel disease: The role of fibre. *Proc. Nutr. Soc. 32:*145–49, 1973.
8. Trowell, H.: Crude fibre dietary and atherosclerosis. *Atherosclerosis 16:*138–40, 1972.
9. Trowell, H.: Coronary heart disease and dietary fiber. *Am. J. Clin. Nut. 28:*798–99, 1975.
10. Burkitt, D. P., Walker, A. R. P., and Painter, N. S.: Dietary fiber and disease. *J.A.M.A. 229:*1068–74, 1974.
11. Van Soest, P. J. and McQueen, R. W.: The chemistry and estimation of fiber. *Proc. Nutr. Soc. 32:*123–30, 1973.
12. Southgate, D. A. T.: The Analysis of Dietary Fiber. In: *Fiber in Human Nutrition.* Spiller, G. A. and Amen, R. J., editors. New York, Plenum, 1976, pp. 73–107.
13. Wells, A. F. and Ershoff, B. H.: Beneficial effects of pectin in prevention of hypercholesterolemia and increase in liver cholesterol in cholesterol-fed rats. *J. Nutr. 74:*87–92, 1961.
14. Ershoff, B. H. and Wells, A. F.: Effects of methoxyl content on anti-cholesterol activity of pectic substances in the rat. *Exp. Med. Surg. 20:*272–76, 1962.
15. Ershoff, B. H. and Wells, A. F.: Effects of gum guar, locust bean gum and carrageenan on liver cholesterol of cholesterol-fed rats. *Proc. Soc. Exp. Biol. Med. 110:*580–82, 1962.
16. Kiriyama, S., Okozaki, Y., and Yoshida A.: Hypocholesterolemic effect of polysaccharides and polysaccharide-rich foodstuffs in cholesterol-fed rats. *J. Nutr. 97:*382–88, 1969.
17. Tsai, A. C., Elias, J., Kelly, J. J., et al.: Influence of certain dietary fibers on serum and tissue cholesterol levels in rats. *J. Nutr. 106:*218–23, 1976.
18. Lambert, G. F., Miller, J. P., Olsen, R. T., and Frost, D. V.: Hypercholesteremia and atherosclerosis induced in rabbits by purified high fat rations devoid of cholesterol. *Proc. Soc. Exp. Biol. Med. 97:*544–49, 1958.
19. Malmros, H. and Wigand, G.: Atherosclerosis and deficiency of essential fatty acids. *Lancet 2:*749–51, 1959.

20. Kritchevsky, D.: Experimental atherosclerosis in rabbits fed cholesterol-free diets. *J. Ath. Res. 4:*103–05, 1964.
21. Kritchevsky, D. and Tepper, S. A.: Factors affecting atherosclerosis in rabbits fed cholesterol-free diets. *Life Sci. 4:*1467–71, 1965.
22. Kritchevsky, D. and Tepper, S. A.: Experimental atherosclerosis in rabbits fed cholesterol-free diets: Influence of chow components. *J. Ath. Res. 8:*357–69, 1968.
23. Moore, J. H.: The effect of the type of roughage in the diet on plasma cholesterol levels and aortic atherosis in rabbits. *Br. J. Nut. 21:*207–15, 1967.
24. Kritchevsky, D., Tepper, S. A., Kim, H. K., et al.: Experimental atherosclerosis in rabbits fed cholesterol-free diets. 4. Investigation into the source of cholesteremia. *Exp. Mol. Pathol. 22:*11–19, 1975.
25. Keys, A., Grande, F., and Anderson, J. T.: Fiber and pectin in the diet and serum cholesterol concentration in man. *Proc. Soc. Exp. Biol. Med. 106:*555–58, 1961.
26. Truswell, A. S. and Kay, R. M.: Bran and blood-lipids. *Lancet 1:*367, 1976.
27. Lopez, A., Hopson, J., and Krehl, W. A.: Effect of dietary pectin on plasma and fecal lipids. *Fed. Proc. 27:*485, 1968.
28. Palmer, G. H. and Dixon, D. G.: Effect of pectin dose on serum cholesterol levels. *Am. J. Clin. Nutr. 18:*437–42, 1966.
29. Durrington, P. N., Manning, A. P., Bolton, C. H., and Hartog, M.: Effect of pectin on serum lipids and lipoproteins, whole gut transit time and stool weight. *Lancet 2:*394–96, 1976.
30. Miettinen, T. A. and Tarpila, S.: Effect of pectin on serum cholesterol, fecal bile acids and biliary lipids in normolipidemic and hyperlipidemic individuals. *Clin. Chim. Acta 79:*471–77, 1977.
31. Kay, R. M. and Trusell, A. S.: Effect of citrus pectin on blood lipids and fecal steroid excretion in man. *Am. J. Clin. Nutr. 30:*171–75, 1977.
