MEDICAL ASPECTS OF DIETARY FIBER

TOPICS IN GASTROENTEROLOGY

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Edited by Gene A. Spiller, Ph.D., and Ruth McPherson Kay, Ph.D.

NUTRITION AND DIET THERAPY IN GASTROINTESTINAL DISEASE
Martin H. Floch, M.S., M.D., F.A.C.P.

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In order to appreciate the requirements of the science, the student must make himself familiar with a considerable body of most intricate mathematics, the mere retention of which in the memory materially interferes with further progress. The first process in the effectual study of the science must be one of simplification and reduction of the results of previous investigations to a form in which the mind can grasp them. The results of this simplification may take the form of a purely mathematical formula or of a physical hypothesis. The disadvantage of a physical hypothesis is that we see the phenomenon only through a medium. So we are liable to a blindness to facts and rashness in assumptions which a partial explanation encourages.

James Clerk Maxwell, 1855
On Faraday's lines of force

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Foreword

Dietary therapy has always been important to medical practice even if it has more often been sacramental than physiological in effect. "You are what you eat" meant a lot to primitive tribes whose new leader had to eat part of his predecessor, and giving diets brought out the priest in the physician even if he or she had heard that "nothing that enters into a man defiles a man." What people eat began to take on new meaning, however, a generation ago when Schoenheimer and others made clear that body fat and muscle protein were not the sluggish unchanging masses they had appeared but instead were storehouses of energy and material influenced by food, activity, and metabolic processes. Fiber, or residue as it was then still called, however, seemed unimportant; even the gastroenterologist concerned with keeping the bowels open by three cooked fruits, three cooked vegetables, and twelve glasses of water each day sometimes felt like a shaman if his cure for constipation worked. Nobody any longer read Arbuthnot Lane's charming Victorian book, *The Way Out,* which placed the blame for most human ailments on constipation; Lane even removed the bowel to cure the costive ills.

Burkitt revived a scientific interest in fiber and the possible connection between diet. constipation, and many physical disorders by observing the volume and frequency of stools on an African diet and on an English diet. His first observation stirred up a whole cauldron of scientific experimentation, and others have taught the evils of the low-fiber diet. Today, high-fiber diets are as popular among the laity as among physicians, who prescribe the amount of fiber in the diet as punctiliously as the degree of blandness a few years ago. Now is certainly the moment for fiber, as interest in high-fiber diets greets the increasing vegetarianism of the children. Spinach today has a finer image than 40 years ago, when it stood for the authority of parents and divided the generations! The father on a high-fiber diet to prevent diverticular disease and colon cancer, and incidentally to scrub his coronary arteries, can meet his vegetarian children in one great if sometimes gassy festival of love. Yet proof of the virtues of fiber is needed, and that is what Spiller and Kay's fine book is all about.

It is hard for the physician to keep abreast of the patient who reads handouts from the local nature food stores, but physician and nutritionist alike should realize what is being learned about the superficially so rigid material. In their fine up-to-date compendium Spiller and Kay and their contributors tell the reader what fiber is, what it does, and how it apparently works. This book has all the latest information, reviewing even the benefits that fiber may have for the patient with high plasma or biliary lipids, and is an example of how workers at the very frontiers of the field can quickly bring what they know to the practitioner. In this book, I learned that fiber is more than a simple substance, that fiber from carrots differs from fiber from bran, and that the role of fiber in human disease depends upon its behavior within the gut, which in turn depends upon the type of fiber and how it affects lipids, carbohydrates, and sterol absorption.

High-fiber diets may be turning eating habits back 50 or 100 years, and that seems to be all for the good. Still, it is important for physicians to separate the wheat from the chaff—even if this book may make them believe that the chaff is better for them. Spiller and his colleagues have given so much useful information that I am delighted to include this book in our series on gastrointestinal problems. I believe the book is important reading for dieticians, nurses, general internists, gastroenterologists, surgeons, and the concerned layman.

Howard M. Spiro, M.D.

Preface

In the late 1970s, our books *Fiber in Human Nutrition* and *Topics in Dietary Fiber Research* were published. The contents of these volumes reflected a systematic effort to clarify nomenclature, chemistry, analytical procedures, and physical properties of fiber. Epidemiological data were reviewed, as were physiological studies in man and animals. In the brief span of four years, considerable progress has been made, particularly in the prophylactic and therapeutic status of fiber in clinical medicine. This volume presents a complete and current analysis of the medical aspects of dietary fiber and is intended for use by physicians, clinical nutritionists, and the growing body of investigators active in fiber research.

The role of fiber in human disease depends on its behavior within the gastrointestinal tract. The fiber content and the composition of the ingesta influence the time required for passage through the gut as well as the rate and site of nutrient absorption. Moreover, disparate effects are observed, dependent on the type of fiber, anatomical location within the gut, and characteristics of the material available for mucosal uptake. Changes in glucose, lipid, and sterol absorption occur that are relevant to disorders of carbohydrate and cholesterol metabolism. Recent clinical studies suggest that fiber may have important therapeutic potential in the treatment of diabetes mellitus (Chapters 10 and 11) and may also influence plasma and biliary lipids (Chapters 8 and 9).

The clinical effects of dietary fiber in the lower bowel are well documented, but responsible mechanisms remain uncertain. Early hypotheses suggesting that the beneficial effect of fiber on colonic function was related to the hygroscopic properties of the ingested material are probably oversimplistic. A series of complex events in the large bowel result in significant degradation of fiber and attendant and important alterations in the bacterial metabolism of other compounds. In the realm of colonic disease, the role of fiber in the treatment of simple constipation and diverticular disease is well established (Chapters 1–3). The link between fiber intake and colonic carcinoma is attractive, but as yet unproven (Chapters 5–7). The effects of the metabolites, such as volatile fatty acids, produced by microbial fermentation of dietary fiber in the

gut, are not well understood. In fact, how do these metabolites affect the gut wall and, after absorption, other body tissues?

Furthermore, the medical implications of altered intakes of dietary fiber must be considered in the context of the entire diet. Fiber and other nutrients undoubtedly interact. An increase in fiber consumption is likely to result in displacement of other dietary constituents, which themselves influence various disease processes. Many investigators have stressed the need for and the difficulty of such a multivariate approach to nutrition and disease. Finally, the pharmacological use of concentrated plant fibers has added a new facet to the study of the effects of high-fiber diets. The use of such highly concentrated sources, e.g., guar gum, in controlling glucose metabolism (Chapter 10) is a challenging concept for the clinical and pharmacological investigator.

Even though Chapters 1–3 of *Fiber in Human Nutrition* thoroughly covered the definition, chemistry, and analysis of dietary fiber, we have added a Glossary on basic terminology as an appendix to this book. As any reader of the literature in this field is aware, definitive nomenclature is still far from being established. We hope this Glossary will be useful in achieving more uniformity. In addition, the Dietary Fiber Workshop of the XI International Congress of Nutrition (Brazil, 1978) elicited some excellent suggestions, which were summarized by us in the *American Journal of Clinical Nutrition* (**32**:2102, 1979). The importance of proper terminology and definition cannot be overemphasized.

We hope this volume will not only function as a valuable clinical and scientific reference but will also stimulate continued research in an important and intriguing area of human nutrition.

We are grateful to Alethe Echols and her assistant Lee Buck for their extensive editorial work.

Gene A. Spiller
Ruth McPherson Kay

Palo Alto and Toronto

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Effect of Fiber on Colon Function

Martin A. Eastwood, William Gordon Brydon, and Kebede Tadesse

I. INTRODUCTION

The most important problem that becomes apparent when discussing the effect of dietary fiber on colonic function is the limited procedures for assessing colonic function. Unlike the measurement of respiratory, cardiac, or renal function in physiology and medicine, no comparable methods exist to assess colon function. The clinician usually asks only if an individual's bowels move regularly, partly because colon function is so poorly defined. The role of the colon is somewhat belittled, as it is possible to live in good health with an ileostomy, i.e., with the colon totally removed. The ileostomy situation, however, does not sufficiently emphasize the absorptive and functional changes that must occur in the ileum to compensate for the loss of the colon. The functions of the colon (Fig. 1) can be summarized as follows.

1. It acts as a reservoir. The existence of such a reservoir requires a controlled expression of feces from the colon. The colon is a propulsive organ which propels intestinal contents from the cecum to the rectum. The feces pass to the descending colon, where there is loss of haustra, and then the sigmoid colon straightens to form a funnel. Mechanical receptors in the colon transmit information to the cerebrum indicating that the colon is full. As a result, intraabdominal pressure increases and relaxes the pelvic floor. The internal sphincter has a locking or flutter-valve effect, which prevents anal canal stimulation. If,

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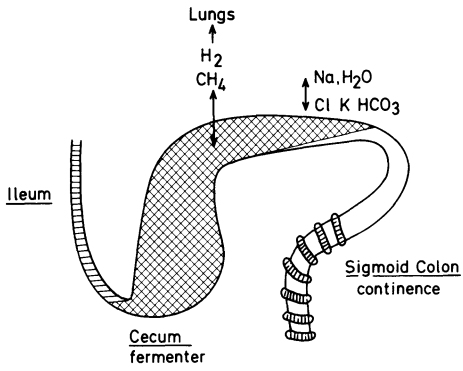

Figure 1. Function along the human colon.

however, feces pass to the anal canal, the anal mucosa is stimulated and the voluntary external sphincter dictates the expression of the stool in circumstances that prevent soiling.

2. The colon conserves water and electrolytes. At least a liter of fluid enters the cecum each day, coming from the ileum. The colon is capable of absorbing several times this volume of water[1] and concentrates this effluent into a stool that may vary in weight from 10 to 500 g. The ileal effluent contains unabsorbed electrolytes and organic material, the absorption of which, in the colon, depends partially on the luminal contents and partially on the absorptive capacity of the colon.

3. The colon contains a large bacterial flora. The flora is mixed but generally consists of strict anaerobes. These bacteria will metabolize chemicals in the ileal effluent. The origin of the substrate will be unabsorbed dietary material and substances that have been excreted by the liver, such as bilirubin glucuronide, bile-acid conjugates, and other conjugated substances. The effect of bacteria on these biliary excretion products is to convert water-soluble, poorly absorbed substances to water-insoluble, readily absorbed substances.[2] Dietary fiber is also partially degraded.

4. The colon absorbs fermentation products of bacterial activity and other substances from the lumen of the colon.

5. Potassium, bicarbonate, chloride, and other materials are absorbed from the plasma and enter the lumen of the colon for elimination with the stool.

6. The colon possibly acts as an endocrine organ.[3]

7. The colon functions in enterohepatic circulation. A further function of the colon is its conserving mechanism. The liver secretes poorly water-soluble materials of a molecular weight in excess of 300. Generally, substances with a molecular weight of less than 300 are excreted in the urine. The function of the liver is either to make molecules that are poorly soluble in water soluble in a micellar bile-acid phase or to render the molecules sufficiently water soluble

to pass out in the bile. Some of the compounds secreted in the bile are subsequently reabsorbed from the intestine and are conserved, a process called the enterohepatic circulation.

The enterohepatic circulation of bile acids[4] appears to have two phases. Bile-acid conjugates are involved in micelle formation and fat absorption in the jejunum, from where hydrolyzed fats are absorbed. However, conjugated bile acids are not actively absorbed but pass to the ileum. Most conjugated bile acids are involved in a rapid turnover, an ileohepatic circulation, which is the major conserving mechanism for conjugated bile acids. A proportion of the pool of bile acids, possibly a quarter in any one day, enters the cecum, where the bile-acid conjugates are hydrolyzed and further metabolized. A proportion are reabsorbed from the cecum, and this constitutes a cecohepatic circulation. The remainder are adsorbed to fiber and bacteria and are excreted in the stool.[5]

The three aspects of the handling of bile acids—rapid ileohepatic, slow cecohepatic, and fecal excretion of bile acids (Fig. 2)—are distinct in their anatomical site and in their qualitative and quantitative effect on the enterohepatic circulation. It is possible that fiber has different effects on the phases of the enterohepatic circulation.[6]

Colonic functional tests are complicated by the meager information available concerning the nature of the material passing into the cecum. It is not sufficient to know dietary intake only, because the material passing into the ileum, and hence into the cecum, will also be made up of biliary excretion products, mucosal cells, and unabsorbed pancreatic secretion.

To interpret what is happening in the colon, it might be useful to regard it as really two organs (Fig. 1). The right side, or cecum, is basically a fermenter. Here, a large mass of bacteria live in anaerobic conditions where they metabolize and ferment materials coming down through the ileum. The left side of the colon, or descending and sigmoid colon, is involved in continence.

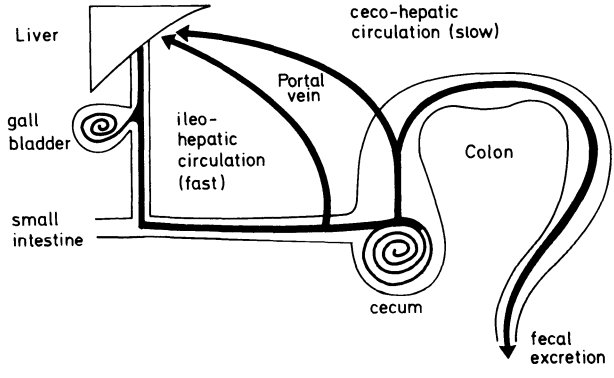

Figure 2. The enterohepatic circulation of bile acid.

The whole colon, though mainly the cecum, is involved in the concentration of feces through the absorption of sodium and water. At the same time, some potassium is excreted depending on luminal concentrations. This allocation of processes is of particular importance when assessing the effect of dietary fiber on colonic function.

Continence will be reflected in stool weight, intestinal transit times, and colonic motility. To some extent, colonic absorptive capacity can be measured by studies with an intubation technique and the use of double lumen tubes. However, such studies can be done only with a colon that has been washed free of its contents. Therefore, the situation that exists in practice with the colon full of bacteria and other substances would not apply in such studies. Fecal weight, dry weight, electrolytes, and bile acids could act as indirect assessments of absorption and secretion. Fecal constituents give little indication of the mechanics of what is happening in the cecum and in the transverse colon. Therefore, fecal constituents will demonstrate the colon only as an organ of elimination.

Some concept of the bacterial fermentation activity in the cecum can be obtained indirectly in various ways. Fermentation products can be studied using feces, flatus, or breath. The population of bacteria voided in the feces are in no way indicative of the spectrum of bacteria in the cecum. Considerable change takes place in this population during the concentration of stool.[7]

The other problem associated with discussing the role of fiber on colonic function is the definition and function of fiber. Much progress has been made in our understanding of the chemistry of fiber.[8,9] Tables are now available that give the fiber content of a great variety of fruits and vegetables.[10] However, the wide range of fruits, vegetables, and cereal products and their quite distinct physiological effects make such data somewhat difficult to convert into nutritional advice. It is not sufficient to select items of food that have the largest fiber content and then to expect a uniform functional response along the gastrointestinal tract.

The studies on the effect of dietary fiber on colonic function in normal subjects include a wide range of approaches. Most studies ask restrained questions and are short term, the period of exposure to a fiber source seeming to vary between 2 and 4 weeks. A feature of these experiments that has been criticized[11] is that most studies have been with self-selected diets and not under metabolic ward conditions. Only 25 of the 57 studies discussed[11] used dietary controls, while the other studies were conducted on subjects consuming self-selected diets to which fiber sources were added. What such a review overlooks, however, is that it is more practical to first make such screening experiments of a novel concept in nutrition. Once the initial screening experiments are completed, a full metabolic study becomes valid. It is unlikely that the advances in our knowledge of fiber in nutrition that have altered many concepts in nutrition would have occurred at all if the rigid, time-consuming studies now necessary had been done at the outset.

II. PHYSICOCHEMICAL EFFECTS OF FIBER

Fiber can be regarded as a physical agent passing along the gastrointestinal tract, i.e., a sponge. Such a sponge will have water-holding capacity and cation exchange capacity; it is an adsorbent, and it provides a matrix and catalytic surfaces. However, in the cecum, fiber is profoundly affected by the flora. The fiber may pass unchanged or modified in physical properties through the cecum to the descending colon. Alternatively, the fiber can be partially or completely hydrolyzed, the end-products of which may be reabsorbed from the cecum into the portal vein; or the hydrolysis products themselves may have biological effects within the lumen of the colon. This concept has been developed previously.[12] The long-term objective of both the chemical analysis of fiber and the description of physical properties is to obtain data that will predict biological activity along the gastrointestinal tract. The chemical composition of the dietary fiber source may affect its metabolism in the colon.[13,14]

The problem is aggravated by the wide spectrum of fruits, vegetables, and cereal products that are available. It has been emphasized repeatedly that bran is not dietary fiber. It is also apparent that different cereal bran sources will be quite distinct in both their chemistry and water-holding capacity. While the particle size of the bran is important,[12] other variables such as the source of the bran are of equal importance, i.e., whether it derives from hard, soft, or durum wheat. There are also differences between varieties of fruits and vegetables. Seed catalogues for the last 100 years show that the available varieties have altered distinctly.[15] For example, the carrot *(Daucus carrotus)* was originally a purple cultivar first found in Afghanistan. In the 9th century, it was eaten as a yellow cultivar and then appeared in Holland in the 17th century both as a white cultivar used for cattle food and as an orange cultivar, which is the origin of the modern carrot. Over the last 100 years there have been changes in the range of cultivars available: Nantes, Altrincham, and Scarlet Perfection, which are old varieties used for eating fresh or for canning; whereas the new varieties, Little Finger, Amsterdam Forcing, Amstel, and Chantenay Red Core have been developed for the changing usage of carrots, such as canning and freezing. The different carrots grow at different rates so that the mean weight at harvest is quite distinct. Such alteration of characteristics applies to many varieties of fruit and vegetables.

