Medical Grand Rounds

Oatmeal or Angioplasty?
The Propitious Effects of Dietary Fiber on Lipid Metabolism

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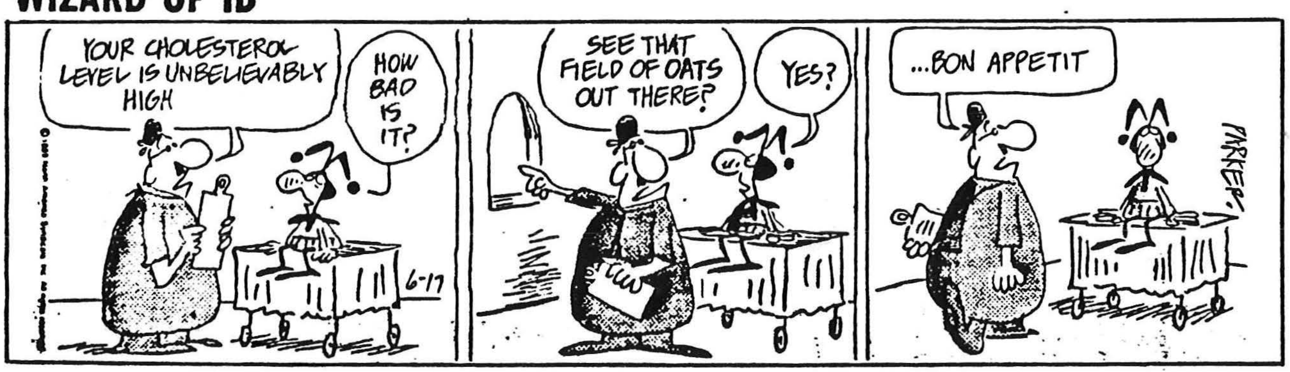


I. Introduction

The threat of premature death from atherosclerotic heart disease provokes a deep anxiety among many Americans, especially men. (1) This well founded fear is based upon the fact that almost 1,000,000 Americans die annually from heart disease and it remains the leading cause of death for American men over the age of 35. (2) Smoking, diabetes, hypertension, and a family history of premature heart disease have been identified as independent risk factors for the development of atherosclerotic heart disease. Additionally, hypercholesterolemia and more specifically, an elevated concentration of low density lipoprotein cholesterol in the blood have been unequivocally linked to the development of premature atherosclerosis. Moreover, epidemiological studies, clinical trials and the genetic analysis of kindreds with familial hypercholesterolemia have conclusively shown that an elevated LDL cholesterol concentration actually <u>causes</u> atherosclerosis and is not simply associated with it. (3,4)

The results of the LIPID RESEARCH CLINICS CORONARY PRIMARY PREVENTION TRIAL became available in 1984 and provided the first definitive evidence that reducing plasma LDL-cholesterol concentrations would reduce the risk of heart disease. (5) This study gave the impetus for the National Heart , Lung and Blood Institute to launch the National Cholesterol Education Program (NCEP) in 1985. A group of experts was charged with developing a consensus on when and how to treat hypercholesterolemia. In October 1987, the NCEP released the Report of the Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2). The report came to the startling conclusion that 27% of adults in the United States have cholesterol levels that put them at "high risk" for developing heart disease (>240 mg/dl or >6.21 mM). They further concluded that an additional 30% of the adult population have cholesterol levels that place them at borderline-high risk (200-239 mg/dl or 5.17-6.20 mM). Thus, a panel of experts in the field have concluded that an astonishing 100,000,000 Americans are in need of treatment for hypercholesterolemia (2). The NCEP algorithm (Figure 23) for the dietary management of those at risk calls for a minimum of five office visits in the first year and twice yearly thereafter. Enactment of this program on a national scale would mean that a typical primary care doctor would be providing about six hundred additional office visits yearly to monitor and counsel these patients.

Clearly, then, economic realities dictate that for most of these 100,000,000 Americans at risk, the only "treatment" that they are likely to get will be in the form of an educational program aimed at modifying their behavior.

II. The Dietary Fiber Hypothesis

Surgeon Captain T. E. Cleave, a physician in the Royal Navy, formulated a hypothesis in 1956 in which he proposed that all diseases particular to Western societies could be attributed to the over consumption of refined carbohydrates. Cleave's "Saccharine Disease" hypothesis, though based on very little data, nonetheless attracted a great deal of attention in post-war Britain. Meanwhile, another British surgeon named Denis Burkitt, while serving in the central African colony of Uganda became familiar with Cleave's saccharine disease hypothesis. Burkitt , who is perhaps best known for his studies on the epidemiology of the peculiar lymphoma that bears his name, was impressed with the virtual absence of certain diseases which he knew to be very common back in Britain. Whereas Cleave had emphasized the consumption of refined carbohydrates, especially sucrose, as the cause of Western diseases, Burkitt proposed that it was the consumption of a diet rich in plant fiber that was protective against these same diseases. In 1975, along with another British physician, Hugh Trowell, Burkitt formulated the dietary fiber hypotheses which is summarized below. (6-8)

The Dietary Fiber Hypothesis

1. A diet rich in foods containing plant cell walls is protective against a range of diseases prevalent in western communities (coronary heart disease, diabetes, stroke, diverticular disease, colon cancer, etc.).

2. In some instances a diet, poor in foods containing plant cell walls, is a causative factor in the development of the disease (e.g. diverticular disease) and in others it provides the conditions where other etiological factors are active.

Denis Burkitt, 1971

III. The "Normal" Human Diet

Implicit in the above hypothesis is the premise that people in Western societies have in some way deviated from the "normal" human diet. Human beings as a species can be correctly classified as omnivores and the normal human diet obviously varies enormously between different ethnic groups and in different geographic areas. For example, the Eskimo people living in the Arctic regions subsist on a diet that is largely of animal origin, whereas people living in technologically primitive societies in sub Saharan Africa exist on a diet that is almost exclusively of plant origin. Before assuming that any one group of people consume a diet that is ideally suited for human beings, it would be useful to consider the evolution of Homo sapiens and attempt to reconstruct the diet consumed by our ancestors at the time natural selection was shaping our digestive systems. (9-12)

Time Course of Human Evolution

Years BP (thousands)	Epoch	Development	Subsistence Activity	Diet
0.2		Industrial revolution	Urbanization, sedentary lifestyle	Ultrarefined cereal grains Marbled meat, tropical oils
10	Modern Times	Agriculture and domestication of animals Glaciers recede	Herding and farming Storage of food surpluses	Rapid shift to cereal grains as predominant calorie source Some aquatic foods
45	Latest Pleistocene	*Homo sapiens sapiens* appears	Mass killings of large game	
80	Late Pleistocene	*H. sapiens neanderthalensis* appears, use of fire	Highly organized hunting/gathering strategy Specialization of large game hunting	Equal portions of meat and vegetables Extensive processing of food
1,600	Early Pleistocene	*H. erectus* present	Gathering fruits and vegetables Scavenging meat Possibly hunting small game	Primarily fruits and vegetables Occasional meat Some non-oral food processing
4,000	Pliocene	Australopithecine divergence, earliest stone tools Bipedal *Australopithecus afranensis* present		
7,500	Late Miocene	African apes and African homonids diverge (inferred from molecular data)		
11,000	Middle Miocene	African and Asian hominoids diverge		
24,000	Early Miocene	Hominoids diverge from Old World monkeys	Tree dwellers	Insects, fruits, unprocessed vegetables

Table 1 above gives a brief outline of human evolution with particular attention to the subsistence activities and an educated guess as to diet . In the early Miocene epoch, when hominoids diverged from Old World monkeys, the primates lived in trees and ate a diet of insects, fruits, and unprocessed vegetables.

The first major dietary transition occurred about one and a half million years ago at the beginning of the Pleistocene epoch with the emergence of Homo erectus. As the name would imply, this hominid lived on the ground, walked upright and spent his time gathering fruits and vegetables and scavenging for meat left behind by other predators. The fossil record would suggest that some of these individuals hunted for small game. Their diet consisted primarily of fruits and vegetables with occasional meat and there is evidence of some non-oral food processing. Eighty thousand years ago, in the late Pleistocene (when glaciers covered much of Europe and Asia) Homo sapiens neanderthalensis appeared. Able to use fire and adept at toolmaking, Neanderthal men pursued a highly organized strategy of hunting and gathering. They began specializing in hunting certain species of large game. Their diet is thought to have consisted of equal portions of meat and vegetables. When anatomically modern man, Homo sapiens sapiens, appeared 45,000 years ago, the fossil record shows continued hunting of large game including several sites of mass killing. (At Solutre in France, one archaeological site has revealed the skeletons of more than 100,000 horses that were killed and butchered by humans.)

The second major transition in the human diet occurred about 10,000 years ago at the time that the glaciers receded. These physiologically modern humans learned to plant crops and domesticate certain animals. They began to store surplus food and for the first time certain members of society were afforded the luxury of pursuing interests other than subsistence behavior. Hence, cities, written languages, art, and science emerged. With the development of agriculture, the typical diet underwent a rapid shift from roughly equal portions of meat and vegetables to a diet in which cereal grains were the predominate calorie source. Although some new foods such as dairy products and aquatic foods were added to the diet at this time, in general the human diet shrank to a very small niche compared with what it had been prior to the development of agriculture. For example, prior to agriculture the typical human would consume a variety of wild game and would gather and eat a hundred or more species of edible plants. After agriculture, cereal grains (e.g., rice, wheat, maize) accounted for up to 80% of the calories.