32. Fahrenbach, M. J., Riccardi, B. A., Saunders, J. C., et al.: Comparative effects of guar gum and pectin on human serum cholesterol levels. *Circulation 32:*11, 1965.
33. Jenkins, D. J. A., Leeds, A. R., Newton, C., and Cummings, J. H.: Effect of pectin, guar gum and wheat fibre on serum cholesterol. *Lancet 1:*116–17, 1975.
34. Stasse-Wolthuis, M., Albers, H. F. F., van Jeveren, J. G. C., 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. 33:*1745–56, 1980.
35. Portman, O. W., and Murphy, P.: Excretion of bile acids and β-hydroxysterols by rats. *Arch. Biochem. Biophys. 76:*367–76, 1958.
36. Leveille, G. A. and Sauberlich, H. E.: Mechanisms of the cholesterol-depressing effect of pectin in the cholesterol-fed rat. *J. Nutr. 88:*209–14, 1966.
37. Kritchevsky, D., Davidson, L. M., Shapiro, I. L., et al.: Lipid metabolism and experimental atherosclerosis in baboons: Influence of cholesterol-free, semi-synthetic diets. *Am. J. Clin. Nutr. 27:*29–50, 1974.
38. Kritchevsky, D., Davidson, L. M., Kim, H. K., et al.: Influence of semipurified diets on atherosclerosis in African green monkeys. *Exp. Mol. Pathol. 26:*28–51, 1977.
39. Eastwood, M. A. and Boyd, G. S.: The distribution of bile salts along the small intestine of rats. *Biochim. Biophys. Acta 137:*393–96, 1967.
40. Kritchevsky, D. and Story, J. A.: Binding of bile salts *in vitro* by non-nutritive fiber. *J. Nutr. 104:*458–62, 1974.
41. Story, J. A. and Kritchevsky, D.: Comparison of the binding of various bile acids and bile salts *in vitro* by several types of fiber. *J. Nutr. 106:*1292–94, 1976.
42. Vahouny, G. V., Tombes, R., Cassidy, M. M., et al.: Dietary fibers. V. Binding of bile salts, phospholipids and cholesterol from mixed micelles by bile acid sequestrants and dietary fibers. *Lipids 12:*1012–18, 1980.
43. Vahouny, G. V. V., Tombes, R., Cassidy, M. M., et al.: Dietary fibers. VI. Binding of fatty acids and monolein from mixed micelles containing bile

salts and lecithin. *Proc. Soc. Exp. Biol. Med. 166*:12–18, 1981.
44. Cleave, T. L. and Campbell, G. D.: *Diabetes, Coronary Thrombosis and the Saccharine Disease*. Bristol, England, Wright, 1966.
45. Keihm, T. G., Anderson, J. W., and Ward, K.: Beneficial effects of a high carbohydrate, high fiber diet on hyperglycemic diabetic men. *Am. J. Clin. Nutr. 29*:895–99, 1976.
46. Anderson, J. W. and Chen, W. L.: Plant fiber. Carbohydrate and lipid metabolism. *Am. J. Clin. Nutr. 32*:346–63, 1979.
47. Anderson, J. W., Chen, W. L., and Sieling, B.: Hypolipidemic effects of high-carbohydrate, high-fiber diets. *Metabolism 29*:551–58, 1980.
48. Jenkins, D. J. A., Wolevar, T. M. S., Haworth, R., et al.: Unabsorbable carbohydrate and diabetes: Decreased postprandial hyperglycemia. *Lancet 2*:172–74, 1976.
49. Jenkins, D. J. A., Wolevar, T. M. S., Haworth, R., et al.: Guar gum in diabetes. *Lancet 2*:1086–87, 1976.
50. Miranda, P. A. and Horwitz, D. L.: High-fiber diets in the treatment of diabetes mellitus. *Ann. Intern. Med. 88*:482–486, 1978.
51. Kay, R. M., Grobin, W., and Track, N. S.: Diets rich in natural fibre improve carbohydrate tolerance in maturity-onset, non-insulin dependent diabetics. *Diabetologia 20*:18–21, 1981.
52. Monnier, L. H., Blotman, M. J., Colette, C., et al.: Effects of dietary fibre supplementation in stable and labile insulin-dependent diabetics. *Diabetologia 20*:12–17, 1981.
53. Jeffreys, D. B.: The effect of dietary fiber on the response to orally administered glucose. *Proc. Nutr. Soc. 33*:11A–12A, 1974.
54. Dam, H.: Nutritional aspects of gallstone formation with particular reference to alimentary production of gallstones in laboratory animals. *World Rev. Nutr. Diet. 11*:199–239, 1969.
55. Bergman, F. and van der Linden, W.: Effect of dietary fibre on gallstone formation in hamsters. *Z. Ernahrungswiss. 14*:217–23, 1975.