Table 1 summarizes most of the studies that have been reported on the effect of diet on colon function in the period from 1975 to 1978. Overall, these studies show that cereal fiber and bagasse behave quite differently from fruit and vegetable fibers. The mass of bacteria in the cecum are probably unable to digest bran. There is considerable degradation of the constituents of fruits and vegetables, presumably pectins and hemicelluloses. Evidence from light microscopy, electron microscopy, and scanning electron microscopy of bran[16] indicates that the outer layer of the pericarp of bran and some of the endosperm are minimally catabolized during passage along the gastrointestinal

Table 1. Studies Involving Fiber Intake and Colonic Function in Normal Subjects (1975–1978)

Reference	Subjects	Diet	Time	Fiber source (g/day)	Measurements
Brodribb and Groves[20]	9 men 12 women	Self-selected	2 weeks	Fine bran (20), coarse bran (20)	Stool weight, bowel action
Cummings *et al.*[21]	6 males	Metabolically controlled	3 weeks	Cereal (45)	Fecal weight, transit time, fecal fat, fecal nitrogen, fecal calcium, fecal electrolytes, fecal volatile fatty acids, fecal bile acids
Raymond *et al.*[22]	5 males 3 females	Metabolically controlled	4 weeks	Plant cell wall (60); Corn, beans, bran, pectin, cellulose (13.2; 22)	Plasma lipids, fecal weight, fecal steroid excretion, intestinal transit time
Kelsay *et al.*[23]	12 males	Defined	26 days	Fruit and vegetables (20 NDF)	Fecal weight, fecal water, fecal energy (K cal), fecal nitrogen, fecal fat, intestinal transit time
Wyman *et al.*[19]	10 males	Self-selected	14 days	Raw wheat bran (12; 20)[a]; cooked wheat bran (13.2; 22)[a]	Fecal weight wet (dry), fecal water, bowel frequency
Durrington *et al.*[24]	12 males	Self-selected	3 weeks	Pectin (15)	Fecal weight, intestinal transit time
Kay and Truswell[25]	4 males 5 females	Controlled	3 weeks	Citrus pectin (15)	Plasma lipids, bowel frequency, fecal weight, fecal fat, fecal steroids
McLean Baird *et al.*[26]	20 females 2 males 2 females	Controlled or metabolic	12 weeks 21 days	Bagasse (8.4 crude fiber), wheat bran (39)	Fecal weight, fecal frequency, fecal steroids, fecal fat, fecal bacteria, transit time
Cummings *et al.*[27]	19 males	Calculated	3 weeks	Dried apple, dried cabbage, dried carrot, bran, guar (17–22)	Fecal weight, intestinal transit time

Kay and Truswell[28]	3 males 3 females	Metabolic ward control	3 weeks	Bran, wholemeal flour (7–11 crude fiber)	Plasma lipids, fecal weight, fecal steroids, intestinal transit time
Williams *et al.*[44]	Not stated	—	Single stools	Variable	Fecal structure, microscopy, scanning electron microscopy
Ismail-Beigi *et al.*[29]	3 males	Metabolic ward conditions	9 or 20 days	Cellulose (10), apple (150), wholemeal breads (35)	Fecal weight, fecal zinc, fecal calcium, fecal magnesium, fecal phosphorus
Jenkins *et al.*[30]	6 males	Metabolic ward conditions	3 weeks	Wheat bran (11.5 crude fiber)	Fecal weight, fecal steroids
Maver *et al.*[31]	165 males	Habitual (diet recall)	1 stool	—	Fecal dry weight, fecal bile acids
Fuchs *et al.*[32]	4 males 2 females	—	3 weeks	Wheat bran, processed (5.4 crude fiber)	Fecal weight, fecal water, bacterial flora
Int. Agcy. Res. Cancer[33]	60 males	Habitual (diet recall)	1 stool	Copenhagen (17), rual Kuopio (31)	Bowel habit, fecal weight, fecal steroids, fecal tryptophan, intestinal transit time
Rendtorff and Kashgarian[34]	115 males	—	8267 stools over 3 years	Unknown	Fecal weight, fecal frequency
Wyman *et al.*[35]	20 males 10 females	—	Repeated 5 days	Unknown	Fecal weight, intestinal transit time
Martelli *et al.*[80]	60 males 54 females	Self-selected	7 days	— (10–18 crude fiber)	Bowel habit, intestinal transit time, anorectal mechanical behavior
Weinreich *et al.*[40]	25 females	Self-selected	5 weeks	Bran (24)	Bowel habit, intestinal transit time
Floch and Fuchs[39]	4 males 2 females	Self-selected	3 weeks	Bran, processed (10 crude fiber)	Stool weight, pH, bacteriology
Sandstead *et al.*[49]	5 males	Metabolic ward control	4–8 months	Wheat or corn bran (26)	Trace elements
Kern *et al.*[81]	2 patients	—	1 week	Fruit and vegetable (5)	Bile-acid adsorption

[a]Two dosages given in varied sequence.

tract. The testa appears to remain intact. Cooking, mixing, and pulverizing bran appear to alter its fate along the gastrointestinal tract.

The effect of processing on feed grains for ruminants has been carefully examined. The various species differ considerably in their response to processed cereals. Evidence exists that, in both cattle and sheep, the extent of processing of cereal supplements can directly influence the voluntary intake of dietary roughage at increased levels of supplementation. It may be that processing methods such as steaming and flaking, which are aimed at increasing the rate of fermentation in the rumen, may adversely influence digestion.[17] Similar observations have been made on the intake, digestion, and utilization of dried herbage.[18] It is clear that chemical and physical changes are induced by the harvesting and processing of forages. Maillard reactions may result from heating, with the development of nonenzymic browning, which occurs mainly as a result of the formation of enzyme-resistant linkages between the carbonyl groups of reducing sugars and amino groups of the protein fraction.

A. *Water-Holding Capacity*

Water-holding capacity is the maximal ability of a fiber source to hold water. Water is held in different ways; hence, there is a complex relationship between the fiber and water: surface water, water trapped in interstices of the fiber, and free water. The summation of surface and interstitial water constitutes the water-holding capacity. However, the measurement of water-holding capacity presents problems. The preparation of fiber can alter its water-holding capacity.[15] The water-holding capacity of a fiber in its native state may be appreciably different from that of the fiber which has been macerated, freeze dried, air dried, or roller dried. This is because the capillary structure of the fiber has been compressed, and consequently the water is unable to expand the collapsed capillaries. The consequences of such differences in preparation on the physiology of the gastrointestinal tract are little understood. Some nutritionists regard fiber only in its natural form, i.e., raw or conventionally cooked bran, fruits, and vegetables. This disregards the requirements of the food-manufacturing industry to produce fiber sources with a prolonged shelf-life. When manufacturers make fiber concentrates, the mode of preparation affects the physical properties.

Few studies of the effects of bran on colon function have included preparation. One such study by Wyman *et al.*[19] showed that unprocessed raw bran was more effective in influencing stool weight than cooked wheat bran at equivalent dosage.

B. *Determinants of Stool Weight*

The single aspect of colonic function which has excited the most interest is that of stool weight.[19–35,38] A remarkable finding, however, is the constancy

of the water content of the stool. In Wyman *et al.*'s[35] study of the variability of colonic function in healthy subjects, the mean percentage water content was 74 ± 3.8% for the females and 75 ± 4.3% for the males. The effect of adding fiber of widely varying water-holding capacity to the diet appears to cause little change in the percentage of water, with one or two notable exceptions. Kelsay *et al.*[23] found that the addition of 20 g of neutral-detergent fiber in the form of fruits and vegetables changed the water content of the feces from 73% to 75% in the enhanced fiber diet. Wyman *et al.* looked at the effect of cooked and raw bran on stool characteristics, and the differences between the water content during the control period (75%), raw bran (76%), and cooked bran periods (73–77%) were not significantly great. Bagasse similarly had no effect on the percentage of water in the stool (75–76%) nor did bran (75–77%), when 39 g of either was added to the diet.[26] Only one study showed a significant decrease in the percentage of water in the stool. When citrus pectin (15 g/day for 3 weeks) was added, the percentage of stool water decreased by 5%.[25] On the other hand, in a metabolic unit taking a liquid diet where an abnormal stool might be anticipated, the percentage of water was between 82 and 89%.[22] The effect of 60 g of a mixed source of vegetable fiber reduced the water content of the stool to 77%. This all suggests some ideal percentage of water between 73 and 79%. The mechanism by which this proportion is established is not at all clear.

Exton-Smith *et al.*[37] have developed a technique to measure stool softness which uses a probe or penetrometer. They found that the mean penetrometer reading for hard stools was 80 ± 44 and for soft stools was 129 ± 52.

The ideal stool weight toward which diet regimes should be directed has not yet been defined. Spiller *et al.*[36] have suggested that an average stool production of 140–150 g/day should be a useful figure to achieve. The intestinal transit time is more predictable above a fecal weight of 140 g/day. It is not clear, however, how reliable transit-time measurements are. The Life Insurance Companies have yet to pontificate on the matter of the ideal stool weight and freedom from disease.

The manner in which food controls the bulk of feces is a matter of conjecture. It has long been recognized that fiber is important in controlling stool weight. Williams and Olmsted[38] determined that, of the three classes of substances that make up the effective portion of indigestible residue, hemicelluloses were more efficacious in increasing stool bulk than cellulose and lignin, the latter being least effective. They thought that the effectiveness of indigestible residues is not due primarily to the mechanical stimulus of distension but rather to chemical stimuli that arise from the destruction of hemicelluloses and cellulose by the intestinal flora. One of the stimulating products was the volatile fatty acids. In addition, the chemical stimulus was aided by the hygroscopic quality of the residue escaping degradation.

Their work tended to be forgotten and, in the renewal of interest in dietary fiber, water-holding capacity became the main emphasis in stool size. The rea-

son for this, perhaps, is that the initial renewed studies on fecal bulking were conducted with cereal bran. The original hypothesis developed by Burkitt, Trowell, and Painter emphasized the prime role of bran. There is no doubt that bran is a most effective source of fecal bulk.[19–21,26–28,30,32,39,40] Brodribb and Groves confirmed previous work showing that the water-holding capacity of bran was related to its ability to influence stool weight, fine bran being much less effective than coarse bran.[12,20] An increase in mean stool weight with coarse bran was 79 g, compared with fine bran at 58 g. There was also absorption of fatty acids from the colon—in the dog, of medium-chain fatty acids[41] and, in man, of volatile fatty acids (VFA).[42] However, when fecal VFA were measured[21] on an enhanced cereal fiber diet of 45 g/day, the concentration of VFA did not increase, but total VFA output increased significantly with the added fiber. Similarly, the fecal organic anion did not change in concentration, but there was a significant increase in output.

McConnell *et al.*[43] demonstrated that the fiber in fruit and vegetables had considerable water-holding capacity. The old experiments by Williams and Olmsted[38] showed that agar had a substantial effect on stool weight, greater than cabbage, greater than carrot, and greater than wheat bran in that order, a fact which suggested that these predictions for water-holding capacity and stool weight were reasonable. However, such rationale did not withstand experimental examination. Durrington *et al.*[24] gave subjects the hygroscopic material pectin (15 g/day) and found that the mean stool-weight increase was from 150 to 186 g/day. Kay and Truswell[25] fed 15 g of pectin per day, and the mean daily wet weight of feces was increased only slightly from 140 to 168 g/day. Kelsay *et al.*[23] looked at the effect of a high-fiber diet containing fruits and vegetables without whole grain cereals or nuts. This diet enhanced the fiber content by 20 g neutral-detergent fiber per day. Fecal fat increased by 28% and the wet fecal weight increased from a mean of 89 to 208 g/day. The fruits and vegetables used in this experiment were in their native or cooked form. However, different effects are obtained if the fiber is given in a prepared form. When prepared fiber is given, the concept of water-holding capacity does not seem to stand.

Cummings *et al.*[27] gave approximately 20 g of concentrated dietary fiber from carrot, cabbage, apple, bran, and guar gum. The fecal weight increased by 127% on bran, 69% on cabbage, 59% on carrot, 40% on apple, and 20% on guar gum. These changes in fecal weight were correlated with an increased intake of pentose-containing polysaccharide from the fiber. In the Williams and Olmsted experiments,[38] the preparations may have differed from those used by Cummings *et al.*[27] There are several interpretations of these results.[23,27,38]

The first is that fiber from fresh fruits and vegetables behaves differently along the bowel than does a prepared concentrate of fiber, and that the use of water-holding capacity as a predictor of their biological effects is not useful for comparisons between these preparations.

The alternative is that water-holding capacity is an indicator of a component of dietary fiber that is readily accessible to bacterial degradation, and that it is the residue of this component, resistant to hydrolysis, which retains its water-holding capacity in the feces. It is conceivable that fresh fruits and vegetables are less exposed to bacterial degradation and therefore are less susceptible to metabolism than is a dried fiber in which, perhaps, the structure is more exposed for bacterial degradation.

A further possibility is that the bacterial flora themselves are responsible for the fecal bulking. It is difficult to get a good indicator of the amount of bacteria in the feces. The electron microscopy work of Williams *et al.*[44] showed that bacteria are a predominant component of the stool, sited on the matrix structure provided by fiber. If the diet provides an easily fermentable carbohydrate source, presumably the fecal mass of bacteria will increase and possibly increase stool weight. The pectin experiments are not consistent with this concept.[24,25] Bornside[45] has reviewed the subject and has shown that the concentration of bacteria remains constant in the stool; as the stool weight increases, the bacterial mass also increases. This leads inevitably to a cause and effect relationship.

C. Cation-Exchange Properties

The existence of cation-exchange properties of dietary fiber is well established.[12] The description of the cation-exchange properties has been extended to include the divalent cation calcium and also zinc and iron.[46,47] These studies, in which fecal electrolytes have been measured,[21,29,48] show that, in association with the enhanced fiber content of the diet, the excretion of fecal electrolytes increases. Although this has caused concern, the studies also show that a high-fiber diet increases the intake of electrolytes. However, the doubts about electrolyte imbalance and fiber must be approached with caution as they were based on studies made in Iran and in the context of the Iranian diet.[47] Sandstead *et al.*[49] have shown that a diet similar to that consumed by many American males, to which 26 g of soft white wheat bran or corn bran was added, affected trace elements only slightly. The soft white wheat bran appeared to decrease retention of zinc in four subjects, but not significantly. Iron retention was similar in all experiments, and copper metabolism was improved by the addition of soft white wheat bran, and, to a lesser extent, by corn bran. The adjustments coincidental to changing the fruit and vegetable content of the diet, i.e., the concomitant increased ingestion of electrolytes, may possibly balance the deleterious effects of the cation exchange. It is odd, however, that in an experiment in which 200 g of carrot were eaten each day[48] and in which there was evidence of metabolism of the carrot fiber, stool weight increased by only 16%, while fecal electrolytes increased by 25%. Factors other than the

binding of electrolytes to fiber may also be important, such as their incorporation into bacteria.

D. Adsorption and Excretion of Bile Acids

Studies of fecal bile-acid excretion in relation to dietary fiber have established that a variety of dietary fiber sources are capable of adsorbing bile acids.[50] The use of adsorption studies has been extended in a study which showed that bile-acid conjugates incorporated into micelles with cholesterol are reversibly adsorbed as micelles onto fiber. Incorporating bile-acid conjugates into micelles with monoglycerides somewhat depresses adsorption of bile-acid conjugates. If fatty acids, monoglycerides, and bile-acid-conjugate-mixed micelles are exposed to cereal fiber, adsorption of bile acids to fiber is diminished. The extent to which the adsorption is diminished is affected by the fatty acid concentration, chain length, and degree of saturation. These experiments suggest that bile-acid conjugates are minimally adsorbed to fiber in the jejunum, but deconjugation and dehydroxylation, as in the cecum, favor adsorption.[51] Further studies showed that the adsorption was reversible and that several phases within the fiber matrix were involved.[52] A recent study questioned the ability of fiber to adsorb[53] and suggested that the saponins in the fiber preparations were responsible for the adsorption; however, the basis for this hypothesis was somewhat indirect.