Paradoxically, as agriculture vastly increased the capacity for food production, humans became vulnerable to famine and malnutrition. The nomadic hunter/gatherer of 30,000 years ago could move on to greener pastures in times of drought, but after agriculture, when the weather was dry and crops failed, famine ensued. Archaeological evidence confirms that famine has increased in incidence with the increasing reliance on agricultural products. Additionally, the very broad omnivorous diet of a hunter/gatherer ensured an adequate supply of vitamins and protein. After the agricultural revolution, however, the narrowing of the dietary niche to a few cereal grains made humans vulnerable to specific vitamin deficiencies and protein malnutrition. Indeed, the mean stature of human beings fell by more than 15 cm after the beginning of agriculture. Only during the last 100 years, during which time meat (and therefore protein) consumption again increased, have we regained the height of our ancestors 30,000 years ago.

The third major dietary transition occurred with the Industrial Revolution barely 200 years ago. We now live a sedentary life style in an urban environment. Technological advances such as steel-roller milling have allowed us to extract more than 90% of the plant fiber present in cereal grains. We now feed corn to immobilized ruminants to produce a marbled meat remarkable for its saturated fat content, and we hydrogenate vegetable oils and import tropical oils in order to create a desirable texture in our processed foods. Most nutritionists and many consumers now agree that our current Western diet is over-processed and too rich in saturated fat for optimal health (13).

Estimated Composition of a Stone-age Diet

	Latest Pleistocene	Current American	RDDA
Total energy (%)			
Protein	34	12	12
Carbohydrate	45	46	58
Fat	21	42	30
P:S ratio	1.41	0.44	1.00
Cholesterol (mg)	591	600	300
Dietary Fiber (g)	45.7	19.7	30-60

Table 2 above shows the estimated composition of a diet eaten by humans 30,000 years ago and compares it to a modern American diet and the recommended daily dietary allowance(11).

Since the glaciers last melted and agriculture was invented, only about 400 generations of human beings have lived and died. From an evolutionary and genetic point of view, we have not yet had time to adapt to the dramatic changes brought about by the agricultural revolution and certainly no time at all to adapt to the dietary changes brought about by the Industrial Revolution. In essence, the human digestive system has not changed from the time of the hunter/gatherer. One should not, therefore, assume that a traditional diet based on the four traditional food groups (two of which emerged only after agriculture) is necessarily the diet for which our evolution has prepared us.

IV. Chemical Definition of Dietary Fiber

Until relatively recently, the dietary fiber content of human food stuffs was rarely measured; rather, the fiber content was measured in animal feeds where it helped determine the price (the more fiber in the hay, the less the hay cost). The assay procedure used to measure fiber content was a simple gravimetric assay of the residue following acid and alkaline extraction of an aliquot of the forage. The assay was termed "crude fiber" and was meant to estimate the cellulose content of forage. The crude fiber assay was never really meant to be applicable to human food stuffs, nonetheless, until 1984 the crude fiber assay was by default the only method recognized by the Food and Drug Administration for quantifying the fiber content of food.

With increasing scientific and consumer interest in dietary fiber, the need arose for a new definition of dietary fiber that was *chemically sound, analytically feasible* and *physiologically relevant*. The currently accepted definition of dietary fiber was proposed by Trowell as follows:

> "Dietary fiber consists of the plant polysaccharides and lignin that are resistant to hydrolysis by the digestive enzymes of man."

Components of Dietary Fiber

Structural Polysaccharides:

- **Cellulose** - straight polymer of glucose linked ß1–>4; extensive hydrogen bonding crosslinks adjacent chains producing insoluble fibril
- **Hemicelluloses** -family of branched matrix polysaccharides; non-covalently (but tightly) binds to cellulose fibrils
- **Pectins** - family of branched matrix polysaccharides; backbone contains negatively charged galacturonic acid residues that bind Ca ions to form gel; rhamnose residues may be covalently linked to hemicelluloses

Storage Polysaccharides:

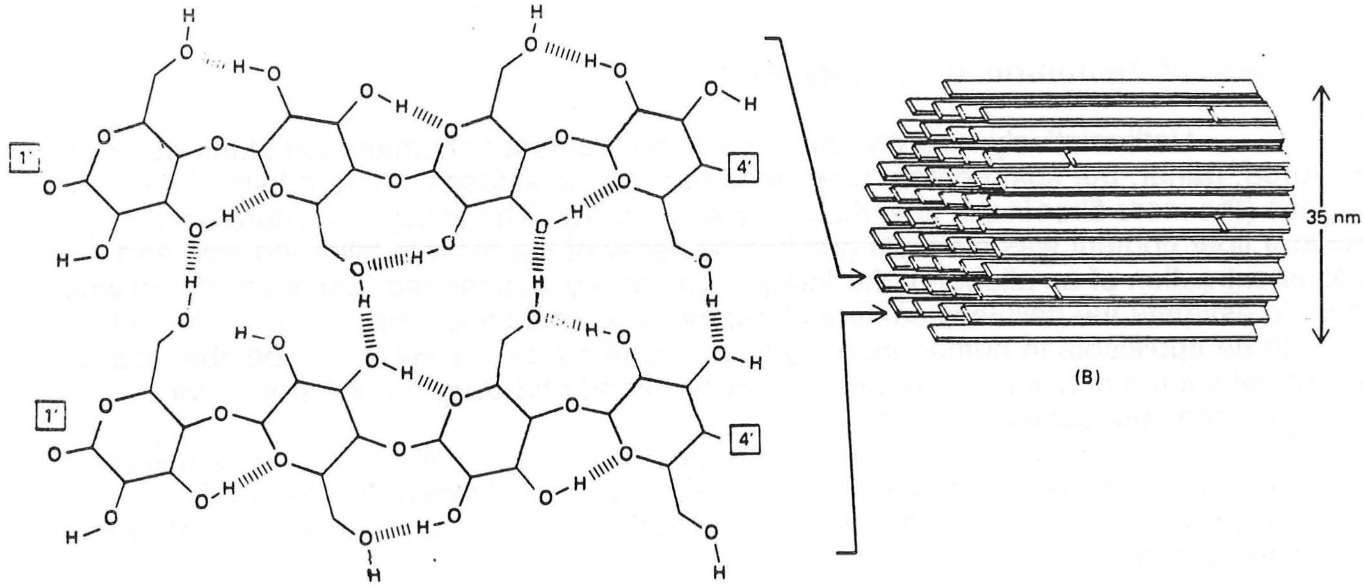
- **Mucilages** - structurally similar to hemicelluloses; found in seeds mixed with endosperm where it retains water and prevent desiccation; soluble in water to form slimy colloidal solution
- **Gums** - non-cell wall complex polysaccharide containing uronic acid residues; true plant gums exude from cut surface of stems; soluble in water to form very viscous gel
- **Alginates** - complex polysaccharides extracted from algae and used as a food additive; slowly soluble in water to form extremely viscous gel

Non-carbohydrate fiber:

- **Lignin** - aromatic polymer of phenylpropane; main component of wood and woody plant tissue; insoluble and indigestible

Table 3 above outlines the individual components of dietary fiber (14,15).

A. Structural Polysaccharides in the Plant Cell Wall



Shown above in Figure 1 is the molecular arrangement of cellulose polymers(15). Note the extensive intramolecular and interpolymer hydrogen bonding that occurs between the free hydroxyl groups in the chain. It is this extensive hydrogen bonding that makes cellulose polymers spontaneously form band-like ribbons that are extremely stable and totally insoluble in water. The ß 1-4 linkage within the cellulose polymer is not susceptible to hydrolysis by amylase and therefore cellulose is indigestible.