56. Borgman, R. F. and Wardlow, F. B.: Serum cholesterol and cholelithiasis in rabbits treated with pectin and cholestyramine. *Am. J. Vet. Res. 35*:1445–47, 1974.
57. Bell, C. C., Vlahcevic, V. R., Prazick, J., and Swell, L.: Evidence that a diminished bile acid pool precedes the formation of cholesterol gallstones in man. *Surg. Gynecol. Obstet. 136*:961–65, 1973.
58. Boyd, G. S. and Eastwood, M. A.: Studies on the quantitative distribution of bile salts along the rat small intestine under varying dietary regimes. *Biochim. Biophys. Acta 152*:159–64, 1968.
59. Osuga, T., Portman, O. W., Tanaka, N., et al.: The effect of diet on hepatic bile acid metabolism in squirrel monkeys with and without cholesterol gallstones. *J. Lab. Clin. Med. 88*:649–61, 1976.
60. Pomare, E. W., Heaton, K. W., Low-Beer, T. S., and Espiner, H. J.: The effect of wheat bran upon bile salt metabolism and upon the lipid composition of bile in gallstone patients. *Am. J. Dig. Dis. 21*:521–26, 1976.
61. Drasar, B. S. and Irving D.: Environmental factors and cancer of the colon and breast. *Br. J. Cancer 27*:167–72, 1973.
62. Modan, B., Barell, V., Lubin, F., et al.: Low fiber intakes as an etiological factor in cancer of the colon. *J. Nat. Cancer Inst. 55*:15–18, 1975.
63. Glober, G. A., Nomura, A., Kamiyama, S. et al.: Bowel transit-time and stool weight in populations with different colon-cancer risks. *Lancet 2*:110–11, 1977.
64. Reddy, B. S.: Role of bile metabolites in colon carcinogenesis. *Cancer 36*:2401–06, 1975.
65. Barbolt, T. A. and Abraham, R.: The effects of bran on dimethylhydrazine-induced colon carcinogenis in the rat. *Proc. Soc. Exp. Biol. Med. 157*:656–59, 1978.
66. Freeman, H. J., Spiller, G. A., and Kim, Y. S.: A double-blind study on the effects of differing purified cellulose and pectin-fiber diets on 1,2-dimethylhydrazine-induced rat colonic neoplasia. *Can-*

*cer Res. 40:*2661–65, 1980.
67. Nigro, M. D., Bhadrachari, N., and Chomchai, C.: A rat model for studying colonic cancer: Effect of cholestyramine on induced tumors. *Dis. Colon Rectum 16:*438–43, 1973.
68. Watanabe, K., Reddy, B. S., Weisburger, J. H., and Kritchevsky, D.: Effect of dietary alfalfa, pectin and wheat bran on azoxymethane or methylnitrosourea-induced colon carcinogenesis in F344 rats. *J. Nat. Cancer Inst. 63:*141–45, 1979.
69. Cassidy, M. M., Lightfoot, F. G., Grau, L. E., et al.: Effect of intake of dietary fibers on the ultrastructural topography of rat jejunum and colon: A scanning electron microscope study. *Am. J. Clin. Nutr. 34:*218–28, 1981.
70. Mower, H. F., Ray, R. M., Shoff, R., et al.: Fecal bile acids in two Japanese populations with different colon cancer risks. *Cancer Res. 39:*328–331, 1979.
71. Reddy, B. S.: Nutrition and Colon Cancer. In: *Advanced Nutrition Research,* Draper, H. H., editor. New York, Plenum, 1979, vol. 2, pp. 199–218.
72. McCance, R. A., and Widdowson, E. M.: Mineral metabolism of healthy adults on white and brown bread dietaries. *J. Physiol. 101:*44–85, 1942.
73. Reinhold, J. C., Nasr, D., Lahimgarzadeh, A., and Hedayote, H.: Effects of purified phytate and phytate-rich bread upon metabolism of zinc, calcium, phosphorus and nitrogen in man. *Lancet 1:*283–288, 1973.
74. Reinhold, J. G., Ismail-Beigi, F., and Favadji, B.: Fiber versus phytate as determinant of the availability of calcium, zinc and iron in breadstuffs. *Nutr. Rep. Int. 12:*75–85, 1975.
75. Davies, N. T. and Nightingale, R.: The effect of phytate on intestinal absorption and secretion of zinc and whole-body retention and secretion of Zn, copper, iron and manganese in rats. *Br. J. Nutr. 34:*242–58, 1975.
76. Reinhold, J. G., Favadji, B., Abadi, P., and Ismail-Beigi, F.: Decreased absorption of calcium, magnesium, zinc and phosphorus by humans due to increased fiber and phosphorus consumption as wheat bread. *J. Nutr. 106:*493–503, 1976.
77. Mistuanaga, T.: Some properties of protease inhibitors in wheat grain. *J. Nutr. Sci. Vitaminol. 20:*153–59, 1974.