Fiber with a substantial bile-acid adsorption property may cause the transfer of bile acids from the fast enterohepatic circulation, that is, from the ileohepatic to the slower cecohepatic cycle.[6] In this situation, there is a possible change from a quantitative control of sterol metabolism to a qualitative control, i.e., following the generation of bacterial degradation products of bile acids.

This is an area of confusion in that one suggested way of reducing serum cholesterol is through an enhanced fecal bile-acid excretion, yet a high fecal bile-acid content is predisposing to carcinoma of the colon.[54] It is clear, therefore, that this paradox is resolved by having a low serum cholesterol and a low colonic bile-acid concentration. This may possibly be achieved through the cecohepatic circulation and the control of sterol metabolism by a feedback mechanism from the cecum.

E. Fecal Bile Acids and Neutral Sterols

Few studies on fecal bile acids in normals have been made. A summary of findings from some studies is given in Table 2, which shows the fiber content of the diet of the subjects and the initial mean fecal sterol results.

The effect of fiber on the excretion of fecal bile acids appears to be complex. It has been shown that the addition of bran to the diet does not alter the excretion of fecal bile acids to any significant extent, but does dilute them.[12,30] Curiously, though, bile-acid excretion increases after bran is discontinued.[12,28]

Table 2. Studies Involving Fiber Intake and Colonic Function in Normal Subjects (1975-1978)

Reference	Dietary fiber content (g)	Bile acids (mg/24 hr)	Neutral sterols (mg/24 hr)
Int. Agcy. Res. Cancer[33]	17.0[a]	420[a]	546[a]
		388[b]	578[b]
Cummings *et al.*[21]	17.0	199	—
Raymond *et al.*[22]	0	194	504
Kay and Truswell[25]	7.3[c]	265	335
McLean Baird *et al.*[26]	3.7[c]	150	344
Kay and Truswell[28]	3.7[c]	251	265
Jenkins *et al.*[30]	12.0[c]	201	602

[a]Urban.
[b]Rural.
[c]Crude fiber.

The effect of fruit and vegetable preparations is quite different from that of bran. Pectin[25] reduces the plasma cholesterol concentration by a mean of 13% and increases the fecal fat excretion by 44%, neutral sterols by 17%, and fecal bile acids by 33%. In this experimental situation, the stool weight had increased by only 5%; therefore, the fecal constituents had changed, but not the fecal weight. In a careful metabolic study,[22] 60 g of plant cell fiber did not change the plasma cholesterol or triglyceride levels; the excretion of both the endogenous neutral sterols was unchanged. Neutral sterols modestly increased from 504 to 636 mg/day and bile acids from 194 to 266 mg/day. However, the total fecal excretion was significantly increased from 699 to 902 mg/day. The authors concluded that the large quantity of dietary fiber from diverse sources had little or no effect on the plasma lipids and sterol balance, although intestinal transit time and stool bulk changed greatly. The curious thing about this experiment, however, is the large fecal bulk on a fiber-free diet. In these experiments, fiber was added to a liquid diet; an experiment where fiber is added to a normal diet may produce different results.

Therefore, it appears that fruits and vegetables act on fecal bile-acid excretion differently from bran, though adsorption studies indicate that they might behave similarly. Again, the effect may be on the enterohepatic circulation prior to degradation by bacteria, or degradation by bacteria in the cecum may alter the environment in the cecum and thus change fecal bile-acid excretion.

F. Matrix Formation

The components of fiber have a degree of order, and the fibrils are arranged in planes. It is conceivable, therefore, that fiber introduces surfaces

into the colon that may influence colonic function and alter the metabolic activities of the bacteria. The alignment of bacteria within the fibrous matrix will be affected by the physical structure of the fibers and the degree of cross linkage. The degree of ion linkage will vary throughout the course of bacterial metabolism and determine the mesh size and the rate of ion exchange. A study in which feces were observed histologically suggests that bacteria are aligned on the surface of intact fiber.[44] As some of the components are metabolized, access to the interior of the fiber will be enhanced, and bacteria can penetrate to further degrade the fiber.

G. Effect of Fiber on Bacteria

Bornside[45] has reviewed the effect of increased dietary fiber on the numbers and types of the major groups of fecal bacteria. In each of the recent experimental studies of the effects of fiber on human fecal bacteria, no change occurred in the bacterial flora. Even on a synthetic diet devoid of dietary fiber, there was no profound reduction or change in fecal flora. Bornside concluded that the major groups of bacteria and the numbers per gram of feces are not altered by diet, either by supplementing with fiber or by removing fiber.

Viable counts of 10^{11} bacteria per gram wet weight appear to be the maximum in feces, suggesting that the nutrient substrate and other conditions that sustain maximal bacterial growth in the colon are not dramatically influenced by the amount of dietary fiber consumed. However, the fecal mass may result from the bacterial mass, so that the total number of bacteria excreted daily per gram of feces is directly related to stool weight, which in turn is related to the dietary fiber content. These studies, however, were all conducted on an enhanced intake of a cereal fiber, bran. It is not known what happens to the fecal flora with a more mixed diet based on fruits and vegetables.

If intact feces are examined with a light microscope and a scanning electron microscope, the matrices of feces are seen to contain large numbers of bacteria intermingled with smaller amorphous particles of food residue. Within this mass, fragments of plant residue are embedded. Around the vegetable fibers, the bacteria are packed closely with many morphological types present, such as gram-positive and gram-negative rods and cocci; generally, these types are mixed in a random manner. However, occasional colonies of gram-positive bacteria and yeast cells were observed. The bacterial mass was closely adherent to the fiber.[44] This suggests that studies on homogenized feces will give results different from those obtained by more direct observation of the fecal mass.

III. METABOLISM OF DIETARY FIBER IN THE COLON

The colon is normally filled with undigested food residue and with variable amounts of water and electrolytes, bacteria, shed mucosal cells, and secreted

or excreted organic and inorganic substances. Dietary-fiber metabolism will thus be governed by the interaction of these colonic contents. The bacteria, particularly, are the most important because of their diversity and wide range of metabolic activities. Over 100 species are identified in human feces and collectively comprise 10–20% of the fecal dry mass.[55] In the normal adult colon, the resident bacterial flora consist of 96–99% anaerobes; about 45% of these consist of a single species, *Bacteroides fragilis*.[56,57]

In addition to the carbohydrates digested by man—the monosaccharides, disaccharides, and starch—colonic bacteria are able to degrade a number of oligosaccharides and polysaccharides of dietary fiber (Fig. 3). Man possesses intestinal enzymes to hydrolyze $\alpha(1\rightarrow4)$-glycosidic bonds and lactase, which hydrolyzes the $\beta(1\rightarrow4)$-bond linkage in the disaccharide lactose. However, bacteria have enzymes to convert plant polysaccharides into shorter-chain carbohydrate molecules and enzymes that cleave $\beta(1\rightarrow4)$, $\beta(1\rightarrow6)$, and $\alpha(1\rightarrow3)$ glycosidic bonds.[58,59] Bacterial degradation of dietary fiber in the colon follows two distinct stages: extracellular hydrolysis of polysaccharides into monosaccharides or disaccharides, and intracellular breakdown of the monosaccharides following absorption.

First, the component polymers of dietary fiber are hydrolyzed into sugars of different chain lengths by bacterial enzymes acting extracellularly. Cellulose is broken down into short-chain oligosaccharides by cellulase. Hemicellulose is cleaved either by specific hemicellulase enzymes (xylanase and xylobiase) or nonspecifically by cellulase. Pectins are degraded to shorter molecules by pectinesterase, pectinhydrolase, and pectinlyase. The free oligosaccharides (raffinose, stachyose, etc.) and the oligosaccharides formed from the polysaccharide as intermediates are then hydrolyzed by the nonspecific extracellular α- and β-galactosidase group of enzymes.[59] Since this metabolism is extracellular, it is

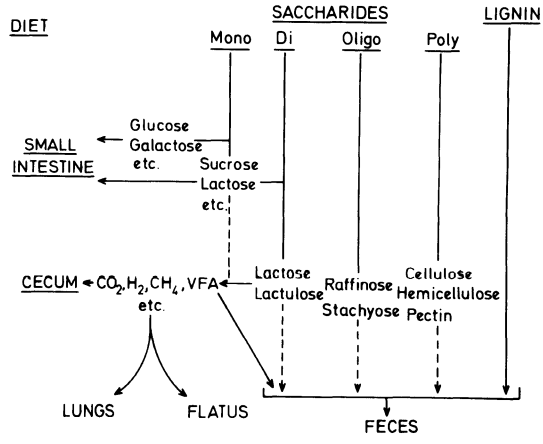

Figure 3. The fate of dietary fiber constituents along the gastrointestinal tract.

influenced by pH, temperature, water activity, movement, and the chemical nature of the luminal content. The physical and chemical states of the substrate polymers determine the degree of breakdown. Cellulose, for example, is a rigid and compact polymer and may be inaccessible to bacterial enzymes, so the bacteria attach themselves to the surface and the enzyme metabolism proceeds slowly.[60] Most of the pectin and hemicellulose is within the plant cell wall between the cellulose fibrils and is difficult for the enzymes to reach. Once the enzymes gain access to the pectins and hemicelluloses, they are relatively easy to hydrolyze.

Other chemical properties of fiber components such as branching, methoxylation, and gelling may affect degradation either by excluding the enzymes from access to the complex or by forming strong bonds resistant to enzymatic attack.[61] The lignin and silica content of the dietary fiber source also affects the degree of breakdown of the fiber in the colon. The reasons for this are not known.[62] Also, individuals may vary in the type and number of bacterial species they harbor, and this may influence the type of enzymes available and hence the polymers degraded. Gorbach *et al.*,[63] in their study of human fecal bacterial flora, have shown wide variations, related to age and diet, in the bacterial flora of individuals. Borriello *et al.*[64] found that a northern Nigerian rural community had fewer bacteroides and NDH +ve *Clostridia* in their feces than Londoners. The bacterial flora also varied with age in both communities.

Once the polysaccharides are hydrolyzed extracellularly to disaccharides and monosaccharides, the sugars are absorbed and metabolized within the bacterial cell. Since most of the bacteria in the colon are anaerobic and the amount of oxygen in this region is very low, the glycolysis which takes place is anaerobic glycolysis, i.e., fermentation. Aerobic and anaerobic glycolysis of monosaccharides is similar as far as the formation of pyruvic acid. After this the two processes diverge. Aerobic glycolysis continues with oxidative decarboxylation of pyruvate and further metabolism in the citric acid cycle. Anaerobic glycolysis ceases at the pyruvate stage and is followed by a variety of reactions to organic compounds and gases. These differences in bacterial metabolism of carbohydrates and the necessity for the bacteria to excrete partially degraded products and gases into the colonic lumen will have several effects on colonic function.

The central problem of anaerobic bacterial metabolism appears to be the accumulation of partially degraded metabolites that must be excreted. Most important is the transfer of the "excess" H^+ ion that is formed to suitable carriers to relieve the limited coenzyme NAD, in order to continue anaerobic phosphorylation.

One of the important ways of disposing of H^+ ions in many anaerobic bacteria of the gut is through the formation of molecular hydrogen (H_2). This is achieved by the hydrogenase enzyme developed to catalyze the following simplified reaction[65]:

$$2e + 2H^+ \xrightarrow{\text{Hydrogenase}} H_2$$

The H^+ ion can also be combined with other organic compounds (pyruvate, fumarate, acetyl CoA, etc.) or inorganic compounds (HCO_3^-, SO_4^{2-}, NO_3^-).[59]

The major by-products of fermentation of dietary fiber are components of volatile fatty acids (acetate about 70%, propionate 18%, and butyrate 12%), acetaldehyde, formate, acetyl CoA, lactate, ethanol, and the gases CO_2, H_2, and CH_4. Of the gases, CO_2 is a constant product and H_2 is formed most of the time. Methane formation requires a specific group of bacteria, methanogenic bacteria, which are very strict anaerobes; formation may require H_2 and formate.[59,66,67]

Which of these compounds are formed during a given fermentation of a fiber polymer and the amount formed depend on various factors yet to be established. The type of bacteria and the chemical nature of the substrate may play a major role. Not all of the diverse bacterial flora of the colon perform the same type of metabolic reactions; hence, intermediate and final products differ to some extent. *Clostridia,* for example, converts pyruvate to CO_2, H_2, and acetyl CoA, while enterobacteria convert pyruvate to acetyl CoA and formate. Many gut anaerobes (e.g., *lactobacillus, streptococcus,* and *bifidobacterium*) reduce pyruvate to lactate.[59] Methane is formed only by methanogenic bacteria, of which only three species are isolated from the rumen and only one from human feces.[68,69] The interdependence of the different bacteria in the gut is well known.[2] The type of substrate available determines not only the intermediates formed but possibly also the type of flora.

Williams and Olmsted[38] showed that hemicellulose was metabolized predominantly to VFA. Hickey *et al.*[70] found that the ingestion of prunes produced high levels of H_2 and low levels of CO_2, while the converse was true for raisins.

Robertson *et al.*,[48] investigating the effect of carrot ingestion on colon function, found that the breath H_2 excretion increased slowly over days, indicating a delay in the change of bacterial flora or in metabolism as a result of carrot ingestion.

IV. EFFECT OF DIETARY FIBER METABOLISM ON COLON FUNCTION

The effects of dietary fiber metabolism on colon function are probably mediated through partially degraded chemical compounds and gases produced in the bacterial cell and excreted into the lumen during fermentation. These fermentation products may be assessed in a number of ways. The gases can be measured in breath or flatus, and in unabsorbed VFA and other compounds in feces.[38,70,71] Hydrogen and methane are not produced by animal cells. It has

been shown that most of the H_2 and CH_4 produced in the colon, under normal conditions, is absorbed into the circulation and excreted by the lungs.[72] Gas chromatographic methods for the detection of the small concentrations in the breath and flatus samples have been developed.[73,74] The measurement of these gases affords an indirect means by which bacterial metabolism in the cecum can be monitored. Tadesse and Eastwood,[75] using breath H_2 and CH_4, studied the metabolism of individual components of dietary fiber in the colon. They showed that raffinose, lactulose, and hemicellulose increased breath H_2, but cellulose, pectin, and lignin did not alter the H_2 excretion. Methane excretion was unaffected by any of the polymers studied. The factors that influence CH_4 production in man are not clear.[76] *In vitro* and ruminant studies indicate a relationship between H_2 and CH_4 production and the influence of carbohydrate substrate on the formation of these two gases.[77] In human experiments, we found that CH_4 excretion was unaffected by a wide range of carbohydrate ingested, even in those individuals who are methane excretors (Figures 4a,b).

The increase of substrates as a result of fiber intake will increase the nutrient available for bacteria in the colon and so enhance their activity and growth. Species that utilize the specific chemical polymers more efficiently than others will increase. Thus the degree and range of bacterial activity in the lumen may change with the amount and type of dietary fiber ingested. The increase of organic anions, particularly VFA, with fermentation was thought to increase fecal bulk by acting as an osmotic cathartic and a stimulant to increase colonic motility.[38] But these substances very possibly are absorbed into the blood circulation without significant contribution to bulking. The absorption of VFA from the cecum and colon has been confirmed in a number of animal experiments, and McNeil *et al.*[42] have indirectly demonstrated VFA absorption from the colon of man. The formation and accumulation of gases in the lumen will distend the colon and stimulate peristalsis, possibly decreasing transit time.[78]

Another effect of gas formation that is often neglected is the introduction of another phase in the luminal environment besides the solid and liquid phase. Pockets of gas may act as a barrier between luminal content and colonic mucosa and between bacteria and substrate. Distension of the colon beyond a certain point may decrease mucosal and muscular activity. However, the effect of gas in the colon is self-limiting since it is either absorbed into the circulation or expelled as flatus.

An indirect contribution of fiber fermentation in the colon is the addition of absorbed VFA and alcohol to the energy intake of the animal. Maintenance of body temperature may result from heat released during fermentation. Both these contributions are significant in a number of animals but are negligible in man, though their importance in population groups with high dietary fiber intake but low overall energy intake cannot be underestimated.