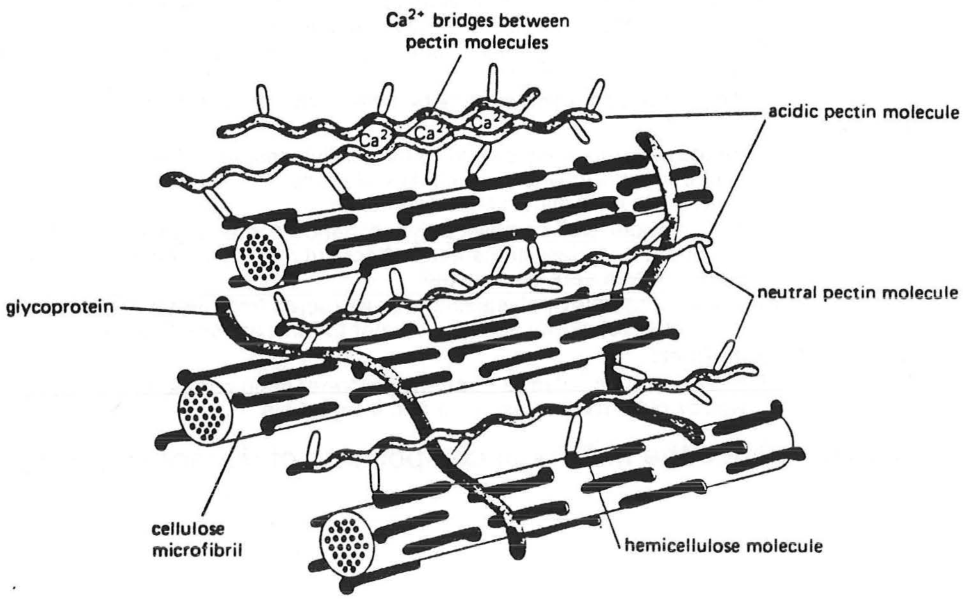
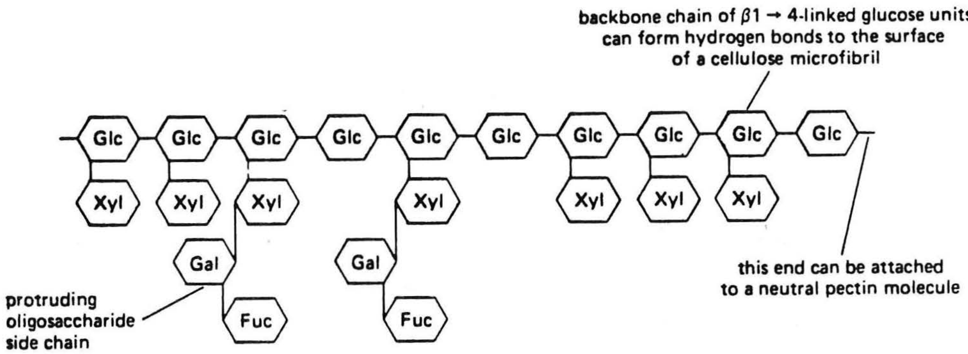
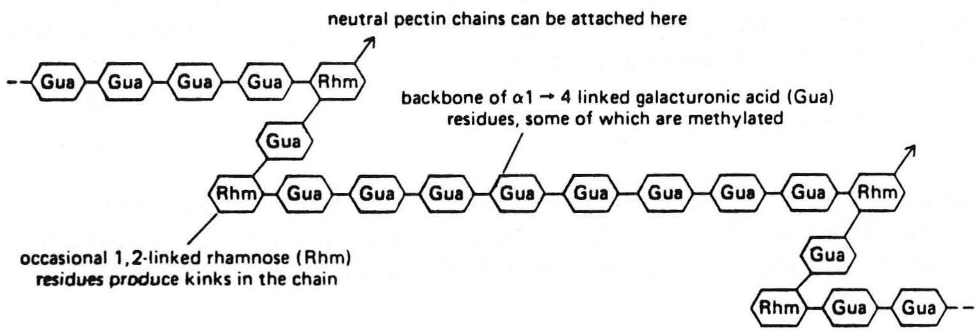


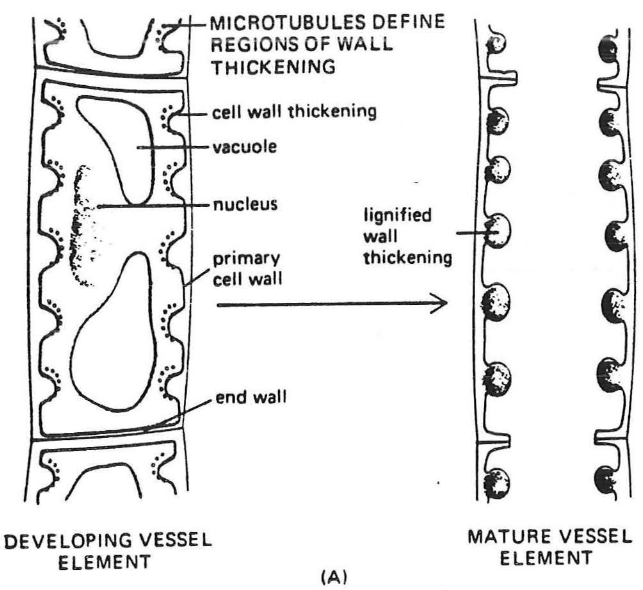
Figure 2 shows the arrangement of cellulose fibrils with the other carbohydrates in the plant cell wall(15). Hemicellulose molecules are held to the cellulose fibril by hydrogen bonding.



In Figure 3 above the chemical structure of a typical hemicellulose polymer is shown(15). Depending on the pH of the surrounding medium, hemicellulose may be water soluble or water insoluble.



In Figure 4 shown above, the chemical structure of a pectin polymer is shown (15). The backbone of the polymer contains galacturonic acid residues some of which may be methylated. The more methylated the pectin molecule is, the more water soluble it is.



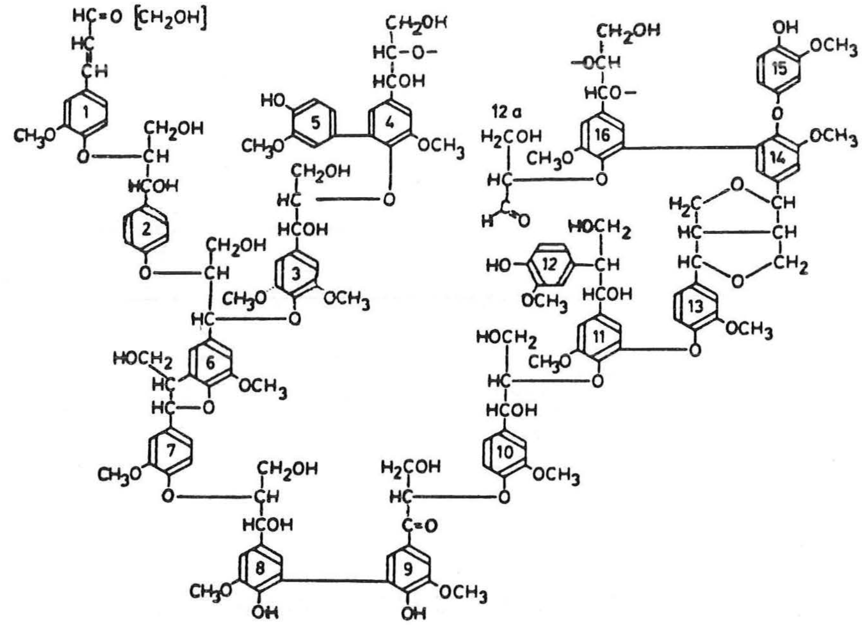


Figure 5 shown on the left above demonstrates the modifications that occur to the plant cell wall with lignification (15). Lignin is a aromatic polymer of phenylpropane and is the main component of wood and woody plant tissue. Figure 6 on the right shows the chemical structure of a lignin polymer. Ordinarily, humans avoid eating lignified plant tissue as it is chemically virtually invert and completely indigestible.

B. Storage Polysaccharides:

Whereas the structural polysaccharides (cellulose, hemicellulose, and pectins) are found in virtually all plant cell walls, the storage polysaccharides are found only in specialized plant tissues. By far the most important of the storage polysaccharides for human nutrition are the mucilages.

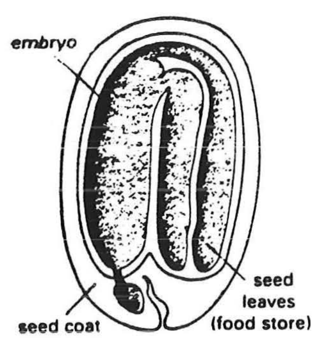


Figure 7 shows a schematic diagram of a typical seed (15). Mucilages are secreted (along with starch) into the endosperm where their hydrophilic properties bind water and prevent desiccation of the seed. The seed coat is composed of cellulose and some lignin and when separated from the endosperm of cereal grains is termed **"bran"**. Thus, bran is not a pure substance but rather is composed of lignin, cellulose, hemicellulose, pectins, mucilages and some starch. Depending on the relative proportions of these substances, the bran may be completely insoluble or mostly soluble. Wheat bran, for example, is predominantly cellulose, hemicellulose and lignin and is largely insoluble whereas oat bran contains large amounts of mucilage and is a good example of a "soluble fiber."

One particular seed that deserves special comment is psyllium. Psyllium is the seed from any of several species of Plantago plants and is unique in its very high content of mucilage. The seed contains little starch and therefore has little nutritive value but it is cultivated as an excellent concentrated source of mucilage. The term "psyllium hydrophilic mucilloid" refers to psyllium husk that have been cleared, ground to a specific size and that have the capacity to swell in a aqueous environment forming a gel.

C. Chemical Analysis

A complete chemical analysis of food for its exact content of these various components of dietary fiber would be extremely laborious and impractical.

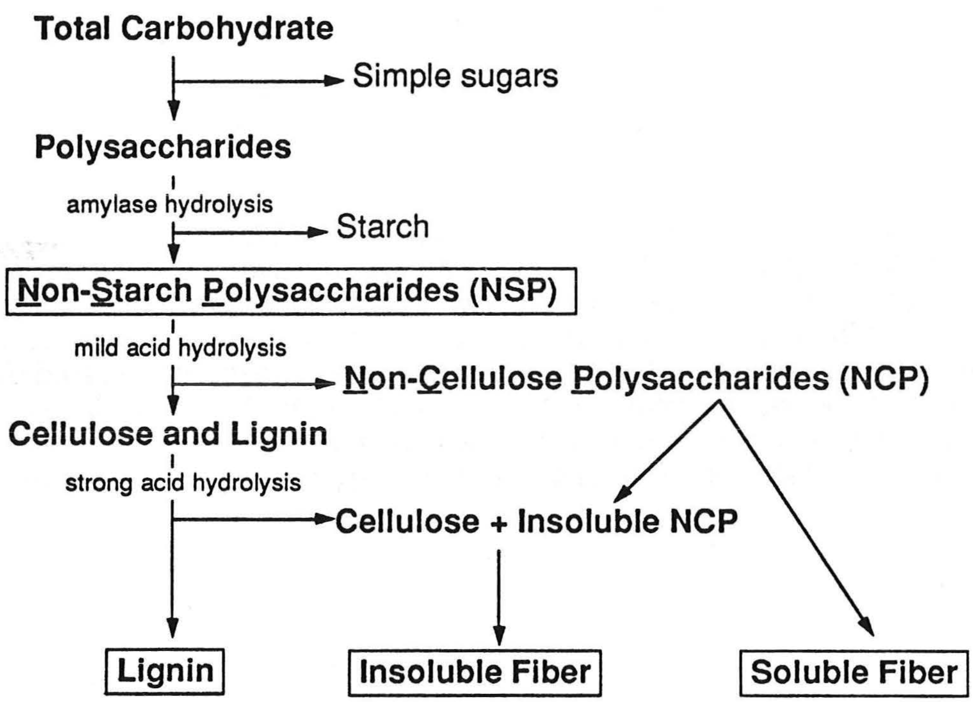


Figure 8 above describes a simplified analytical technique in which the simple sugars and starch are removed from a food sample by enzyme hydrolysis(8). The remaining carbohydrate (which also includes the non-carbohydrate lignin) is termed non-starch polysaccharide and represents the total dietary fiber content of food. In some instances, the NSP is analyzed further and separated into its soluble fiber fraction (which would include most mucilages, gums, pectins and some hemicellulose) and the insoluble fiber fraction which includes mostly cellulose and some lignin.

When you read the label on a box of breakfast cereal and it lists a value for the total dietary fiber content, that value in essence represents the non-starch polysaccharide content.

V. Clinical Observations and Clinical Trials

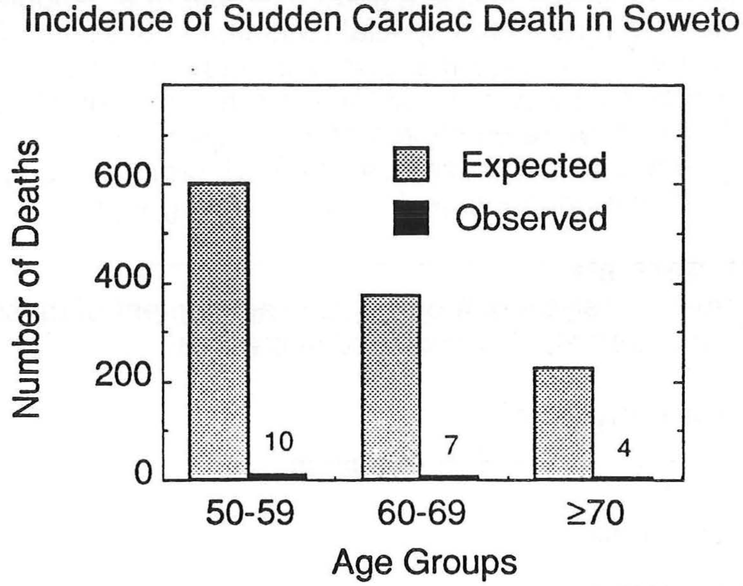
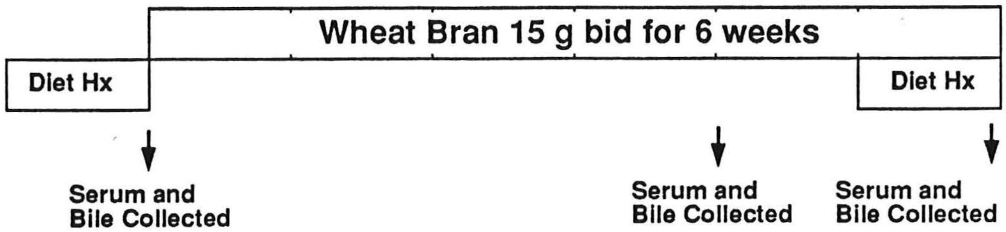


Figure 9 shown above plots the number of sudden cardiac deaths noted in the township of Soweto in South Africa. The people who live in Soweto are mostly black Africans and they consume a diet that is rich in fiber and low in saturated fat. In this study, Walker (17) calculated the expected number of sudden cardiac deaths based on the incidence of these events among whites in South Africa. As shown, the age-adjusted incidence of heart disease was extremely low compared with that seen in the white population that consumed a more refined diet. It was observations such as these, repeated over and over again , that led to the formation of the dietary fiber hypothesis described above(16-23).

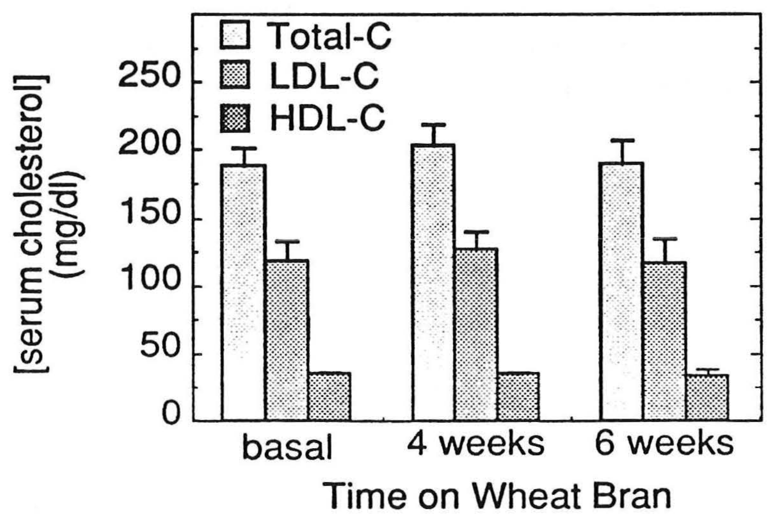
A. Wheat bran studies

Wheat Bran Supplementation in Healthy Men



	Before	During
Energy (kcal/day)	3094 ± 127	3282± 211
Carbohydrates (g/day)	294 ± 19 (45%)	319 ± 25 (45%)
Protein (g/day)	95 ± 5 (15%)	100 ± 8 (14%)
Fat (g/day)	119 ± 10 (40%)	132 ± 11 (41%)
P:S ratio	0.14 ± 0.01	0.14 ± 0.01
Fluid (l/day)	3.1 ± 0.2	3.2 ± 0.2
Cholesterol (mg/day)	397 ± 59	390 ± 57
Dietary Fiber (g/day)	16 ± 2	30 ± 2

Figure 10 above shows the design of a representative study (24) that examined the effect that wheat bran supplementation had on serum and bile cholesterol concentrations in ten healthy volunteer males. As shown, the dietary histories taken prior to and after the six-week wheat bran test period showed that the diets remained comparable with the exception of a doubling in the total dietary fiber content during the wheat supplementation. It should be emphasized that wheat bran is representative of the class of insoluble fibers.



The results are shown in Figure 11 above. There was absolutely no difference in the total or LDL or HDL cholesterol concentrations with wheat bran supplementation.

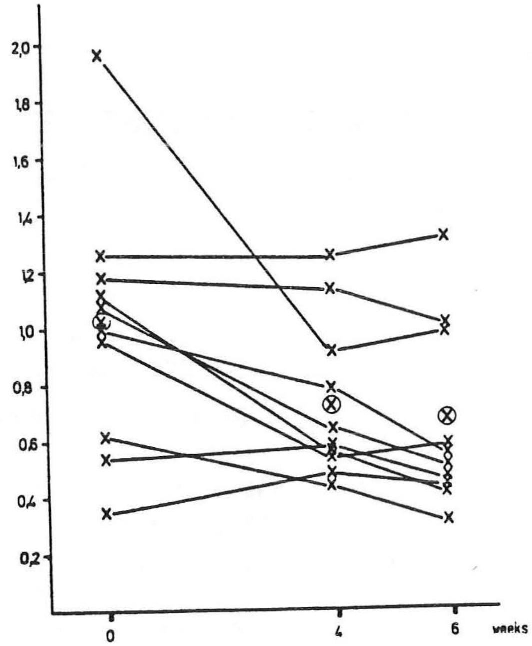


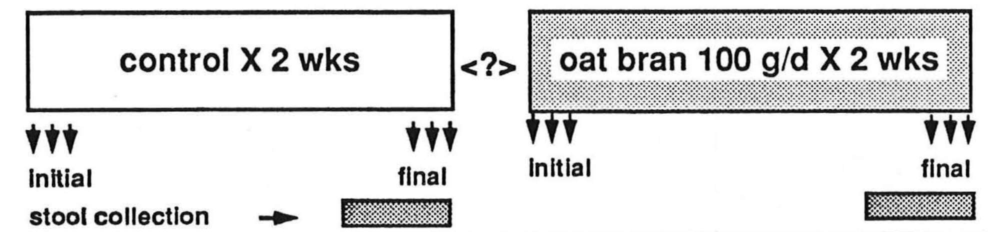
Figure 12 plots the cholesterol saturation index of the bile in these ten subjects in the basal state and after 4 and 6 weeks of wheat bran supplementation. The mean cholesterol saturation index fell from a value of 1.01 ± 0.14 to 0.67 ± 0.11 after 6 weeks.