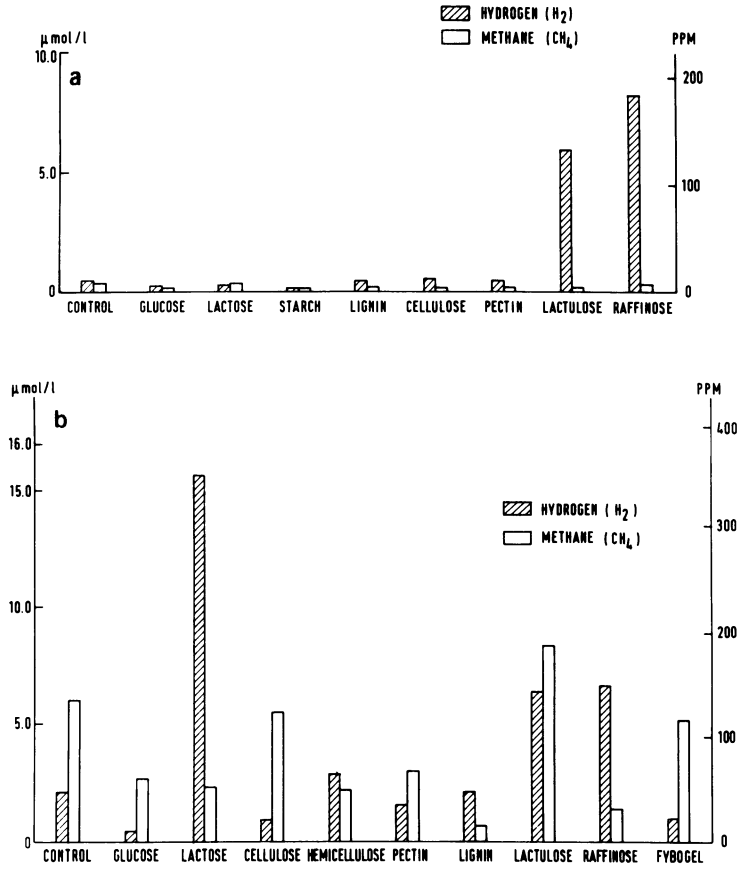

Figure 4. Breath hydrogen and methane excretion in response to ingestion of different carbohydrates (20 g). Fybogel (ispaghula), 7 g; raffinose, 10 g; lactose, 50 g; hemicellulose, 10 g. Values are the total of eight end-expiratory samples taken at 1-hr intervals. a: Methane nonexcretor. b: Methane excretor (lactase deficient).

V. EFFECT OF FIBER ON STOOL WEIGHT

A. Normal Fecal Weight

A wide range of normal values are accumulating for control periods in studies in which fiber was added to the diet. In addition there are studies in which either stool weight or fecal constituents or both are measured in populations who show propensity or resistance to certain diseases.

It has been suggested that part of the confusion in studies on dietary fiber is due to the failure to study patients in metabolic units. This criticism is rea-

sonable, but it has to be seen in the light of our contemporary lack of knowledge of the factors that control fecal output in the normal. It is only when the factors that affect stool weight are known that variations can be introduced. At the moment the emphasis is on dietary fiber, though other factors could exist that are totally unexplored. This becomes apparent when the available results are appraised (Table 3).

Spiller *et al.*[36] have suggested that a fecal output of 140–150 g/day be used to establish the minimum amount of a particular dietary fiber for the

Table 3. Studies Involving Fiber Intake and Stool Weight in Normal Groups or Populations (1975-1978)

Reference	Diet	*N*	Mean daily stool wt (g)
Brodribb and Groves[20]	Habitual (uncontrolled)	21	140
Cummings *et al.*[21]	2800 kcal, 351 g cholesterol, 122 g fat, 88 g protein, 17 g fiber	6	79
Raymond *et al.*[22]	Fiber free, low cholesterol	8	196
	Fiber free, +1 g cholesterol	—	192
Kelsay *et al.*[23]	2800 kcal, 95 g protein, 115 g fat, 350 g cholesterol, low fiber (1 g crude fiber)	12	89
Wyman *et al.*[19]	Habitual	10	131
Durrington *et al.*[24]	Habitual	12	150
Kay and Truswell[25]	2350 kcal, 275 g cholesterol, 86 g fat, 90 g protein, 7.3 g crude fiber	9	140
McLean Baird *et al.*[26]	Unrestricted	20	88
	Metabolically controlled	4	93
Cummings *et al.*[27]	2784 kcal, 385 g cholesterol, 85 g protein, 22 g diet fiber	29	117, 88, 95, 141, 120
Kay and Truswell[28]	10.14 MJ, 90 g protein, 91 g fat, 282 g cholesterol, 3.7 g crude fiber	6	125
Jenkins *et al.*[30]	2800 cal, 350 g cholesterol, 120 g fat, 90 g protein, 12 g crude fiber	6	71
Eastwood and Kay[6]	Habitual	—	103
Int. Agcy. Res. Cancer[33]	City (Copenhagen)—17 g fiber, 79 g fat, 53 g protein, 7.9 MJ energy	30	150
	Rural (Finland)—31 g fiber, 91 g fat, 88 g protein, 10.2 MJ energy	30	200
Wyman *et al.*[35]	Habitual (males)	10	131
	Habitual (females)	10	126
Glober *et al.*[82]	Japanese, native	28	194
	Japanese, living in Hawaii	67	120
	Caucasians	25	119
Manousos *et al.*[83]	Rural (Greece)—high fiber	22	172
	Urban (Athens)	14	131

average adult to consume daily. The individuals participating in some of these studies came close to this level before the start of the study. There are only a few detailed studies on stool patterns. One that gave remarkable detail[34] was in a Federal Correction Institution at Seagoville, Texas, with information on 8267 stools for 115 individuals, taken between 1950 and 1953. Unfortunately, the only dietary information given was that the diet was adequate and well balanced nutritionally and consisted of approximately 3500 calories per day. The average weight of stool of 115 subjects, aged 20–57 years, was 124 ± 40 g (range 35–224 g).

B. Addition of Wheat Bran to the Diet

Given this variation in initial values, the wide differences in response to ingestion of wheat bran are not surprising. Brodribb and Groves[20] looked at the effect of bran particle size on stool weight and compared a coarse bran with a water-holding capacity of 7.3 g water per gram dry weight to a fine bran with a water-holding capacity of 3.9 g water per gram dry weight, the chemistry of the two brans being approximately equal. With coarse bran, the stool weight was significantly greater than with the fine bran. The increase in mean stool weight with coarse bran was 79 g and with fine bran 59 g. Wyman *et al.*[19] showed that cooking bran changed its effect on stool weight. The size of individual stools was increased with raw bran (12 g/day) but paradoxically not with 20 g/day. It was suggested that the reason for this apparent discrepancy was that the 12-g dose was the first to be taken, and tolerance to bran developed.

A further clue to complexities is given in a study by Wicks *et al.*[79] on the effect of bran (30 g/day) on biliary bile acids. It is clear that there is a delay in the changes in the biliary bile acids. Only by the sixth week was there a significant decrease in deoxycholic acid and an increase in chenodeoxycholic acid. There are no comparable studies on the effect of bran on fecal constituents, or on dose response and time course using defined brans. As has been emphasized in this chapter, individual variations complicate studies.

In the study by Cummings *et al.*[21] on the effect of cereal fiber on fecal weight, increasing the dietary fiber with cereal bran from 17 to 40 g/day resulted in an increased fecal output from 79 to 228 g/day. Fuchs *et al.*[32] showed that supplementing the diet with 3 oz of processed wheat bran (5.5 g of crude fiber) increased the mean daily stool weight from 103 ± 40 g to 220 ± 90 g. Kay and Truswell,[28] enhancing the crude fiber content of the diet with cereal bran from 3.7 to 8.6 g, showed an increase in mean stool weight from 125 to 225 g/day. In a study by Jenkins *et al.*,[30] adding 36 g of wheat bran fiber for 3 weeks increased the stool weight from 71 ± 6 g to 217 ± 12 g. When bagasse is given as a supplement (5.2 g of crude fiber per day), the stool

weight increased from 88.3 to 139 g/day. In all of these studies, the effect of bran is to increase stool weight by the retention of water.

C. Addition of Fruit and Vegetables to the Diet

In one study, 200 g of raw carrot taken each day produced an increase in fecal constituents but only a minimal effect on stool weight,[48] indicating that it is possible to alter fecal constituents without increasing fecal weight. Kelsay *et al.*,[23] however, found that by giving a diet containing a wide range of fruits and vegetables, the stool weight increased from a mean of 89 to 208 g/day. The details of the diet showed this to be a manageable dietary intake. Raymond *et al.*,[22] in a metabolic ward study using a basal liquid diet, gave 60 g of plant-cell-wall material (approximately five times the fiber intake of the typical American diet), which increased stool weight from 176 to 240 g/day. Cummings *et al.*,[27] in their study of fiber concentrates, showed that fecal weight increased 127% on bran, 69% on cabbage, 59% on carrot, 40% on apple, and 20% on guar gum. These changes in fecal weight correlated with an increased dietary intake of pentose-containing polysaccharide. They indicated that individual variations in response to a given fiber intake are also important. The extent to which pentose-containing polysaccharides are digested could thus determine individual response to a given fiber. In studies where pectin has been added to the diet, the increase in stool weight was 25%[24] and 5%.[25]

VI. SUMMARY

Clearly, these studies show that dietary fiber has a distinct influence on stool weight and that individuals respond differently to fiber. The method by which the fiber is prepared—whether it is cooked or processed—may affect stool weight. Water-holding capacity, as a predictor of effect on stool weight, may be limited to wheat bran. The water-holding capacity of fruit and vegetable fiber perhaps indicates the accessibility of the dietary fiber to bacterial degradation.

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2

The Measurement of Intestinal Transit Time

Adam N. Smith and Martin A. Eastwood

I. INTRODUCTION

Intestinal transit is the phenomenon accomplished by what is at first food, later chyme, and still later feces in making the journey of about one or two days along the alimentary canal. Transit is an important function to study, first because of its relationship to the change from food to chyme; at this stage, digestion is the principal activity affecting intestinal transit, mainly in the small bowel. Second, transit is studied in relation to the production of the formed feces; the retention and the excretory functions of the gut are the activities then under examination. "Intestinal transit" is most often measured as the total intestinal transit time along the whole alimentary tract and as such is mainly a function of propulsion in the small and large intestine. Yet, since there are variable periods of delay in the stomach, cecum, and rectum, such total measurements may be rendered capricious. The contribution of the various sectors of the alimentary tract physiologically to gastrointestinal transit will be summarized first.

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II. PHYSIOLOGICAL RELATIONSHIPS

The contribution of esophageal motility is in moving the bolus along the esophagus by peristalsis. On arrival at the stomach, the swallowed material is accommodated by receptive relaxation of the upper stomach. Contractions invoked by a possible pacemaker in the body spread into the antral area and serve to reduce the food to a smaller particle size. The pylorus relaxes and allows food and H ions to enter the duodenum, but acid in the duodenum inhibits further gastric emptying until neutralization has taken place, when emptying resumes. It does so at the height of another antral wave when osmotic relationships and particle size have been adjusted and are synchronized with pyloric duodenal relaxation, the three components—the antrum, the pylorus, and the duodenum—acting as a unit.

Onward transmission in the duodenum and small intestine is both peristaltic and segmenting in nature. The former is now regarded as the rarer event; the latter mixes the contents to and fro. As a result of contractions that are of greater amplitude and frequency proximally than distally, segmentation drives the chyme downwards along the alimentary tract, though much more slowly than by peristalsis. Measurements of intestinal activity made by radio telemetering capsules show that movement is in abeyance for very long periods; this is true of recorded pressure waves as well. The factors controlling these periods of activity and inactivity are imperfectly understood. Bursts of electrical activity, the interdigestive spike potentials, are recorded between meals and are thought to represent the motor activity of the intestinal tract emptying itself of its contents: according to Code and Martlett—"the housekeeper sweeping the house clean."[1] They are related to neural, parasympathetic activity and possibly also to motilin release.[2] They are inhibited by the further intake of food.

Transmission of contents in the colon is achieved by mass peristalsis, but here also a fundamental role is played by segmentation. This motor activity is, however, more likely to facilitate the slow turnover of contents locally to aid water absorption and thus the conversion from liquid to solid or semisolid feces. It is not known how closely the solidification of the contents to form feces by segmentation and mass peristalsis are related. Mass peristalsis, which occurs mainly postprandially, after breakfast in the majority, leads to feces entering a zone of sensory awareness and to the desire for defecation. Mass peristalsis is also facilitated, it appears, by somatic activity. A relationship of the so-called gastrocolic reflex to hormone release has been sought, but the involvement of any particular hormone such as gastrin is as yet unconfirmed. However, it is classically well documented that food increases the segmenting motor activity, and it has alternatively been postulated that a humoral material derived from the duodenum or upper small intestine may affect the sigmoid colon. Cholecystokinin stimulates motor activity of the sigmoid colon in man, whereas secretin and glucagon inhibit it.

III. METHODS OF MEASURING GASTROINTESTINAL TRANSIT

A. Gastric Emptying Time

It is clear that the methods for measuring gastric emptying time will influence the emptying time. If the marker that is used to measure emptying time is a solid, the value obtained is quite distinct from one that measures the liquid phase. On the other hand, changes in gastric emptying time that result from enhancing the fiber content of the diet may affect liquid emptying time and solid emptying time. Thus, a complication is added to measurements of this particular phase of intestinal transit.

Studies of the rate at which refined and unrefined carbohydrates leave the stomach of normal subjects have produced conflicting results. McCance *et al.*[3] measured the rate of emptying of barium sulfate given with food. But Grimes and Goddard[4] used radioactive tracer techniques and were able to measure the rate at which both the solid and liquid components were emptied from the stomach. McCance and his colleagues had indicated that whole-meal bread left the stomach more rapidly than white bread, whereas Grimes and Goddard, using their technique, found no difference in the rates at which the solid phase of the gastric content left the stomach. Liquid left the stomach significantly more rapidly with white bread than with whole-meal bread. Furthermore, the amount of liquid leaving the stomach unaccompanied by solids was significantly greater with white bread than with whole-meal bread. Grimes and Goddard[3] suggested that an interpretation of McCance *et al.*'s previous work on the barium image of the stomach (that the stomach outline after white bread was small and more concentrated than after whole-meal bread) suggested a more rapid emptying of liquid after white bread. Obviously, in analyzing the results of gastric emptying studies, it is essential to know precisely what is measured by each technique.

An alternative technique is to measure the gastric emptying time by the rate of absorption of some nutrient. Such a technique has been used by Haber and his colleagues.[5] In this study, 10 normal subjects ingested test meals based on apples, each of which contained 60 g of available carbohydrate. The apples were given pulverized, as juice, or whole and intact. There was no significant difference in the rate of rise of plasma glucose or the time or amplitude of peak value.

B. Small-Intestinal Transit Time

Measuring transit time in the small intestine presents formidable problems. Essentially, this technique is the estimation of the mouth-to-cecum transit time. Such a transit time will be influenced by the period of residence within the stomach and therefore, to an extent, it represents duodenum-to-cecum transit. A variety of factors will affect this transit time. Solids, liquids,

and other materials pass along the gastrointestinal tract at differing rates. Another variable may be the intestinal contents; therefore, factors such as the osmolality of the intestinal contents could be important. Another factor is the presence or absence of fiber from the test meal or the habitual diet of the person being studied. A temptation is to measure intestinal transit time in patients with ileostomies[6,7] and to assume that the appearance of markers in the ileostomy bag is representative of what would have happened in the intact person. Almost certainly, however, adaptive changes have occurred in the ileum of ileostomy patients so that to some extent ileal tissue is beginning to adopt some of the function of the removed colon. Therefore, extrapolation from the ileostomy situation to the intact individual may be invalid.

A method that is widely quoted and used in clinical practice uses the head of barium passing along the gastrointestinal tract to give some indication of transit time. However, this again has considerable errors. Barium is a material of substantial specific gravity and therefore merely indicates a facet of the diagnostic technique which perhaps has little physiological relevance.

Kirwan and Smith[8] developed a transit-time method which incorporated an isotope capsule. Localization of the capsule, which contained ^{131}I, was made possible by a portable collimated sodium iodide scintillation counter. The time for capsules to pass from mouth to cecum was always within 8 hr. The techniques used, however, are to an extent artificial. The consequence of the technique can be illustrated by the method developed by Bemair and his colleagues.[9] They used an externally applied magnetic transducer, which senses the presence of an ingested ferromagnetic material as it passes along the small intestine. The mean transit time in a group of 20 normal subjects was found to be 157 $\pm$ 64 min, much less than measurements obtained by capsules. It is of interest that the magnesium ferrite remained finely dispersed and did not clump together even after most of the meal was absorbed from the small intestine.

An alternative method of measuring mouth-to-cecum transit time is the utilization of the phenomenon of gas production by colonic bacteria. The three major gasses formed in the colon—hydrogen, carbon dioxide, and methane—are excreted predominantly in the breath. The hydrogen is normally produced almost solely in the colon, and the production depends on the presence of exogenously supplied fermentable substrate, primarily carbohydrate. Bond and Levitt[10] found that variations in the dose of bran influenced their results, so that 10 g of bran had no effect on pulmonary hydrogen excretion, whereas 20 and 30 g of bran caused an increase in pulmonary hydrogen production, which came between 90 and 120 min after ingestion of the bran. On the other hand, they found that only 10 g of lactulose, with a transit time of only 48 $\pm$ 6 min, gave a more vigorous response in terms of hydrogen production. Adding bran to lactulose did not significantly alter its rate of movement through the small bowel. The transit time of lactulose with and without bran averaged 52 $\pm$ 8 min and 58 $\pm$ 14 min (SEM), respectively. Jenkins and his colleagues[11] mea-

sured the mouth-to-cecum transit time of a variety of fiber analogues: guar, gum tragacanth, pectin, and cholestyramine. They measured the point at which the breath hydrogen began to increase as reflecting the mouth-to-cecum transit time. In their control subjects, the mean transit time was between 90 and 120 min. Guar, gum tragacanth, pectin, and cholestyramine delayed transit time by 75, 30, 15, and 15 min, respectively. Methylcellulose had no effect on transit time, and bran reduced transit time by 45 min. The gums were related to the viscosity of a 1% solution at room temperature, guar having a viscosity of 1.3, gum tragacanth 0.2, pectin 0.21, and methylcellulose 0.07. There was a direct relationship between the mouth-to-cecum transit time and the viscosity ($r = 0.885$; $p < 0.02$).

The only problem with this technique is that the increase in breath hydrogen is reflecting the fermentation of the lactulose when it is given with the gum or cholestyramine or bran. The presence of the gums or bran could be influencing the onset of hydrolysis of the disaccharide.

The effect of these various polysaccharides on mouth-to-cecum transit time may be important in the enterohepatic circulation. The reduction in cycling frequency due to the presence of mucilaginous polysaccharides might be expected to reduce feedback inhibition of bile-acid synthesis and to increase the bile-acid pool size. This effect is relevant since cholelithiasis is commonly associated with a decreased pool of bile acids, perhaps because there is less bile acid in the gallbladder to dilute the more saturated bile secreted by the liver during an overnight fast. Therefore, altering small-intestinal transit time may cause various fibers to influence the bile-acid pool and the propensity for cholesterol gallstones.[12]

C. Cecal Residence Time

Very few studies have been made that accurately establish the influence of fibers on the bile-acid pool. It is possible using barium enemata to show that there is a remarkable constancy in the sequence of colonic contractions. The initial contraction usually takes place immediately distal to the cecum. Not only is there segmentation with symmetrical contractions, but the whole cecum may rise up relative to the ascending colon. Frequently only part of the cecal contents are expressed, and mixing therefore occurs, a fact which may have considerable metabolic importance. A considerable clue to this has been given by feeding multiple markers on serial days for 1–3 days and estimating the appearance of the first and last of these in the feces. This gives an estimation of colonic turnover, from which a cecal emptying time can be calculated.[13]

D. Total or Transintestinal Transit Time

The rate of passage of material from mouth to anus, total or transintestinal transit time, varies from person to person and even in individuals. Early

measurements were made with dyes and then with spheres, which were modified to plastic barium-impregnated pellets; this last refinement made observations more aesthetically acceptable by permitting collection of feces in plastic bags and X-raying them, rather than finding and counting the spheres! Early observations using the spheres indicated that those swallowed first were not always the first to be passed in the feces and that, to have a representation of gastrointestinal transit, it was necessary to have a whole series of "markers." In the technique introduced by Hinton and his co-workers[14] and widely followed, 40 markers are swallowed, and the time until 80% of these have been returned is taken as the "transit time." The marker technique thus elaborated by Hinton *et al.* has been criticized by Eastwood *et al.*[15] and Cummings.[16] Eastwood *et al.* hold that individuals in the same trial might vary by as much as 46 hr, and Cummings pointed out how much transit measured by markers was dependent on the clearance of the last of the markers, which might merely reflect a delay in rectal emptying. A subject might be recorded as having a slow transit because of slow ejection, rather than a slow transit because of prolonged propulsion throughout the alimentary canal.

E. *Modification by Fiber*

Any effect of diet on transit has to be set against the great variability of the methods of estimation. Obviously, different sources of fiber influence intestinal transit time in different ways. Little information exists on the minimum effective dose of bran or on comparisons of different types of bran and transit time. Most studies have been conducted on individuals taking a self-selected diet[17] rather than on carefully controlled populations.

Wyman and his colleagues[18] have emphasized the variability of transit time in healthy subjects. In their study, 20 healthy subjects eating their habitual diets made repeated 5-day stool collections, the 10 females making their collections over 4–6 successive weeks. There were striking differences in transit time, the mean transit time in females being 82.4 $\pm$ 16.7 hr; however, the range for each individual was considerable, e.g., 47 and 123 hr in the same individual. There were no obvious changes related to the phases of the menstrual cycle. In the males, the mean transit time was 65 $\pm$ 27 hr with a considerable range, though the study in these individuals was less detailed.

In another study, Wyman and his colleagues[19] examined the effect of raw and cooked bran in different doses on intestinal transit and fecal bulk. The diet was essentially low fiber; details were not given, but all fiber-rich cereals and breads were omitted and fruits and vegetables were limited to six specified small portions per day. Significant changes from control values were achieved only with raw bran at 20 g/day. Cooked bran at either dosage had no significant effect on intestinal transit time. They suggested that the cereal manufacturing process alters wheat bran so that cooked bran has less effect on the

intestine than does a comparable amount of raw bran. Other factors inherent in the fiber itself are also important. Kirwan *et al.*[20] found that 20 g of a coarse bran accelerated slow transit, whereas the same amount of a fine bran had no effect. These effects were paralleled by pressure changes; there was a reduction of pressure by the coarse bran, no reduction or even an increase of intraluminal pressure with the fine bran. Thus, fiber supplements that increase transit speed may have different implications even though they share the common property of bulk expanders.

The effects of other sources of fiber are quite distinct. Kay and Truswell[21] looked at the effect of 15 g/day of citrus pectin on transit time in a metabolically controlled situation. Pectin was consumed as a gel with fruit and sugar in divided doses with meals. The mean intestinal transit time was not altered. Sugar cane fiber, bagasse, has also been studied in normal ambulant volunteers over a 9-month period.[22] Though there was a significantly higher stool mass with bagasse supplements, the mean intestinal transit times for the radiopaque shapes used were lower but not of statistical significance. At the same time, they measured the mean carmine transit time; this showed that the bagasse biscuit supplement had a significantly lowering effect. This again emphasizes the problems of both diet and method of measuring transit time.

A study by Cummings *et al.*[23] of the colonic response to fiber from cabbage, carrot, apple, and bran showed pronounced individual variation, but most of these materials did affect transit time. The effect of bran on the mean colonic transit time was profound, reducing it from 73 $\pm$ 24 hr to 43 $\pm$ 7.5 hr. The effects of cabbage and apple were less distinct. Cabbage decreased time from a control value of 80 $\pm$ 26 hr to 64 $\pm$ 20 hr and apple from 80 $\pm$ 21 hr to 43 $\pm$ 16 hr. The differences were significant at the 5% level, whereas carrot had no significant effect on transit time. These results underline the varying effects of different fiber sources on intestinal transit.

Walker[24] has looked at the effect of a shorter transit time in South African Negro schoolchildren on a higher fiber regime. These children had a substantial excretion per day of fecal solids, nitrogen, fat, and other components. The average transit time on their habitual diet was about 9.5 hr. Supplements of fiber-rich food only slightly shortened the transit time to an average of about 8.5 hr, indicating that the daily intake of fiber of the children was acting maximally in respect of transit time. Walker was able to show that under conditions of high fiber intake, subsequent dietary supplementation with protein, fat, and carbohydrate had no effect on the fecal constituents, showing no malabsorption. Therefore, such a rapid transit time is not nutritionally disadvantageous.

Markers, being particulate, may not disperse throughout the fecal mass: as particles they will not reflect the transit of the gut contents when these are liquid, as in diarrhea. Specific gravity is important in the measurement of transit time. Kirwan and Smith[8] showed that a capsule with a specific gravity heavier or lighter than the gut contents travels faster than one more closely

related to the specific gravity of feces. The supposition was that, as the capsules were lighter or heavier, they would take up a position closer to the gut wall and be transported by its muscular action more readily. Kirwan and Smith suggested that the differential rate of particle transport through the gut may be one reason why bran, which is known to increase stool weight, can increase the rate of intestinal transit. They suggested, too, that other forms of vegetable fiber could alter the transit rate by altering the specific gravity of the colonic contents. There is also evidence that when fiber increases bulk and weight of feces excreted per day, the transit rate is increased; there is an exponential relationship, with short transit time being associated with high stool weight.[25,26]

F. Colonic Transit Time

Further studies by Kirwan and Smith[27] and Waller[28] have shown that there is little change in the small-bowel transit between normal subjects, those with constipation and those with diarrhea. Though Rosswick *et al.*[29] have shown that considerable unexplained transit delay exists in the small intestine in ulcerative colitis, the greatest change in transit in subjects with constipation and diarrhea is in the colon; colon transit is also abnormal in diverticular disease.

The isotope capsule tracked by a hand-held monitor lends itself to this type of study because of the regular topography of the colon. It is fairly easy to follow the capsule from the right colon through the transverse to the left colon and past the pelvic loop to the rectosigmoid. Difficult areas of comparison leading to errors of postural estimation are mainly between a low-lying transverse colon and a long pelvic colon extending inward towards the midabdomen. Serial plots of the maximum radioactivity of the isotope (sodium iodide with ^{131} I) sealed within the capsule allow subsequent correction of any false estimate of the localization of the emission source and thus the capsule site. It can be shown that in normal subjects, transit is slower in the left colon than in the right. In diverticular disease, it is relatively slower by a few hours in all zones when measured by isotope capsule. In contrast, the delay in constipation is mainly in the splenic flexures and rectosigmoid areas and, especially in the latter zone, may be 10–20 hr or more greater than in normals, and in some dyschezic subjects, 50 hr or so. Waller[28] has shown the slow rate of passage of the capsule in constipation and the correction of this by the administration of purgatives such as senna; and we have shown that bran accelerates the passage of the capsule in all the segments of the colon.[27] Waller has also shown fast transit in postvagotomy diarrhea and its reduction by codeine.

Both Kirwan and Smith[8] and Waller[28] have compared the isotope capsule with Hinton markers, with similar results: the time of excretion of a capsule of specific gravity 1.1 corresponded statistically in the Kirwan and Smith series with excretion time of 81.8 $\pm$ 5.3% of the radiopaque pellets. (It is of interest

that a lighter capsule of specific gravity 0.53 gave a figure of 62.50% of radiopaque pellets, and a heavier one of specific gravity 1.35 gave an excretion time corresponding to 72.3 ± 7.8% of radiopaque pellets.) In constipation, there was a significant correlation between the two methods, the results falling about a line the regression coefficient of which is 0.99; but in diarrhea, the correlation between the methods did not reach statistical significance, as the isotope capsule tended to be excreted earlier than 80% of the radiopaque pellets.

G. Differential Colonic Transit Time

Colonic transit time can be recorded by estimating the passage of a radioisotope capsule along the length of the colon. This can be done by subtracting 8 hr from the time it takes to pass along the entire length of the gastrointestinal tract. Eight hours is the average time from mouth to cecum and, according to Kirwan and Smith and to Waller, is relatively constant when measured by the radioisotope method. In 10 normal subjects, the estimated colonic transit time was 23 ± 8 hr, while the time measured directly was 25 ± 8 hr. In 5 constipated subjects, the estimated colonic transit time was 187 ± 85 hr, while the direct colonic measured time was 192 ± 92 hr. The time taken averaged 24 hr to pass the hepatic flexure, 78 hr to pass the splenic flexure, and a further 82 hr to pass the rectosigmoid. This was in contrast to 5 normal subjects in whom the capsule took an average of 10 hr to pass the splenic flexure and 20 hr to pass the rectosigmoid.[30]

H. Mean Transit Time

The most common technique for measuring transit time at the present is to record the passage of 80% of 40 swallowed radiopaque pellets.[14] Repeated measurements in the same subjects show wide variations, the average coefficient of variation being about 30%, according to Cummings.[16] The mean transit time (MTT) determined by repeated observations was shorter than the 80% transit time, which was 1.6 times the MTT.[31] The 80% transit time, as has already been stated, is probably imprecise because it depends on collecting the total markers; this, in turn, is affected by the expulsion of the last of these in defecation, which varies depending on timing and clearance of the remaining markers. To overcome this and minimize the disadvantage of estimating transit at one point in time, a technique was evolved by Cummings and his co-workers to estimate a MTT by feeding small doses of markers over a period of weeks and estimating the turnover. A more accurate MTT could be obtained by reducing the day-to-day irregularities through the expression of the results as a 5-day running average.

This technique showed variations in MTT unrelated to the frequency of defecation, however, and it was deduced that there were other factors, probably

relating to diet. Studies to determine the influence of low and high fiber on MTT established that high fiber caused a fall in MTT.[16] The changes obtained by the 5-day-average method and the 80%-transit-time method were made more statistically significant by combining with the low- and high-fiber tests. Yet the between-subject variation in MTT is still very great, e.g., 33–117 hr for normal subjects, and must reside in some individual or consititutional factor. Studies with Cummings's MTT method in subjects on control diets and after added fiber showed that those with the slowest initial MTT show a more dramatic change than subjects with fast initial transit, who often show very minimal effects. Harvey *et al.*[32] postulated that whereas fiber speeded the transit of those with a slow transit, this may be reversed in subjects with a fast transit, and thus the concept of a normalizing role for fiber in gut action was introduced.

The variation in the MTT cannot be reduced when the subjects take a constant diet; the only factor that appears to reduce the fluctuation in the MTT is the addition of fiber to the diet, which, by reducing the time of transit, appears to suppress the variation. The cause of the variation is unknown, though Cummings suggests that it may relate to the amount of exercise taken. Holdstock *et al.*[33] found that exercise initiated motor activity. Brocklehurst and Khan[34] and Eastwood[35] suggested that lack of exercise might be one of the factors prolonging transit in the elderly and thus contributing to the constipation which they so often develop.

IV. TRANSIT IN RELATION TO OTHER FUNCTIONS

A. Relation to Pressure

The motility paradox of Connell[36] was that diarrhea was associated with low-pressure and constipation with high-pressure waves. This may depend on the local conditions or the manner in which the motor phenomenon is being studied; e.g., a contraction spreading along an open length of bowel may lead to the equilibration of the pressure change thoughout its length with little incremental effect. The physical nature of the contents is also important, since pressure will be more readily generated in the "spaces" near to solid fecal contents. The raised pressure of diverticular disease is further attributable to the subdivision of the bowel into small compartments by the excessive segmenting action of the circular muscle. This might imply delayed transit, but Kirwan and Smith[27] found that in diverticular disease patients, pressure and transit were reciprocally related. Spriggs and Marxer[37] and Manousos *et al.*[38] further suggest that transit can be faster than normal in diverticular disease subjects who have, for example, an underfilled colon. They also found that the subjects had distinctive patterns and that individuals varied greatly.

The increase in rate of transit caused by administration of wheat fiber might have nutritional consequences apart from any effects caused by binding or precipitation by phytates. Studies done at a time of enhanced transit showed an increased fecal fat nitrogen and calcium output. The output of volatile fatty acid was increased, as was that of the fecal bile acids. Colonic water content may be controlled by the VFA concentration. It has been mentioned that water content of the feces is kept as far as possible under control in the fecal lumen. Perhaps a factor such as this is inherent in the finding of Harvey *et al.*[32] the "Bristol group," that wheat bran speeds transit when intestinal transit is slow, but also slows down fast transit.

B. Relation to Fecal Weight

Burkitt *et al.*,[39] Connel and Smith,[40] Spiller *et al.*,[25] and Findlay *et al.*[26] confirmed a reciprocal relationship between transit and fecal weight. Spiller *et al.* found that transit time decreased up to an output of 150 g/day, but beyond this there was no further decrease. The scatter of transit time was small (approximately ± 1 day) above a fecal weight of 140 to 150 g/day. This was no so with lesser fecal outputs, when the variation could be ± 2 days or more. The colonic activity was more predictable (in terms of transit) at fecal outputs of 140 to 150 g when the transit averaged 2–3 days. They set the amount of fiber (or equivalent) for a standard diet as the amount that is required to produce a transit of not longer than 3 days and that will yield moist, formed, easily expelled feces, with a wet weight of no less than 140–150 g/day. At this level of fecal output, transit may be compared more uniformly in relation to other variables such as drug action and hormones.