In many respects, this one study is representative of a very large number of clinical trials (24-30) that have been carried out examining the effect of wheat bran on lipid metabolism. Wheat bran consistently shortens gut transit time, increases the fecal weight and the number of bowel movements, slows the absorption of carbohydrates from the diet and thereby dampens the postprandial glycemic response and decreases insulin secretion. A few studies such as this one have shown that insoluble fiber supplementation may reduce the saturation index of bile with respect to cholesterol. However, the vast majority of studies using wheat bran supplementation have conclusively demonstrated that this insoluble fiber does <u>not</u> lower plasma cholesterol levels.

B. Oat bran studies

Whereas wheat bran is a convenient means of adding insoluble fiber to a variety of foods, oat bran, though less versatile from a culinary point of view than wheat bran, can nonetheless be added to muffins and breakfast cereals as an additional source of soluble fiber. Two studies using oat bran are presented.

Oat Bran Supplementation in Hypercholesterolemic Men



	Control	Oat Bran
Energy (kcal/day)	1954 ± 84	1954± 98
Carbohydrates (g/day)	209 ± 9 (46%)	211 ± 11 (46%)
Protein (g/day)	95 ± 5 (21%)	93 ± 5 (21%)
Fat (g/day)	82 ± 4 (33%)	82 ± 4 (33%)
(saturated fat)	30 ± 4 (12%)	32 ± 3 (13%)
Cholesterol (mg/day)	435 ± 11	424 ± 12
Dietary Fiber (g/day)	20 ± 1	43 ± 1
(soluble fiber)	7 ± 1	19 ± 1
Oat Bran	0	94 ± 2

Figure 13 above shows the design of a study that was carried out on a metabolic ward on 8 men with hypercholesterolemia (31). Oat bran was administered during the test period in the form of hot oatmeal for breakfast and 5 oatmeal muffins throughout the rest of the day. As shown, the diets were comparable with the exception of a 2-fold increase in total dietary fiber and a 3-fold increase in the soluble fiber content.

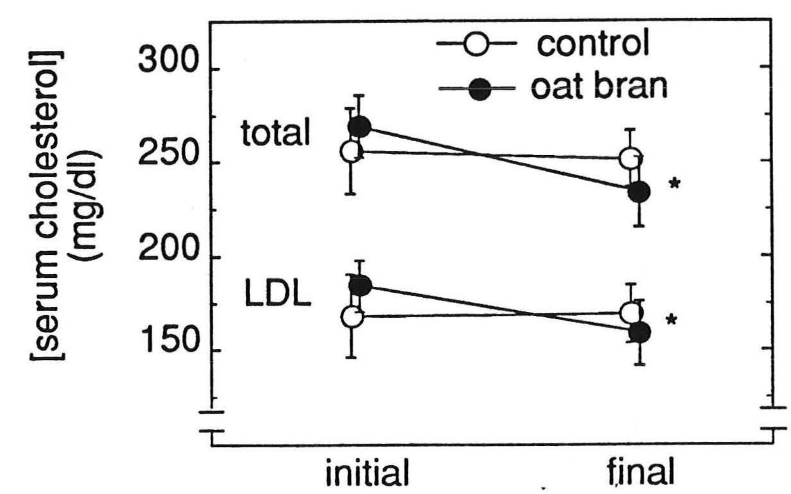


Figure 14 above shows the results of this study. The control group showed no change in either the total or LDL cholesterol concentration between the initial and final measurements. On the other hand, during the oat bran period, total cholesterol concentrations fell by 18% and LDL-cholesterol concentrations by 14% when compared with the initial measurements. There was no change in HDL cholesterol concentrations.

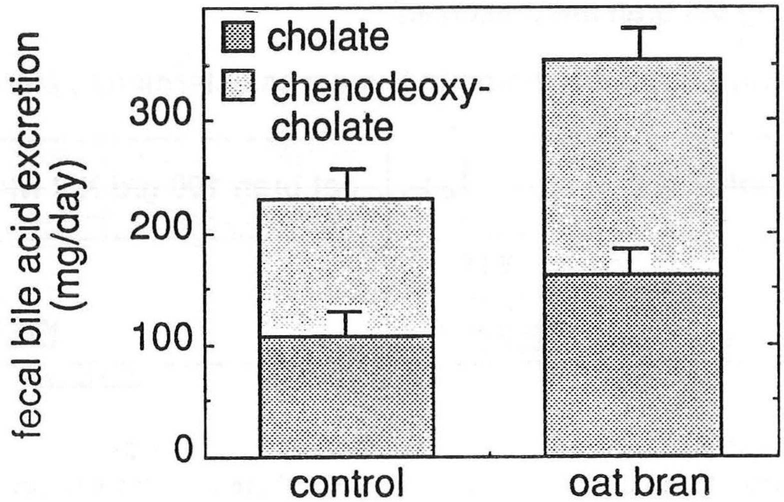
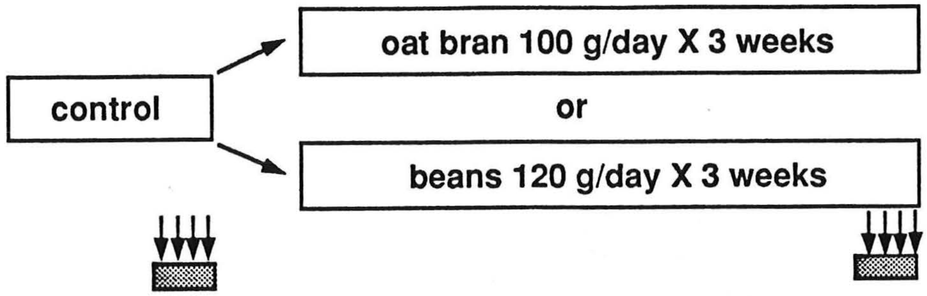


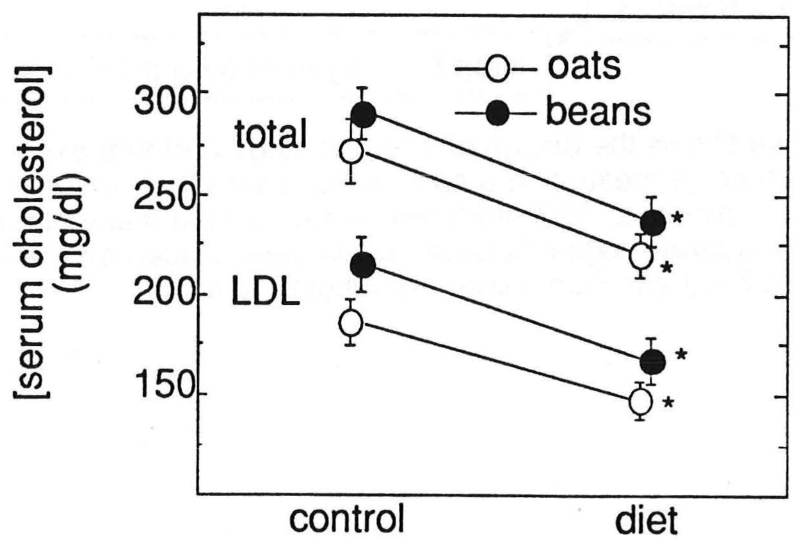
Figure 15 above shows that the total fecal bile acid excretion increased significantly by 54% during the oat bran period.

Studies such as this one are consistent with a model in which soluble fiber in the gut lumen interferes with the enterohepatic circulation of bile acids resulting in increased fecal bile acid excretion. Since bile acids are synthesized in the liver from cholesterol, the increased need for cholesterol by the liver to make replacement bile acids would result in increased expression of hepatic LDL receptors and an increased clearance of LDL cholesterol from the plasma compartment.

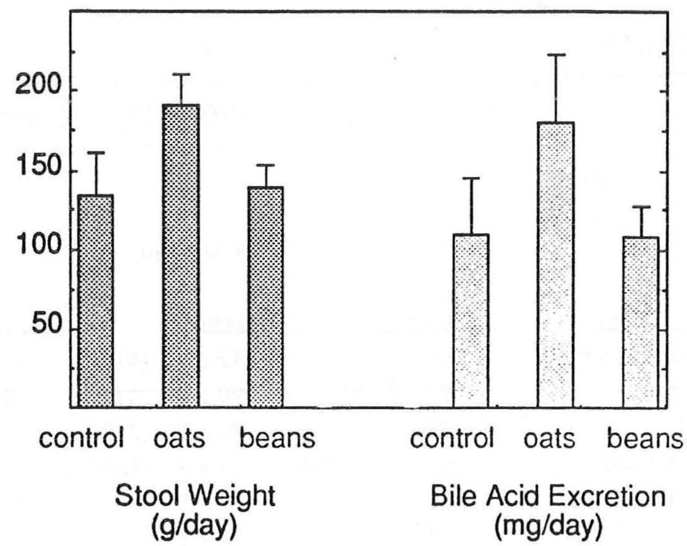


	Control	Oat Bran	Beans
Energy (kcal/day)	1938 ± 63	1948± 74	1742 ± 64
Carbohydrates (g/day)	208 ± 7 (47%)	212 ± 7 (47%)	189 ± 7 (47%)
Protein (g/day)	97 ± 3 (21%)	98 ± 3 (21%)	87 ± 3 (21%)
Fat (g/day)	78 ± 3 (31%)	78 ± 3 (31%)	71 ± 3 (31%)
(saturated fat)	31 ± 2 (13%)	31 ± 2 (13%)	29 ± 1 (13%)
Cholesterol (mg/day)	439 ± 4	436 ± 5	423 ± 5
Dietary Fiber (g/day)	19 ± 1	47 ± 1	44 ± 2
(soluble fiber)	6 ± 1	17 ± 1	16 ± 1
Oat Bran	0	98 ± 1	0
Beans	0	0	101 ± 4

Figure 16 above shows the design for another study (32) examining the effect of oat bran or bean supplementation carried out in 20 hypercholesterolemic men on a metabolic ward. After ingesting a control diet for 1 week, the men were randomly assigned to a diet rich in oat bran or a diet in which beans had been isocalorically substituted. As shown, the diets were essentially comparable with the exception of a reduced total caloric intake in the bean-fed group. Apparently the 10 men randomized to bean group were only able to consume 88% of the beans given them. This was a well-designed study in that both of the treatment arms received a 2.5-fold increase in the total dietary fiber intake and a 3-fold increase in the soluble fiber intake.



In Figure 17 above the results of this study are shown. In this study, both oats and beans reduced the total plasma cholesterol by 19% and the LDL-cholesterol by 23 and 24%, respectively. These were statistically significant decreases.



In Figure 18 above, the stool weight and the fecal bile acid excretion are plotted. Beans had no effect on either stool weight or bile acid excretion, whereas, total bile acid excretion was 65% higher on the oat bran diet.

Obviously, though oats and beans have a similar content of both total fiber and soluble dietary fiber, the mechanism whereby they both bring about a 19% reduction in plasma cholesterol must be different. This study very nicely illustrates that we understand the phenomenology of the hypocholesterolemic effect but that we do not yet understand its mechanism(33-38).

C. Psyllium studies

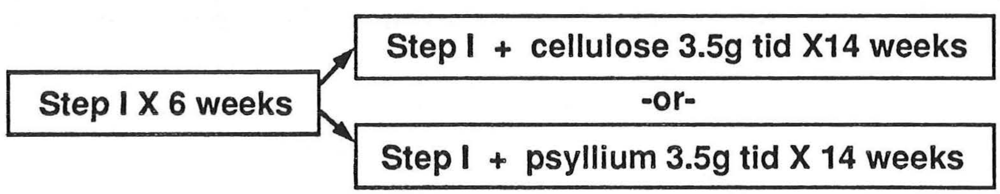
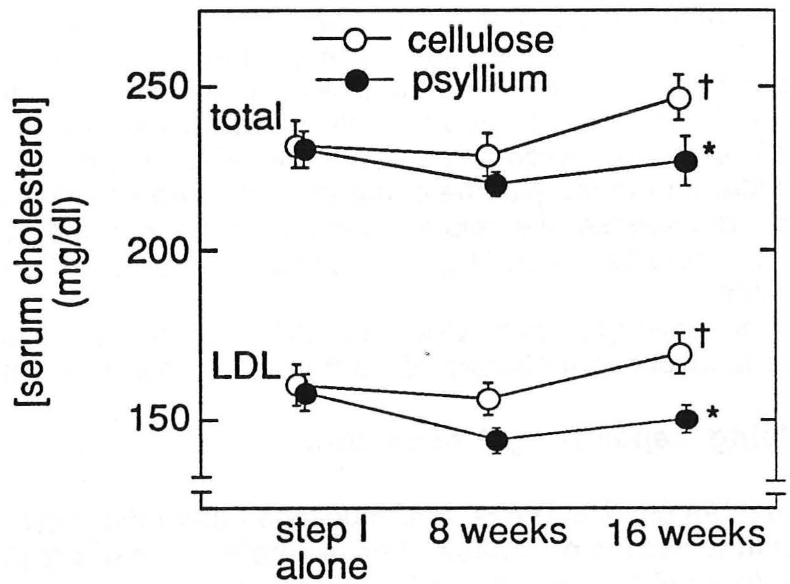


Figure 19 above shows the design of a recent study (39) that examined the effect of psyllium supplementation (representing a soluble fiber) with that of cellulose supplementation as the placebo. This study was different from many others in that the 75 patients with mild to moderate hypercholesterolemia were placed on the National Cholesterol Education Program Step 1 diet throughout the study.

	Typical American	Step I	Step II
Energy		(adequate to maintain IBW)	
Nutrients (% total calories)			
Fat	40 %	≤ 30 %	≤ 30 %
saturated fat	15 - 20 %	≤ 10 %	≤ 7 %
monounsaturated fat	14 - 16 %	10 - 15 %	10 - 15 %
polyunsaturated fat	7 %	7 - 10 %	7 - 10 %
Carbohydrates	40 %	50 - 60 %	50 - 60 %
Protein	20 %	10 - 20 %	10 - 20 %
Cholesterol (mg/day)	400	300	200

As shown above in Figure 20, step 1 of NCEP diet reduces total fats to less than 30% of the total calories, saturated fats to less than 20% and total cholesterol intake to less than 300 mg per day. Thus in this well-designed study one is able to see what the additive effect of a soluble fiber would be when superimposed on a low-fat, cholesterol restrictive diet.



The results are shown in Figure 21 above. At the outset, while on the Step 1 diet alone, the two groups were comparable in their total cholesterol and LDL cholesterol concentrations. After 8 weeks, the control group showed no change in cholesterol concentrations but in the psyllium group the total and LDL cholesterol levels had fallen by 4 and 8%, respectively. Despite the large number of patients, these small decrements in cholesterol concentrations were not significant. At 16 weeks, the cellulose-treated group actually increased their total and LDL cholesterol by 6% compared with the basal period whereas the psyllium-treated group maintained a mild reduction in total and LDL cholesterol of 2 and 5%, respectively. Overall, when comparing the psyllium with the cellulose group at 16 weeks, total and LDL concentrations were decreased by 7.7% and 11.8%.

Thus, the hypocholesterolemic effect of soluble fibers is not as evident when the fiber is added to a NCEP Step 1 (low-cholesterol, low-saturated fat) diet; however, the addition of the soluble fiber did further reduce cholesterol concentrations and seemed to protect against the gradual loss of efficacy of the Step 1 diet alone that was noted in the cellulose group.

Taken together, these short-term clinical trials suggest that soluble fiber, when incorporated into a regular American diet, effects a 10-20% reduction in LDL cholesterol concentrations. When added to a low saturated fat/low cholesterol diet, soluble fiber may further reduce LDL cholesterol by a modest 5-10%. While these reductions may be small, the LIPID RESEARCH CLINICS trials indicate that for every 1% reduction in plasma cholesterol concentration, a 2% reduction in heart disease risk ensues. Thus, for millions of Americans, a 10% reduction in their plasma cholesterol concentration (moving them from an "at risk" category into a desirable range) would seem to be a worthwhile goal.

VI. Possible Mechanisms of the Hypocholesterolemic Effect

Unfortunately, as was illustrated in the study comparing oat bran and beans, the mechanism whereby soluble fiber reduces circulating LDL cholesterol concentrations is poorly understood. The conventional wisdom has held that fiber has a "cholestyramine like" effect of binding bile acids in the gut lumen and thereby interrupting the enterohepatic circulation so that fecal bile acid excretion is increased. Since bile acids are synthesized in the liver from cholesterol, the increased need for cholesterol by the liver to make replacement bile acids would result in increased expression of hepatic LDL receptors and an increased clearance of LDL cholesterol from the plasma compartment. The problem with such a model is that not all soluble fibers increase bile acid excretion (e.g. beans) and some insoluble fibers that do increase bile acid excretion (e.g. wheat bran) have no effect on plasma cholesterol concentrations.

In general, the mechanism (or mechanisms) of the hypocholesterolemic effect should be related to one of the functional capabilities of plant fiber in the gut lumen. These include:

A. Water holding capacity, gel formation

Soluble fibers such as pectins, gums, and mucilages have the capacity of tying up large amounts of water in a viscous gel phase. For example, 1.0 g of dry psyllium will, when added to water, swell into a gel that occupies 40 ml. This gel phase in the stomach will delay gastric emptying and perhaps produce a state of early satiety. In the small intestine, the viscous gel creates diffusion barriers that delay nutrient absorption and in some cases may cause malabsorption of difficult to absorb molecules such as sterols. All fibers that are known to lower plasma cholesterol concentrations also are capable of swelling in water to form a gel phase (44-48).