C. Hormonal and Metabolic Influences

Almost all the hormones of the APUD series affect small-bowel motility and may affect colonic motor function as well. Several hormones have been investigated in regard to transit through the entire gastrointestinal tract. Gastrin has been studied in relation to the diarrhea of the Zollinger–Ellinson syndrome, and gastric inhibitory peptide (GIP) with possible release in the dumping syndrome. Motilin, which may affect gut transit, may act as a coordinator in the adjustment of motility to the delivery of nutrients at rates sufficient to fulfill calorie expenditure ratios. Secretin may have opposite functions, but whether these are part of a physiological mechanism of control is unknown. Prostaglandins, though not of the APUD series, have been related to the diarrhea of medullary carcinoma of the thyroid, and their effects on the intestinal transit have been directly studied. Prostaglandin E_1 increased the transit rate through the small intestine and the colon and produced abdominal colic and the passage of fluid and feces per rectum. Transit was examined in this study

using radioactive pellets; there was a concomitant increase of colonic pressure activity. Thyroxine is also said to increase transit rate, and this may be an explanation of the occasional diarrhea of thyrotoxicosis. Bile acids also cause clinical diarrhea, but motor activity of the intestinal tract has not been intensely studied in such patients, as it was hitherto believed that the main action of the bile salts in the causation of the diarrhea was on mucosal secretion. Motor activity has been shown to be excessive in the distal colon in patients with cholerrheic enteropathy,[41] and it is likely that colonic transit at least is accelerated. Animal experiments have confirmed the motility change in rabbits and have shown that this is due mainly to the secondary bile acid, deoxycholic acid, with prostaglandin release as an intermediary mechanism.[42] In the colon, many of the changes in transit have been related to bacterial activity and the production of metabolites in response to stasis. Fecal ammonia levels measured by the dialysis bag technique of Wrong *et al.*[43] were greater on a high-protein diet but less on a high-protein and high-fiber diet, which presumably reduced the transit time. Cummings[16] quotes unpublished work by Bond, Hill, and himself who have also recorded a relationship between urinary phenol and transit, the higher values being associated with slow transit. Urinary sulfate and phenol are bacterial metabolites of dietary protein. It is of some interest that there is a relationship between urinary sulfate and transit in children which is also altered by the presence of fiber in the gut.

D. *Changes in Colonic Disease*

Differences in transit have been explored particularly in relation to theories of bowel carcinogenesis reviewed by Eastwood *et al.*[44] In prolonged transit, the colon may harbor bile-acid-splitting organisms, particularly anaerobes of the NDH clostridial type. Short transit times have been recorded in Nigerians and Japanese who have a low bowel-cancer incidence; but when people of these nationalities migrate to the United States, their intestinal transit time increases significantly, to that of the indigenous American, and their incidence of bowel cancer increases. Attention has therefore been directed to the fecal flora and the bowel habits of other population groups that are considered "high" and "low risk" for colonic cancer. Two populations were compared in two areas of Denmark and Finland with a fourfold variation in colon cancer incidence.[45] The relation to other known factors such as dietary fat, neutral or acid steroids. and bacterial metabolites was inconclusive, but it appeared that there was a higher intake of dietary fiber in the low-incidence area, suggesting a possible protective role for fiber. Nevertheless, the mouth-to-anus transit times were unchanged in the two groups. The protective role of fiber may be more subtle than merely expediting the clearance from the colon of a hypothetical carcinogenic compound.

The irritable colon syndrome, which in incidence accounts for about 25% of hospital gastrointestinal outpatient attendance has, as one of its forms of clinical presentation, diarrhea rather than the more common sympton, abdominal pain. The transit time in this type is worthy of more complete investigation. In diverticular disease, motility changes and electrolyte shifts suggest some basic disturbance of Ca and Mg ions in the fecal output or perhaps in the wall of the bowel. This decreased electrolyte excretion in association with an enhanced colonic pressure may, however, merely reflect the amount of cation in the colon, as a result of the reduction in fiber and its cation-exchange properties. In diverticular disease, the classical view following the many studies by Painter[46] is that pressure increases in the distal bowel lumen, and this is the cause of the mucosal extrusion through the wall that becomes the diverticulum. Evidence has been presented in this review that, in diverticular disease, an isotope capsule passes through all the segments of the colon slowly and that it is expedited by bran; yet in other studies, pressure and transit were reciprocally related.[27] Does this imply that there is in some patients an obstructive factor with a rise in pressure and thus a faster transit, and in others, perhaps with stasis, a more prolonged transit with a reduced intraluminal pressure? We have come to doubt that pressure change is the initial change in the diverticular disease state.[47] It could depend on which patients are examined and at what time. Attisha and Smith[48] measured the pressure in diverticular subjects, proceeding to myotomy, and found it to be invariably high preoperatively; yet Eastwood *et al.*[47] found that the intraluminal pressure, the intestinal transit, and the stool weights were the same in 46 subjects with diverticular disease as in a normal population residing in the same part of Edinburgh. This must raise doubt as to the exclusiveness of some of the features of diverticular disease, such as low stool weight, prolonged transit, and high pressure, which could be more related to stasis in the distal bowel. These subjects may produce waves of larger amplitude at an early stage of the condition before moving into a later, more continuously maintained high-pressure phase of the disease and the full development of the characteristic "triad." It is of interest that bran is more productive of transit change than fybogel or lactulose and was the only one of these compounds to influence consistently the high-pressure waves.[49]

V. CONCLUSIONS

Published studies on intestinal transit times show that they are subject to great individual variation. Methods need standardization and improvement, not only in relation to transit as an aspect of gut motility, but also in refining the measurement of intestinal absorption,[50] of which the rate of transit is but one variable. Measurement of intestinal transit has become of paramount

importance with the emergence of the study of dietary fiber in relation to gastrointestinal function. Alteration in transit time is one of the characteristic changes described as a response to the administration of cereal fiber.[51] Refining the measurement of transit may enable us to detect abnormalities in diseases attributed to the lack of "roughage" in the Western diet.

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3

Dietary Fiber in Diverticular Disease of the Colon

A. John M. Brodribb

I. INTRODUCTION

In 1971, Painter and Burkitt[1] published a hypothesis in the *British Medical Journal* suggesting that diverticular disease of the colon was caused by a deficient intake of dietary fiber. The publication of this theory stimulated a number of detailed research investigations, the results of which are now becoming available and enabling critical reevaluation of the hypothesis.

The investigation of an etiological agent in a chronic disease has proved to be far more complex than the identification of a causative organism in an acute bacterial infection. Multiple factors are frequently involved, the time scale is usually slow, and it is often difficult to test for specificity of effect. The principles underlying Koch's postulates for identification of a causative agent are, however, equally applicable to chronic disease.[2]

In this chapter, the relationship between dietary fiber and diverticular disease will be considered from four different viewpoints.

1. Is the prevalence of diverticular disease related to the intake of dietary fiber?
2. Is there physiological and pathological evidence to suggest that it is both reasonable and predictable that a reduction in fiber intake could produce changes of colonic function resulting in the development of diverticular disease?
3. Do fiber-depletion studies in animals confirm these predictions?

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4. What is the effect of increasing fiber intake in subjects who already have diverticular disease? If a lack of dietary fiber is important in the production of the disease process, will additional fiber have a therapeutic effect?

II. FIBER INTAKE AND THE PREVALENCE OF DIVERTICULAR DISEASE

The relationship between the prevalence of diverticular disease and fiber intake has been studied in three ways. The incidence of diverticular disease in various communities throughout the world consuming diets with very different fiber values has been compared. The historical change in the prevalence of diverticular disease within a given community and the change in fiber intake of that community over the same period of time has been studied. Finally, the fiber intake of individuals within a given community has been assessed and the presence or absence of diverticular disease determined.

A. Geographical Distribution

Painter and Burkitt's[3] data from many different sources indicate that diverticular disease is almost unknown in sub-Saharal Africa, apart from European communities, and is uncommon in the Indian subcontinent, the Middle East, the Far East, and South America. This contrasts sharply with the very high incidence in much of Europe and North America and appears to indicate that the prevalence of diverticular disease is closely related to economic development. Developing countries tend to eat a traditional cereal-based staple diet rich in fiber, whereas more economically advanced countries eat highly refined and fiber-depleted foods. They suggested that it took about 40 years for a community to develop a high prevalence of diverticular disease after departing from its traditional eating habits.

This view is supported by reports that diverticular disease has recently become more common in Japan[3] and also in the urban South African population. For many years diverticular disease was practically unknown to the clinicians, radiologists, and morbid pathologists at Baragwanath Hospital, Johannesburg. Segal *et al.*[4] have recently reported increasing numbers of Africans with diverticular disease at the same hospital. The patients were relatively young (mean age 48.9 years), urbanized, eating a low-fiber diet, and tending to have sedentary occupations. They had enjoyed a "Western" life-style for at least 20 years.

The incidence of diverticular disease in Europe varies considerably. The prevalence in Finland is lower than in Sweden.[5,6] In Scotland the number of cases admitted to hospital is double that for England per 100,000 population,

and in the north of Scotland the rate is double that for Scotland as a whole.[7] The prevalence in parts of Southern Europe appears to be low.[3] These differences within Europe are, to a certain extent, paralleled by differences in fiber intake.[8,9]

Unfortunately, much of the available data has, of necessity, been anecdotal and based on clinical material rather than specific epidemiological surveys. Since the actual dietary fiber intake of many communities is still unknown, such evidence is open to a number of criticisms.[6]

Data from hospital records, be they from post-mortems, barium enemas, or the clinical diagnosis of patients, may not reflect the true incidence of a disease within the community, particularly in areas where medical services are sparse and rudimentary.

Routine barium enema studies,[5,6,10–12] autopsy studies,[8,13,14] and barium follow-through studies[5,15] all demonstrate that the prevalence of diverticular disease in western communities increases rapidly with age from approximately 20% in the sixth decade to approximately 40% in the eighth decade. Marked differences in age distribution exist between the populations of economically developed and underdeveloped countries. Without age-specific prevalence data, the real incidence of the disease may be seriously distorted. For example, Antia and Desai[16] reported a prevalence of diverticular disease of 23.6% in Bombay for persons over the age of 70, higher than other figures from India, although the fiber intake in this community may have been abnormal.[17] The difference between countries, however, appears to be so great that it cannot be accounted for by differences in age distribution.[18]

Some racial groups may be more prone to the condition than others. However, black Americans of African origin have shown an increased incidence of diverticular disease as their maize consumption has declined. Their prevalence of diverticular disease was 30% less than Caucasian compatriots in 1937[19] but is now comparable.[20] Similarly, the prevalence of diverticular disease among Japanese who have emigrated to Hawaii is higher than in Japan.[21] Racial factors do not appear to be as important as those of environmental origin. Although the geographical prevalence of diverticular disease correlates quite closely with fiber intake for most countries, both the Masai tribe in Africa and the Eskimo, who eat most unusual diets, appear to be exceptions to the general rule. It has been suggested that the Eskimos eat a large amount of animal fat, skin, and hair with their meat, which acts as "animal fiber." They tend to have a moderately fast oral–anal transit time and pass soft motions.[15]

Although the geographical evidence has been widely criticized since it was originally published by Painter and Burkitt,[1] the general conclusion that those communities on high-fiber diets have a low prevalence of diverticular disease has not been seriously challenged by substantial contradictory evidence. This does not prove that a low-fiber intake is of etiological importance. Differences in fiber intake are associated with differences in other dietary components such

as fat and meat.[22,23] The fiber content of a diet is also indicative of the economic development of a community, differences in standards of public health and personal hygiene, social customs, life-style, and so on.[24–27]

B. Historical Changes in Prevalence

The prevalence in diverticular disease in Western societies appears to have increased greatly over the last 100 years. Painter has made a detailed study of the British and American literature and has argued convincingly that the disease has changed, within the space of a century, from a rare pathological curiosity to a major medical problem and the most common colonic disorder.[3,28]

Certain difficulties are inherent in this type of analysis, especially when the diagnosis is usually made by barium enema, a technique not available to earlier clinicians. It is salutory to note that two early German autopsy series by Graser in 1899 and Sudsuki in 1900 found the prevalence of diverticular disease to be very high (64% and 37.5%, respectively).[5] Similarly, Mourges in 1913 found diverticula in 30% of 100 consecutive autopsies on aged subjects.[8]

It has been suggested that the dietary fiber intake in Britain has declined over the period in which the disease has become more common. A reduction in fiber intake occurred between 1860 and 1880, associated with changes in milling technology.[3] Painter and Burkitt argued that this was responsible for the increasingly common appearance of diverticular disease 40 years later. Southgate and Bingham[29] have calculated the fiber intake from food-supply data and have found there has been very little change between 1880 and the present (24 to 21 g/day). Since 1880, the daily intake of cereal fiber has fallen from 12 to 8 g but consumption of vegetable fiber has increased. However, during World War II and until 1953, fiber intake rose to nearly 40 g/day. The consumption of cereal fiber particularly increased. During the period 1940–1953, the increase in mortality from diverticular disease seen in Britain during the 20th century was halted.

The historical correlations between fiber intake and diverticular disease have been hotly debated and cannot be regarded as proven.[25,27,30] Historical considerations are of limited value, as many other factors of possible etiological significance have changed over the same period.

C. Comparisons between Individuals in a Single Community

Epidemiological studies within a single community are likely to be much more specific than larger scale studies in determining whether the prevalence of diverticular disease is related to fiber intake.

Manousos and colleagues in Athens[31] compared 59 patients with diverticular disease with three age- and sex-matched controls for each patient. They found the disease occurred most frequently in those who were prosperous (2.8

times more) and lived in urban areas (3 times more). There was less diverticular disease in the poorer rural community. They arbitrarily divided subjects into those with high- and low-cellulose consumption. Unfortunately, this is unlikely to provide an accurate index of dietary fiber intake. There was no significant difference in prevalence between two cellulose groups. This was surprising as they claimed that the prosperous urban community with a high prevalence of diverticular disease had a much more Westernized diet than the rural community. They have subsequently reported that the transit time was faster and daily stool weight heavier in the rural population.[32] This strongly suggests that their fiber intake was greater than in the urban areas.

Brodribb and Humphreys[33] compared the crude fiber intake of 40 patients with symptomatic diverticular disease and 80 age- and sex-matched controls in Reading, England. The mean crude-fiber intake for the patients with diverticular disease was 2.6 g crude fiber per day, while that of the controls was 5.2 g. Fiber intake was determined by diet history. This study suggested that a low-fiber intake increased the risk of diverticular disease, but it was open to a number of criticisms. The patients with diverticular disease had symptoms and may have altered their diet after the development of the disease. The selection of the control group could have included some subjects with an abnormally high fiber intake. Unfortunately, dietary fiber values were unavailable at the time and so only crude fiber could be determined. The results of this study indicated that more detailed research was required.

Such a study, of two groups aged 45 or over, has recently been completed at Oxford.[34] The first group was broadly representative of the general population and comprised 264 subjects from the lists of local general practitioners. The second group comprised 56 symptomless members of the Vegetarian Society of the United Kingdom, living in southern England. Of these, 12 had been vegetarians since childhood, 14 for more than 25 years, and the remainder for at least 10 years. The dietary intake of each subject was determined by a comprehensive questionnaire validated by 3-week diaries. The presence or absence of symptomless diverticular disease was determined using a barium follow-through technique.[35]

The total dietary fiber intake of the vegetarians was much greater on average than that of the nonvegetarians (41.5 and 21.4 g/day). Diverticular disease was consistently found more frequently in the nonvegetarians (see Table 1). Vegetarians with diverticular disease appeared to have a lower mean intake of cereal fiber than those unaffected by the disease.

The prevalence of diverticular disease increases with age. Subjects 60 years or over with diverticular disease also had a lower total mean fiber intake than those unaffected in both vegetarian and nonvegetarian groups (see Table 2).

The difference in fiber intake was chiefly accounted for by difference in cereal fiber consumption in both vegetarians and nonvegetarians. The differ-

Table 1. Prevalence of Diverticular Disease in Nonvegetarians and Vegetarians by Age and Sex

Subjects	45–59 yr		Over 59 yr	
	Number studied	Number with diverticular disease	Number studied	Number with diverticular disease
Males				
Nonvegetarians	62	19 (31%)	56	21 (38%)
Vegetarians	14	2 (14%)	8	1 (13%)
Females				
Nonvegetarians	82	17(21%)	64	31 (48%)
Vegetarians	19	0	15	4 (27%)

Table 2. Mean Fiber Consumption of 100 Nonvegetarians and 23 Vegetarians Aged 60 yr or over with and without Diverticular Disease[a]

Type of fiber	Nonvegetarians		Vegetarians	
	With diverticular disease (n = 51)	Without diverticular disease (n = 49)	With diverticular disease (n = 5)	Without diverticular disease (n = 18)
Total dietary fiber	19.5 ± 6.6	22.7 ± 8.6[b]	27.7 ± 9.5	42.7 ± 9.9[d]
Cereal fiber	6.5 ± 5.0	9.3 ± 7.1[c]	10.9 ± 7.2	18.0 ± 6.3[e]
Vegetable fiber	9.7 ± 3.8	9.4 ± 5.3	7.8 ± 4.4	13.9 ± 4.7[f]
Fruit fiber	2.3 ± 1.7	2.6 ± 2.1	8.7 ± 2.8	9.2 ± 4.0

[a]Values are given in g ± SD.
[b–g]Differences between subjects with and without diverticular disease are as follows: [b]t = 2.11, p = 0.037; [c]t = 2.31, p = 0.023; [d]t = 3.03, p = 0.006; [e]t = 2.16, p = 0.042; [f]t = 2.56, p = 0.018.

ences in fiber intake between those with the disease and those without was much greater among the women than the men, and was also much less obvious among younger subjects. In fact, the younger nonvegetarians with diverticular disease had a greater mean vegetable fiber consumption than those unaffected.