B. Adsorption of organic materials

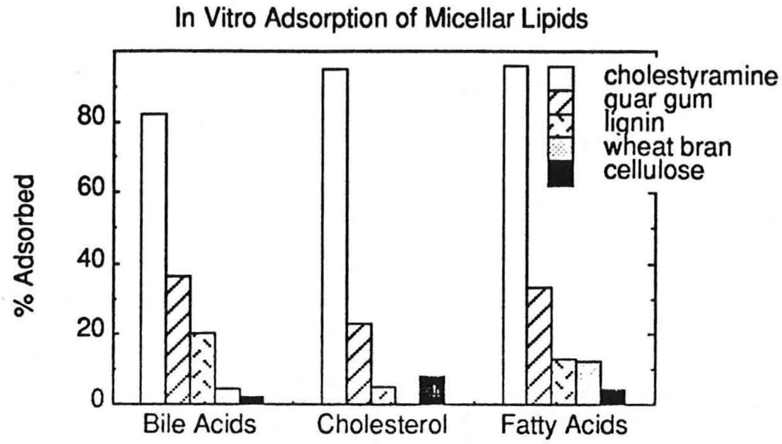


Figure 22 above compares *in vitro* adsorption of micellar lipids by a variety of fibers with that of cholestyramine (45). On a gram for gram basis, none of the fibers tested were nearly as potent as cholestyramine at binding either bile acids or cholesterol. Moreover, *in vitro* bile acid binding capacity of fibers does not predict the fibers effect on fecal bile acid excretion *in vivo.*

C. Susceptibility to bacterial enzyme degradation

Most soluble fibers are thoroughly metabolized in the cecum into volatile short chain fatty acids that are absorbed into the portal circulation and taken up by the liver. Some investigators have proposed that these volatile fatty acids suppress hepatic cholesterol synthesis and that this may be the mechanism of the hypocholesterolemic effect (57-58). Though widely quoted, these studies are flawed by profound methodological errors in the measurement of hepatic cholesterol synthesis such that their data are uninterpretable. Studies carried out here (by Steven Turley, PhD) and elsewhere have shown that in fact soluble fibers (psyllium) have a significant stimulatory effect on rates of hepatic cholesterol synthesis, presumably as a compensatory response to either diminished cholesterol absorption or increased fecal bile acid excretion.

D. Inducing morphologic adaptation of the gut mucosa

In animal studies, the presence of soluble fiber in the lumen of the small intestine is necessary for the normal maturation of the villi. Animals weaned to a fiber free diet continue to exhibit immature "finger like" villi rather than the mature "leaf shaped" villi seen in animals weaned to a standard chow diet. The significance of these findings to humans ingesting different diets is not known (60,61).

VII. Recommendations

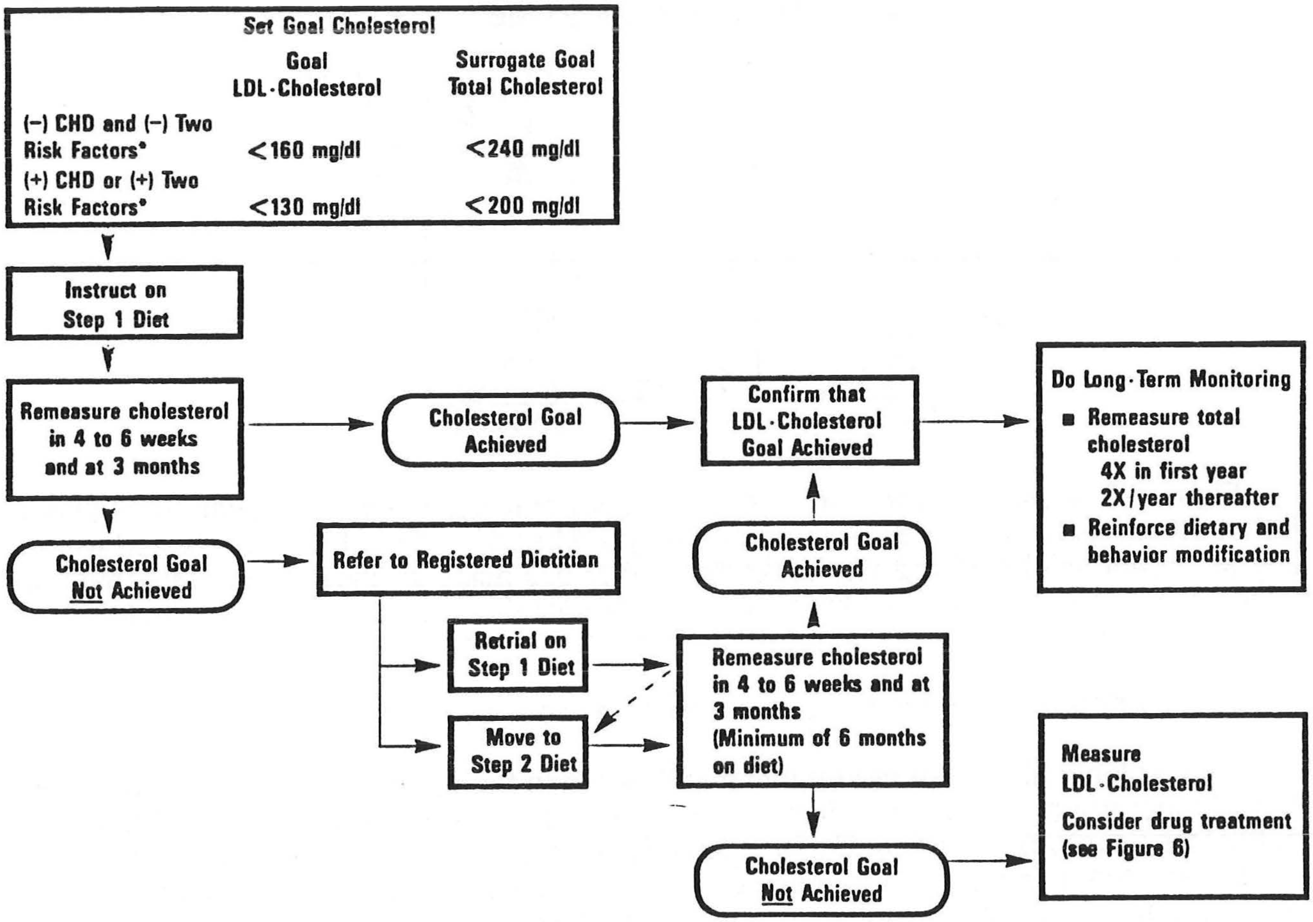


Figure 23 above shows the algorithm recommended by the National Cholesterol Education Program (NCEP) for the dietary management of hypercholesterolemia (2,62). For patients without known coronary heart disease and lacking two risk factors, the goal should be a total plasma cholesterol of <240 mg/dl. If the patient is known to have heart disease or has two or more risk factors (simply being male is considered a risk factor) then the goal is a total serum cholesterol of <200 mg/dl. To achieve that goal, the patient should be instructed in the NCEP Step I diet (Figure 20).

Based on the large number of clinical trials, a few of which are presented here, I think it would be prudent to **include in the Step I diet, specific information to the patient on the beneficial effects of soluble fiber**. Some patients may find it onerous to alter their diet to increase their soluble fiber intake, but others may not.

Because long term data are lacking, I would stop short of recommending that a high soluble fiber diet be used in lieu of the NCEP Step I diet. Of course, there are many patients who will not meet the serum cholesterol target goal with dietary management alone and will require pharmacologic intervention, but that is a different topic.

1. Personal observation, unpublished
2. Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. National Cholesterol Education Program. NIH Publication No. 88-2925, January 1988.