Information collected in this study was of present dietary habits, but an attempt was made to assess whether these were stable eating patterns throughout adult life. When only those subjects with the most stable diet were studied, the results were similar.

This study has demonstrated a relationship between symptomless diverticular disease and the consumption of dietary fiber. Furthermore, fiber of cereal origin appears to be the most important component of dietary fiber for protection against diverticular disease.

III. DIVERTICULAR DISEASE: PATHOGENESIS AND THE EFFECT OF FIBER

A. Pathogenesis

The pathological changes that occur in the sigmoid colon in diverticular disease have been known for many years.[36] The colon is narrow and contracted, with thick walls and redundant mucosa. The diverticula are acquired mucosal hernias, usually occurring where the bowel wall is weakened by penetration of blood vessels.[14,37] Early in their development diverticula, like other hernias, are reducible[8] and may not be found in the resected or postmortem specimen even though they have previously been demonstrated by barium enema.[38]

The teniae coli are thick and appear contracted, bunching up the pericolic tissues and the appendices epiploica, creating redundant folds of mucous membrane, and partially obstructing the lumen internally.[39–41] The circular muscle is thickened and corrugated, giving a characteristic appearance.[8,38] This thickening does not appear to be due to true cellular hypertrophy or muscle cell hyperplasia. Morson[38] concluded that the muscle abnormalities are important in the pathogenesis of diverticular disease and that pulsion probably plays a major role in the formation of the diverticula.

It has been demonstrated that abnormally high intraluminal pressures occur within the sigmoid colon in diverticular disease.[42,43] Cineradiography showed that this was due to closed segments developing along the bowel as the circular muscle contracted. Any further contraction increased the tension of the wall of the closed segment and rapidly increased intraluminal pressure with peaks of up to 100 mm Hg. These high pressures appeared to act as a pulsion force for mucosal herniation.[44] It was observed as long ago as 1926 that diverticula could appear and increase in size as the sigmoid colon contracted.[45]

Not all patients with diverticula show the muscle changes. Recently it has been reported that many patients with asymptomatic diverticular disease do not show abnormally high intraluminal pressures.[46] It is possible that the muscular abnormalities are reversible and that the disturbance in motility is only present at certain stages of the disease process.[47]

Diverticula formation appears to depend on two processes: the generation of high intraluminal pressures acting as a pulsion force and the inability of the tissues to resist that force, resulting in mucosal herniation.

B. Effects of Dietary Fiber on the Normal Colon

It has been known since Hippocrates that fiber-containing foods increase daily stool weight. Normal daily wet stool weight varies from approximately 100 g in the United Kingdom, with its low-fiber diet, to 500 g in rural Uganda.[48] Fiber-feeding studies demonstrate that fiber from different sources

differs in its ability to increase stool weight, and that cereal fiber in the form of bran increases stool weight more than most other fiber sources.[49] This may be related to the fact that colonic bacteria digest bran less readily than most other types of natural fiber.[50] Stool-weight response to bran varies with its particle size[51] and from one individual to another. Most feeding experiments suggest that for every gram of extra cereal fiber consumed each day, mean wet stool weight increases from 3 to 9 g daily.

Although substantial increases in dietary fiber intake have only minimal effects on the water content of the stool,[52] the effect on the consistency of the stool is usually obvious. The low-fiber stool is compact and has the consistency of firm clay, whereas the high-fiber stool is soft, gelatinous, and easily deformable. This change in consistency has not been adequately explained but may be partly due to entrapped gas.[53,54]

The effect of dietary fiber on oral–anal transit time has been well documented. Transit is slow on a low-fiber diet and accelerates on a high-fiber diet. Not all individuals on a low-fiber diet have a slow transit time, however. Studies using a continuous marker technique found that transit times tend to become increasingly unstable on a low-fiber diet.[55]

Daily stool weight seems to be related to transit time[32,48,56,57] and this gives some indication of the total amount of fecal material passing through and filling the colon. Colonic filling is extremely difficult to assess accurately, as transit time may vary along the bowel, and water will be absorbed, fiber digested, and bacterial and epithelial debris increased. Furthermore, the left colon is emptied to a varying extent with defecation.[58] There does not appear to be a precise regulatory mechanism modifying transit time with variations in fecal bulk. Without such a mechanism, periods of underfilling of the colon are likely on a low-fiber diet.

Colonic filling has been studied radiologically[59] using a barium follow-through technique. The descending colon was commonly empty and displayed the greatest range of filling. Subjects with the irritable bowel syndrome were more likely to have a partially empty descending colon, and the radiopaque material was broken up into ball-like masses of high radiodensity, suggesting that there was less fecal material to dilute it and that the feces were hard and more likely to form fecal plugs.

Although major differences in fecal flora have been reported between Western communities and those in developing countries[60,61] and also between similar communities eating high- and low-fiber diets,[62] it is not known whether these differences in flora are due to the differences in fiber content. Short-term studies do not show a marked effect by fiber feeding on fecal flora.[63] A high-fiber diet may increase the relative number of anaerobes to aerobes.[52] Similarly, a fiber-free diet increased the relative aerobe population.[64] The ecology of the fecal flora remains a most difficult field for investigation, but little evidence exists that alteration in fiber intake results in any striking qualitative changes

in the bacterial population that might exert a profound influence on colonic function.

The chemical composition of the feces varies with fiber intake. Short periods of fiber feeding resulted in an increased daily output of fecal fat, nitrogen, and calcium. The 24-hr output of fecal bile acids was also increased, but as fecal weight increased more, the concentration of bile salts decreased. Total output of sodium, potassium, magnesium, and chloride increased, but only the concentration of sodium increased significantly. Total volatile fatty acid output also increased, but the concentration did not change significantly.[65] It has been suggested that changes in the electrolyte concentration of the intraluminal contents may affect intestinal motility.[66] Eastwood[67] and Goy *et al.*[68] reported that the fecal content of potassium, calcium, and magnesium cations were lower in patients with diverticular disease than in healthy young adults. There was an inverse relationship between the postfood motility index and fecal magnesium and calcium content. The lower the cation content, the higher the index. It is possible that the cation content of the feces may be an indirect indicator of the fiber content of the diet. Volatile fatty acids have been thought to stimulate colonic function,[69] and bile salts also have an effect.[70]

It appears unlikely that the bacterial changes occurring with a fiber-depleted diet could cause diverticular disease. Possibly, chemical changes in the intraluminal contents of the bowel could stimulate motor activity. Both bile salts[30] and electrolyte changes[66] have been considered. The most serious objection to any biochemical explanation of the pathogenesis of diverticular disease is that the disease apparently can develop and progress in a bowel that has been permanently removed from the fecal stream by a defunctioning colostomy[71,72] or for use as an esophageal replacement.[73]

C. *Dietary Fiber Depletion*

The most striking difference in the feces produced by high- and low-fiber diets is in its physical properties. The defunctioned bowel distal to a colostomy is known to become narrow and contracted[74] and it is possible that underfilling of the colon with a fiber-depleted diet over a long period of time would produce a similar narrow, contracted bowel. On a low-fiber diet, the colon also has to propel small, firm fecal masses. The narrowing of the bowel with redundant folds of mucosa would increase resistance to movement, and this would result in compensatory thickening of the muscle layers. The colon appears narrow radiologically in both diverticular disease and the irritable bowel syndrome. This has been confirmed when measuring the diameter with inflatable balloons.[75]

Almy[76] observed that La Place's law may apply to intraluminal pressure within the bowel. The narrower the bowel lumen, the higher the intraluminal pressure will be for a given tension in the wall. Closed segments of bowel

observed by Painter and colleagues[44] were formed more easily in the narrow, contracted bowel with redundant mucosa. The presence of hard plugs of feces would further aggravate the situation. A low-fiber diet could, therefore, be expected to produce maladaptive changes in the colon resulting in high intraluminal pressures. Patients with diverticular disease show an inverse relationship between transit time and intraluminal pressure.[77] Those patients with a fast transit, and therefore the least fecal filling, had the highest pressures.

If underfilling of the colon is an important etiological factor in diverticular disease, it seems illogical to treat the condition by a proximal defunctioning colostomy. Considerable clinical evidence shows that such a colostomy, whether temporary or permanent, does not help to control the disease process.[78–81] Bolt and Hughes[82] compared the results of colostomy with simple laparotomy without colostomy for acute diverticulitis. They concluded that a colostomy not only was ineffective but allowed contraction of the affected bowel, increasing the risk of inflammatory complication. Defunctioning the bowel also seems to increase the muscular abnormality histologically.[8]

IV. FIBER DEPLETION STUDIES IN ANIMALS

Lubbock *et al.*[83] found that rats fed on a low-fiber diet, simulating that of the working-class community of Peterhead, developed diverticula[84] of the colon. This occurred only in older rats and was less common in those that were given supplementary greens and milk. Large diverticula were noted in three elderly rats fed on a high-fat, low-fiber diet for 90 weeks or more.[85] Morgan and Ellis[86] fed black and white Lister rats a low-fiber diet for 50–70 weeks without producing diverticula, though the colon was invariably contracted and contained little food residue. Carlson and Hoelzel[87] carried out extensive lifespan studies on Wistar rats. Diverticula of the proximal colon developed in 57% of the rats over 100 weeks old which were fed a low-residue diet, and they all had contracted colons not atypical of the muscular changes of human diverticular disease. The addition of bulk in different forms to the diet resulted in a lower prevalence and at an older age. Only 1 of 25 rats over 100 weeks old in whom the diet was supplemented with 5% psyllium seed husk developed diverticula. A vegetarian diet gave an incidence of 10% (2 of 20). The highest incidence of diverticula was in those rats initially fed a high-bulk diet and then changed to a low-residue diet before they were 30 weeks old; 8 out of 10 rats over 100 weeks old developed diverticula.

The rabbit colon is somewhat more similar to man's, as it has teniae coli. The effect of a low-fiber diet on these animals has been studied for periods of 4 months. On a low-fiber diet, the rabbits became constipated, with a marked reduction in fecal output; the colon became thick and contracted. Areas of

hypersegmentation occurred after injection of prostigmine. On measuring intraluminal pressure, the colonic motility index increased significantly with a low-fiber diet.[88] The mean diameter of the bowel of control rabbits increased from 1.7 to 2 cm proximally and 1.3 to 1.7 cm distally, whereas those on a low-fiber diet narrowed from 1.9 to 1.33 cm proximally and 1.5 to 1.0 cm distally. Histology of the colon showed some irregularity of the circular muscle similar to human diverticular disease.[89]

The rat and the rabbit are rather poor experimental models for human colonic disease. Recently, fiber-feeding experiments have also been carried out with stump-tailed monkeys, which eat an omnivorous diet more similar to that of man.[90] Six stump-tailed monkeys were preconditioned to sit in restraint chairs. The sigmoid colon was chronically instrumented with an extraluminal strain gauge force transducer, a bipolar serosal electrode, and a Thomas cannula to provide access for determining luminal pressure with a perfused open-tipped catheter. Diets containing 0, 5, 10, 15, and 20 g dietary fiber daily were fed in varying sequences, each for periods of 3 weeks, and observations were made during the last week of each diet. Fecal stool weight increased predictably as the fiber content of the diet increased. Colonic intraluminal pressure, represented as a motility index, increased significantly when feeding low-fiber diets, but the electrical spike discharge activity and the contraction frequency of the colon circular muscle were not affected. This study suggested that a low-fiber diet had a rapid effect in increasing intraluminal pressures, and that it did so not by increasing muscular activity in the wall, but by changing the fecal content within the lumen.

While it would be wrong to assume that the behavior of the animal colon is necessarily similar to that of the human bowel, animal experiments do support the view that fiber intake is an important factor in determining colonic function, and that a low-fiber diet produces adaptive changes that may predispose to diverticula formation.

V. TREATMENT OF DIVERTICULAR DISEASE WITH DIETARY FIBER

Half a century ago, a high-fiber diet was recommended for both diverticular disease[91] and the irritable colon syndrome.[92] A low-residue diet was known to cause problems for the colon.[93] However, a low-residue diet became increasingly fashionable for patients with diverticular disease.[81,94–97] The efficacy of such a diet has never been proven[3] or shown to arrest the development of diverticula or prevent complications.[98] There is no evidence that pips or seeds within diverticula cause diverticulitis.[99] Indeed, some evidence shows that a low-residue diet causes symptoms to persist. Eusebio and Eisenberg[100] found that patients who followed their doctors' orders and ate a low-residue diet had

far more persistent symptoms than those who failed to restrict their diet. In the last 10 years, a number of clinical trials have been reported in which patients with diverticular disease have been placed on a high-fiber diet.

A. Treating Symptoms

Painter and his colleagues[101] treated 62 diverticular disease patients with a high-fiber, low-sugar diet, and sufficient additional bran to ensure that their bowels were open once or twice daily without straining. Fifty-two percent of symptoms were eliminated and a further 36% relieved after a mean follow-up period of 22 months. In another study, 48 patients with symptomatic diverticular disease were treated with a high-fiber crispbread (approximately 4.5 g dietary fiber daily). In 69% of patients, pain was effectively controlled, and in 71% all symptoms were satisfactorily treated. Fourteen patients were subsequently changed to a low-fiber crispbread but, as three deteriorated rapidly, a crossover study was abandoned.[102] Hodgson[103] reported that six patients given methylcellulose daily became symptom-free within 6 months.

Parks[104] treated 40 patients with diverticular disease with a high-fiber diet and bran supplements. Improvement in bowel function was found to be the most noticeable benefit. He emphasized that abdominal discomfort, distension, and flatulence may be accentuated at first, but this seldom lasted more than 3–6 weeks and was less troublesome if fiber was increased gradually.

Srivastava and colleagues,[105] using a symptoms score to compare therapeutic efficacy, reported that bran (20 g per day) was more effective in both the relief of pain and the overall improvement of the symptoms than sterculia. If the antispasmodic alverine citrate was added to sterculia, it was similar in effectiveness to bran. In 20 patients, the total score was reduced to approximately one-quarter of its initial value after bran. Pain scores were reduced to one-third of their pretreatment level, with discomfort reduced to trivial levels in 80% of patients.

Bran in tablet form, sterculia with alverine citrate, and a high-residue diet (unspecified) were compared in a crossover study by Taylor and Duthie.[106] Twenty percent of patients became symptom-free with a high-residue diet, 40% after sterculia, and 60% with bran tablets. The increase in mean stool weight was much greater with bran than with the high-residue diet (42 and 23 g/day), suggesting that the latter contained considerably less fiber than the bran tablets.

In a preliminary report, Tarpila and Miettinen[107] described a year's treatment of 26 patients with diverticular disease. Half had a high-fiber diet of bran porridge and whole-grain zwiebacks and the others a low-fiber porridge and zwiebacks. After an initial decline, the clinical condition was subjectively improved by the high-fiber diet; this was associated with a regular bowel habit and a significant increase in stool weight.

Brodribb and Humphreys[108] studied 40 patients with symptomatic diverticular disease. After taking 3 heaped tablespoons of bran daily for 6 months, 33 patients were extremely satisfied with their symptomatic relief. Five patients still had some troublesome symptoms and two patients showed minimal improvement. Although patients in this series initially complained of many symptoms, after the bran regimen 60% of all symptoms were abolished and a further 28% relieved. All types of abdominal pain were improved; generalized lower abdominal pain showed the greatest improvement, with 76% of patients pain free and 20% relieved. Intestinal colic was abolished in 61% and relieved in the remainder. Of those who initially complained of left iliac fossa pain, half obtained complete relief and the remainder partial relief. Of patients with right iliac fossa pain, 54% were free of it after the bran program and 40% were improved. In those patients who still suffered from pain, it was trivial in all but four. Straining on defecation was abolished in 69% of patients. Many patients initially passed either liquid or fairly hard motions, some alternating between the two. Bran effectively thickened liquid motions and softened hard motions. Similarly, patients with very frequent bowel actions defecated less often, and constipation was also relieved. Only 2 out of 12 patients who initially took laxatives continued to do so with bran.