Note: this publication is highly recommended and may be obtained by writing to:
National Cholesterol Education Program
C-200
4733 Bethesda Ave.
Suite 530
Behtesda MD 20814

3. Goldstein JL, T Kita, MS Brown. Defective lipoprotein receptors and atherosclerosis. Lessons from an animal counterpart of familial hypercholesterolemia. N. Engl. J. Med. 1983; 309:288-296.
4. Brown MS, JL Goldstein. Receptor mediated pathway for cholesterol homeostasis. Science 1986; 232:34-47.
5. Lipid Research Clinics Program. The Lipid Research Clinics Coronary Primary Prevention Trial Results: I. Reduction inthe Incidence of Conronary Heart Disease. JAMA 1984; 251:351-364.
6. Trowell H, D Burkitt, K Heaton et al. Dietary Fibre, Fibre-Depleted Foods and Disease. Academic Press, Orlando, FL , 1985.
7. Spiller GA, RM Kay. Medical Aspects of Dietary Fiber. Plenum Medical Book Company, New York, 1980.
8. Vahouny GV, D Kritchevsky et al. Dietary Fiber. Basic and Clinical Aspects. Plenum Press, New york, 1984.
9. Washburn SL. The evolution of man. Sci. Am.1978;194-207.
10. Pilbeam D. The descent of hominoids and Homi. Sci. Am. 1984; 250:84-96.
11. Eaton SB, M Konner. Paleolithic nutrition. A consideration of its nature and current implications. N Engl. J. Med 1985; 312:283-289.
12. Gordan KD in Nutritional Anthrophology. Johnston FE.ed. Alan R. Liss, Inc., New York, 1987.
13. Marshall E. Diet Advice, with a grain of salt and a large helping of pepper. Science 1986; 231:537-539.
14. Kay RM. Dietary fiber. J. Lipid Res. 1982; 23:221-242.
15. Alberts B, D Bray, J Lewis et al. Molecular Biology of The Cell. 2nd edition. Garland Publishing Company, New York, 1989.
16. Walker ARP, UB Arvidsson. Fat intake, serum cholesterol concentration, and atherosclerosis in the South African Bantu. Part I. Low fat intake and the age trend of serum cholesterol concentration in the South African Bantu. J. Clin. Invest. 1954; 33:1358-1365.
17. Walker ARP. Studies bearing on coronary heart disease in South African populations. S. Afr. Med. J. 1973; Jan 20:85-90.
18. Walker ARP. The epidemiological emergency of ischemic arterial diseases. Am. Heart J. 1975; 89:133-136.19.
19. Sacks RM, WP Castelli, A Donner, EH Kass. Plasma lipids and lipoproteins in vegetarians and controls. N. Engl. J. Med. 1975; 292:1148-1151.
20. Phillips RL, FR Lemon, WL Beeson, JW Kuzma. Coronary heart disease mortality among Seventh-Day Adventists with differing dietary habits: a preliminary report. Am. J. Clin. Nutr. 1978; 31:S190-S198.

21. Hallfrisch J, JD Tobin, DC Muller, R Andres. Fiber intake, age, and other coronary risk factors in men of the Baltimore Longitudinal Study (1959-1975). J. Gerontol. 1988; 43:M64-68.
22. Barrow JG, CB Quinlan, RE Edmands, PT Rodilosso. Prevalence of atherosclerotic complications in Trappist and Benedictine monks. (Abstract) Circulation 1961; 24:881.
23. Anderson JW, J Tietyen-Clark. Dietary fiber: hyperlipidemia, hypertension, and coronary heart disease. Am. J. Gastroenterol. 1986; 81:907-919.
24. Wechsler JG, H Wenzel, W Swobodnik, H Ditschuneit. Influence of increased fibre intake on biliary lipids. Scand. J. Gastroenterol. 1987; 129:185-191.
25. Marcus SN, KW Heaton. Effects of a new, concentrated wheat fibre preparation on intestinal transit, deoxycholic acid metabolism and the composition of bile. Gut 1986; 27:893-900.
26. Heaton KW. Cholesterol-rich gallstones. Molec. Aspects Med. 1987; 9:89-96.
27. Floren C-H, A Nilsson. Binding of bile salts to fibre-enriched wheat fibre. Scand. J. Gastroenterol. 1987; 129:192-199.
28. Marcus SN. The effect of Testa Triticum Tricum on intestinal transit, deoxycholic acid metabolism and the cholesterol saturation of bile. Scand. J. Gastroenterol. 1987; 129:200-204.
29. Hillamn LC, SG Peters, CA Fisher, EW Pomare. Effects of the fibre components pectin, cellulose, and lignin on bile salt metabolism and biliary lipid composition in man. Gut 1986; 27:29-36.
30. Gariot P, JP Digy, P Genton et al. Long-term effect of bran ingestion on lipid metabolism in healthy man. Ann. Nutr. Metab. 1986; 30:369-373.
31. Kirby RW, JW Anderson, B Sieling et al. Oat-bran intake selectively lowers serum low-density lipoprotein cholesterol concentrations of hypercholesterolemic man. Am. J. Clin. Nutr. 1981; 34:824-829.
32. Anderson JW, L Story, B Sieling et al. Hypocholeterolemic effects of oat-bran or bean intake for hypercholesterolemic man. Am. J. Clin. Nutr. 1984; 40:1146-1155.
33. Van Horn LV, K Liu, D Parker et al. Serum lipid response to oat product intake with a fat modified diet. J. Am. Diet. Assoc. 1986; 86:759-764.
34. Anderson JW, L Story, B Sieling et al. Hypocholesterolemic effects of high-fibre diets rich in water-soluble plant fibres. J. Can. Diet. Assoc. 1984; 45:140-148.
35. Anderson JW, NJ Gustafson. Hypocholesterolemic effects of oat and bean products. Am. J. Clin. Nutr. 1988; 48:749-753.
36. Van Horn L, LA Emidy, K Liu et al. Serum lipid response to a fat-modified, oatmeal-enhanced diet. Prev. Med. 1988; 17:37-386.
38. Linder P, Moller B. Lignin: a cholesterol lowering agent? Lancet 1973; II:1259-1260.
39. Bell LP, K Hectorne, H Reynolds et al. Cholesterol-lowering effects of psyllium hydrophilic mucciloid. JAMA 1989; 261:3419-3423.
40. Anderson JW, N Zettwoch, T Feldman et al. Cholesterol-lowering effects of psyllium hydrophilic mucilloid for hypercholesterolemic men. Arch. Intern. Med. 1988; 148:292-296.
41. Abraham ZD, T Mehta. Three-week psyllium-husk supplementation: effect of plasma cholesterol concentrations, fecal steroid excretion, and carbohydrate absorption in man. Am. J. Clin. Nutr. 1988; 47:67-74.
42. Forman DT, JE Garvin, JE Forestner et al. Increased excretion of fecal bile acids by an oral hydrophilic colloid. PSEBM 1968; 127:10601063.
43. Cassidy MM, FG Lightfoot, LE Grau et al. Effect of bile salt-binding resins on the morphology of rat jejunum and colon. Dig. Dis. Sci. 1980; 25:504-512.
44. Silk DBA. Progress Report: Fibre and enteral nutrition. Gut 1989; 30:246-264.

45. Vahouny GV, MM Cassidy. Dietary fibers and absorption of nutrients. Proc. Soc. Exp. Biol. Med. 1985; 180:432-466.
46. Cerda JJ, FL Robbins, CW Burgin, GA Gerencser. Unstirred water layers in rabbit intestine: effects of guar gum. JPEN 1987; 11:63-66.
47. Story JA. Dietary fiber and lipid metabolism. Proc. Soc. Exp. Bio. Med. 1985; 180:447-452.
48. Sugano M, S Watanabe, A Kishi et al. Hypocholesterolemic action of Chitosans with different viscosity in rats. Lipids 1988; 23:187-191.
49. Kritchevsky D, SA Tepper, S Satchithanandam et al. Dietary fiber supplements: effects on serum and liver lipids and on liver phospholipid composition in rats. Lipds 1988; 23:318-321.
50. Stewart JR, EB Fryer, HC Fryer. Effects of dietary fiber, carbohydrate, lipid and protein levels on serum and liver lipids in rat. J. Nutr. 1987; 117:650-659.
51. Gallaher D, BO Schneeman. Intestinal interaction of bile acids, phospholipids, dietary fibers, and cholestyramine. Am. J. Physiol. 1986; 250:G420-G426.
52. Sandhu JS, GJ Hudson. The gel nature and structure of the carbohydrate of ispaghula husk ex Plantago ovata forsk. Carbohydr. Res. 1981; 93:247-259.
53. McDougall RM, L Yakymyshyn, K Walker, OG Thurston. Effect of wheat bran on serum lipoproteins and biliary lipids. Can. J. Surg. 1978; 21:433-435.
54. Walker ARP. Dietary fibre and mineral metabolism. Molec. Aspects Med. 1987; 9:69-87.
55. Behall KM, DJ Scholfield, K Lee et al. Mineral balance in adult men: effect of four refined fibers. Am. J. Clin. Nutr. 1987; 46:307-314.
56. Vahouny GV, R Khalafi, S Satchithanandam et al. Dietary fiber supplementation and fecal bile acids, neutral steroids and divalent cations in rats. J. Nutr. 1987; 117:2009-2015.
57. Propionate and cholesterol homeostasis in animals. The hypocholesterolemic effect of fermentable fiber may be due, in part, to gut fermentation of propionate. Nutr. Rev. 1987; 45:188-190.
58. Kelley MJ, JA Story. Short-term changes in hepatic HMG-CoA reductase in rats fed diets containing cholesterol or oat bran. Lipids 1987; 22:1057-1059.
59. Eastwood MA, WG Brydon, DMW Anderson. The effect of the polysaccharide composition and structure of dietary fibers on cecal fermentation and fecal excretion. Am. J. Clin. Nutr. 1986; 44:51-55.
60. Sigleo S, MJ Jackson, GV Vahouny. Effects of dietary fiber constituents on intestinal morphology and nutrient transport. Gastrointest. Liver Physiol. 1984; 9:G34-G39.
61. Tasman-Jones C, RL Owen, AL Jones. Semipurified dietary fiber and small-bowel morphology in rats. Dig. Dis. Sci. 1982; 27:519-524.
62. Oat bran for lowering blood lipids. The Medical Letter 1988; 30:111-112.

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