In a double-blind control in Oxford,[109] patients with large-bowel symptoms and radiological evidence of diverticular disease (but without evidence of complications or of other colonic disorders) were given nine crispbread biscuits to eat daily for 3 months. Each patient completed a detailed symptomatic questionnaire on dyspeptic symptoms (nausea, vomiting, heartburn, eructation, abdominal distension), abdominal pain, and symptoms of "bowel dysfunction" (passage of excessive wind per rectum, the need to strain, anal pain on defecation, abnormal frequency of evacuation, abnormal consistency of the motion, presence of blood or mucus, feeling of incomplete emptying of the rectum after defecation, the use of laxatives). Each symptom was scored 0–6 for frequency and 0–6 for severity on a standard descriptive scale; the score for pain was doubled to give it weighting similar to the other two symptom groups. The pharmacist supplied patients with either low-fiber wheat or high-fiber bran crispbread according to a code (randomized in groups of six). Nine wheat crispbreads supplied approximately 0.6 g and nine bran crispbreads approximately 6.7 g dietary fiber daily. The biscuits were similar in shape and appearance and were supplied unlabeled. The change in mean symptomatic scores for the two groups over a 3-month period are shown in Figs. 1 and 2. The change of total symptom scores showed a highly significant difference (high fiber, 34.2 to 8.1; control, 42 to 35.1). The difference in change of pain score was significant (high fiber, 11.1 to 1.1; control, 12.7 to 10.2). The changes in dyspeptic and bowel function scores did not reach statistical significance. Two patients in the control group required further treatment during the 3-month period, but none in the high-fiber group. Initially, a strong placebo effect appeared, but it

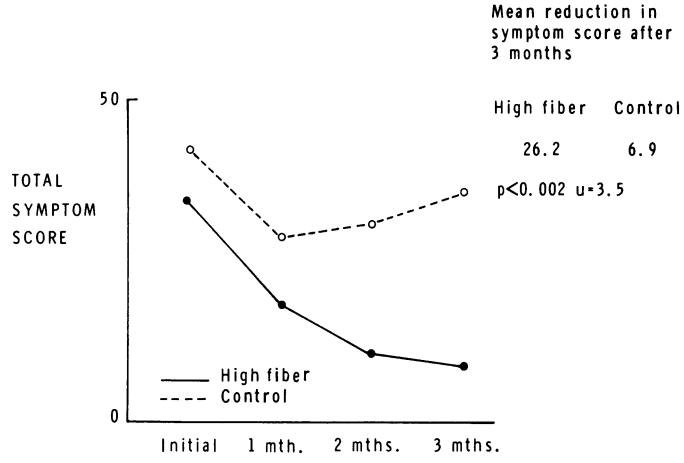

Figure 1. Changes in mean symptom score over 3 months for high-fiber and control groups.

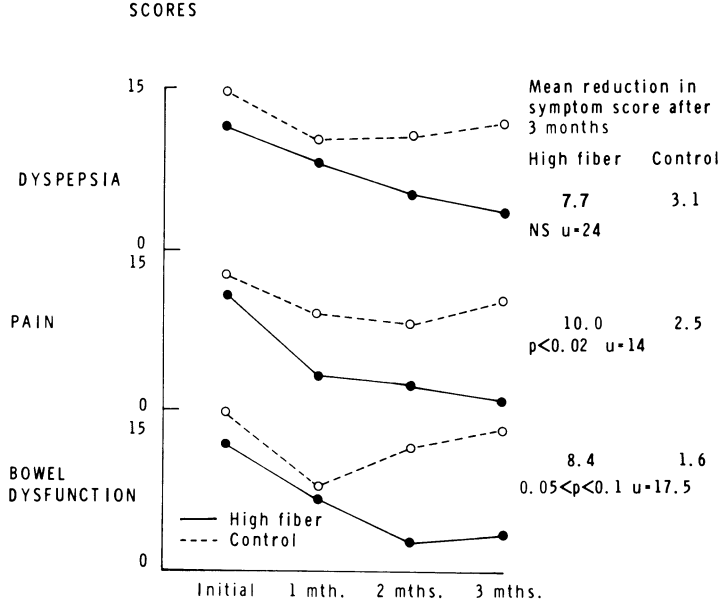

Figure 2. Changes in mean sympton score over 3 months for high-fiber and control groups for dyspepsia, pain, and bowel dysfunction symptoms.

was gradually lost after the first month. The effectiveness of treatment with a high-fiber diet increased with time, and might have been greater had the patients been studied for a longer period.

Weinreich[15] carried out a control trial with 105 patients suffering from symptomatic diverticular disease. The patients were randomized to treatment with either unprocessed bran, hyoscyamine, or placebo and reassessed after 3, 6, and 12 months. At 3 months, bran was significantly better than placebo by clinical assessment, while no difference was found between hyoscyamine and placebo. At 6 months, the therapeutic value of bran continued to increase, and after 1 year the group on bran still showed the greatest improvement, though even the placebo group had many fewer symptoms than at the start of the trial.

A number of similar studies using bran have been conducted with patients with the irritable bowel syndrome. Piepmeyer[110] found that only 3 of 26 patients treated for 4 months failed to show satisfactory improvement. Soltoft and colleagues[111] carried out a randomized double-blind trial with 52 patients and found no significant improvement after 6 weeks on bran. This was at variance with most other studies and has been criticized on grounds of the small particle size of the bran,[112] the effect of cooking and compressing the bran,[113] and the short trial period[109] (many patients suffer from abdominal distension and flatulence in the first few weeks after suddenly starting a high-fiber diet). Patients continued to use irritant purgatives. Manning and Heaton[114] also noted that no evidence was presented to show that the control and treatment groups were comparable.

A similar study was made of high- and low-fiber diets given to 26 patients with the irritable bowel syndrome in Bristol. Those on the high-fiber diet experienced a significant reduction in frequency and severity of pain after 6 weeks.[115] There was also an objective reduction in colonic motor activity.

A direct comparison between medical and surgical therapy is impossible as it is likely that only subjects with severe symptoms who have failed to respond to simpler measures are subsequently subjected to an operation. It is, however, worth noting how unsatisfactory surgical treatment has been. Of 103 patients undergoing elective resection at St. Mark's Hospital for uncomplicated symptomatic diverticular disease, one-third continued to have symptoms postoperatively.[116] In another series of 100 consecutive patients with diverticulitis reviewed 5–15 years after laparotomy, 59% treated by resection remained symptom-free compared with 58% treated by laparotomy alone without resection.[82]

Of 39 patients with symptomatic uncomplicated diverticular disease treated by colonic resection at St. Bartholomew's Hospital, London, only 14% were subsequently symptom-free.[117] Of 25 patients who had had a distal colomyotomy for uncomplicated diverticular disease, 40% had recurrent symptoms 3–7 years later.[118]

It is concluded that a high-fiber diet is an effective treatment for symp-

toms in uncomplicated diverticular disease. The maximum therapeutic advantage is not achieved until approximately 3 months after starting treatment; indeed, during the first few weeks on a high-fiber diet, patients frequently complain of increased abdominal distension and wind.

B. Preventing Complications

No data are available to confirm whether a high-fiber diet protects patients with diverticular disease from developing inflammatory complications. Anecdotal evidence suggests that fewer patients develop complications while on a high-fiber diet compared with the previously recommended low-residue diet, and patients with diverticulitis rarely give a history of high fiber intake. It has been suggested that inflammatory complications are caused by a micro- or macroscopic perforation of a diverticulum.[119] Such an event might be expected to occur as a result of persistent high pressures within the bowel. A reduction in pressure might, therefore, be expected to reduce the risk of diverticulitis. A number of studies have been carried out to assess the effect of a high fiber intake on intraluminal pressure.

Hodgson[103] found a significant reduction in colonic motility index at the rectosigmoid junction in 6 diverticular disease patients after they had taken methylcellulose for 6 months. Findlay and colleagues[56] studied 7 patients before and after 4 weeks of bran consumption (20 g/day). Basal, postprandial, and postprostigmine motility indices were reduced after bran, but only the latter was statistically significant. Kirwan and colleagues[120] studied 13 patients. After bran, the basal colonic motility index was reduced to only 38% of its initial level. After food it was only 40% and after neostigmine 56% of its previous value. All three reductions were statistically significant.

Smith *et al.*[121] compared the colonic motility index of 50 patients with diverticular disease before and after surgery. Sigmoid colectomy was carried out on 25 patients and myotomy on the other 25. Postoperatively, 5 patients in each group were given 20 g bran daily. The patients were followed up with motility studies at 3 months, 3 years, and 5 years after surgery. There was no reduction in mean motility index after resection. The reduction after myotomy was only transient, returning to preoperative levels after about 5 years. The recurrence of high-pressure activity after myotomy had previously been reported.[122] Five patients took bran regularly after each operation. The motility index was reduced in those who had had a sigmoid resection and remained low in those who had had a sigmoid myotomy. It appeared that increasing the fiber content of a diet was more effective in controlling high-pressure activity in the bowel than either surgical procedure. Srivastava *et al.*[105] compared 10 patients with diverticular disease treated with sterculia to 10 others on sterculia and alverine citrate for a similar 4-week period. While sterculia with alverine cit-

rate resulted in a reduction in colonic motility index similar to that resulting from coarse bran, sterculia alone resulted in an increase in motility index.

Taylor and Duthie[106] carried out a crossover trial on 20 patients with diverticular disease comparing sterculia, a "high-roughage diet" (unspecified), and compressed bran tablets. Patients were given each for a period of 1 month. The percentage of basal recording time showing pressure activity was compared with that before treatment. The bran tablets halved pressure activity time, but the other two treatments had no effect.

Brodribb and Humphreys[108] compared intraluminal pressures in the sigmoid colon of 39 patients before and after 6 months of treatment with bran. The results were analyzed by counting the number of pressure waves of different heights rather than calculating a motility index. The number of pressure waves was markedly reduced, particularly during and after eating. This reduction was maximal for waves of high amplitude. Waves greater than 50 mm Hg were reduced to only 20.6% of the pretreatment number while eating and 17.1% after eating.

Weinreich,[15] comparing bran, hyoscyamine, and placebo for 1 year, also found that the motility index fell significantly with bran and hyoscyamine. With hyoscyamine, the reduction in pressure activity was rapid, but with bran it continued to fall throughout the 12-month period.

It is concluded that bran reduces pressure activity.

The effect of treatment with bran for 6 months on the barium-enema appearance of the bowel was also studied in 33 patients with diverticular disease by Brodribb and Humphreys.[108] The number of diverticula did not change significantly, but colonic spasm was reduced. Patients who initially showed small diverticula appeared to have normal sigmoid colons after treatment.

VI. CONCLUSIONS

Available evidence suggests that subjects on a low-fiber diet are more prone to develop diverticular disease. The known physiological effects of dietary fiber on the colon are compatible with the hypothesis that a low-fiber diet may produce maladaptive changes similar to the pathological features seen in diverticular disease. Fiber-depletion studies in animals support this hypothesis.

When patients with diverticular disease are treated with a high-fiber diet, the symptoms are effectively relieved and the abnormally high intraluminal pressures within the sigmoid colon are reduced.

Present knowledge indicates that dietary fiber is an important factor in the etiology of diverticular disease. The evidence, however, must not be viewed in isolation from reports suggesting other possible factors.

Several possible factors have been suggested which have either been subsequently disproved or for which there are no satisfactory supporting data. These include obesity,[124] venous distension,[125] degenerative changes of colonic muscle,[126] bacteriological toxic damage,[124] colonic distension particularly due to flatus,[127] and the voluntary retention of flatus for social reasons.[26] Constipation with excessive intestinal stasis and fecal loading of the distal bowel was suggested by a number of early writers.[128–130] The incidence of constipation in diverticular disease is, however, no greater than that of the general population,[124] and transit times have been found to be faster than in normal subjects.[131] Barium enemas have seldom shown demonstrable diverticula in patients with large colons and redundant loops of sigmoid colon.

It has been observed in all epidemiological studies that the prevalence of diverticular disease increases progressively with age from the fifth decade onward. It could be argued that the older the subject, the longer an environmental factor, such as a low-fiber diet, operates. Alternatively, the tissues of the bowel will possibly weaken with age, increasing the risk of mucosal herniation.

An association between diverticular disease and varicose veins was reported by Latto *et al.*[132] In a well-controlled study, 73% of 110 patients with diverticular disease had varicose veins compared with 33% of 330 age- and sex-matched controls. An association between diverticular disease and hiatus hernias has been reported by many authors.[133–136] Similarly, an association with abdominal hernias has been reported.[137,138] Brodribb and Humphreys[33] compared 40 patients with diverticular disease with 80 age- and sex-matched controls. Those with diverticular disease showed a significantly greater incidence of varicose veins, hiatus hernias, abdominal hernias, and hemorrhoids. Ten percent of patients had all five conditions and 47.5% had three of the quintet. All five conditions can be regarded as a failure of connective tissue to resist a pulsion force, whether this be exerted across the bowel wall, diaphragm, abdominal wall, venous valves, or anal sphincter.

In those diseases where there is a pathological weak connective tissue, such as the Ehlers–Danlos syndrome, Cutis laxa, or Marfan's syndrome, an abnormally high risk of developing intestinal diverticula, hiatus hernia, hemorrhoids, and external hernias has been reported.[139–142]

Some families are reported to be particularly prone to developing diverticular disease.[143,144] Although families may tend to eat as their parents do,[28] it has also been suggested that in every chronic disease a genetic condition exists upon which environmental variables work.[145] In the classical rat studies of Carlson and Hoelzel,[87] all the rats were the offspring of two males and four females. All the most severe examples of colonic diverticula were found among the 32 offspring of one female. This female was not on a low-residue diet and did not develop diverticula, but she was the only breeding female to have depressions

in the colonic mucosa compatible with the earliest stages of diverticula formation.

In the past, those who believed that diverticula were the result of an excessive pulsion force have been in conflict with those who believed that the bowel was abnormally weak and unable to resist normal intraluminal pressure (the blow-outs versus the drop-outs). Most likely, both factors are interacting. Those people with the greatest inherent weakness of the bowel wall develop diverticular disease most readily and at a younger age, while others may be able to withstand very high intraluminal pressures caused by a fiber-depleted diet and never develop diverticula, even in old age.

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4

Effects of Dietary Fiber on the Structure and Function of the Small Intestine

Clifford Tasman-Jones

I. INTRODUCTION

Because of a suggested relationship between dietary fiber and a number of diseases of the large bowel, most studies have concentrated on the effects of dietary fiber on the function and morphology in the large bowel. However, as large-bowel changes may be the result of reactions taking place farther upstream, there is an increasing interest in the effects of diet on the internal milieu of the small intestine.

The highly dynamic digestive and absorptive activities of the gut lead to a constantly changing physical and chemical environment. Food degradation products, the result of host and bacterial enzyme digestion, meet with the actively regenerating intestinal epithelium. This interacting and constantly changing milieu puts a constant stress on the structure and function of the small intestine.

The light microscopy appearance of the human small bowel shows that the jejunal mucosa in apparently healthy residents from tropical countries has features that would be considered abnormal if seen in residents of temperate climates.[1-3] In the human fetus the jejunal villi are regular and fingerlike. This pattern is maintained throughout life in advanced Western countries. In trop-

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ical areas, within a few weeks, the regular fingerlike villi become broad, developing leaf-shaped forms, and in time, an increasing number of ridges and convolutions.[3] The morphological changes seen in the less well-developed tropical areas have been considered abnormal and the pattern seen in the temperate climate postulated as the desirable morphology. Nutritional deficiencies, particularly protein deficiency, have been suggested as a probable etiology for the changes, but this seems unlikely as many of the people from tropical areas have diets adequate in energy and nutrient content. Further, hypoproteinemia occurring in temperate areas is not associated with changes in the morphology of the small bowel.[4] Recently, Owen and Brandborg[5] observed that healthy vegetarians have leafed and some ridge-shaped villi similar to those seen in the tropical countries; that observation suggests the possibility that the jejunal morphological changes described in both vegetarians and residents of tropical areas are related either to a reduced intake of meat or to a higher fiber diet. What, then, is the more appropriate adult morphology, that seen in the temperate climate with the morphology more closely resembling that of the immature fetus, or the modified morphology as seen in patients in the tropical climates? This question cannot be answered with the present incomplete knowledge.

II. DIETARY EFFECTS ON SMALL-BOWEL STRUCTURE

At birth, young rats have regular finger-shaped small-bowel villi similar but not identical to the villi seen in human infants. As these animals mature on standard laboratory diets, the villi become leaf-shaped and then ridged.[6] In an environment as complex as that existing in the lumen of the small bowel, there are many factors that may influence morphological changes and that may be influenced by changes in morphology.

Fasting and feeding lead to subtle ultrastructural changes. In the hamster, the microvilli on the cells from orally fed animals are approximately 25% longer than those from fasted animals. Other ultrastructural changes distinguish the fasting small bowel from the fed bowel.[7] Intravenously fed rats have an increased microvillous length.[8] The changes of the microvilli would thus seem to be more dependent on the total nutritional status than on the feeding route.

Variations in the composition of orally ingested food substances are associated with variations in small intestinal structure and function. In complete starvation there is mucosal atrophy and reduced intestinal function.[9,10] If the intestinal food load is eliminated but the animals maintained on a normal caloric intake by parenteral nutrition, there is a reduced villous height, a decrease in gut weight, and a reduced disaccharidase activity. The changes are greatest in the proximal small bowel and least in the distal small bowel.[11,12]

When an isolated intestinal loop in an otherwise normally fed animal is infused with glucose, galactose, or sodium chloride there is an increase in villous height in the isolated loop.[13] A chemically defined bulk-free diet is capable of stimulating the mucosa of the small intestine to an adaptive hypertrophy.[14]

The effects of increased food load have been tested by adding bulk to the diet or by altering the load by resection of a portion of the alimentary tract. The addition of an inert bulking agent, kaolin, to the diet does not result in small-bowel hypertrophy.[15]

When there is extensive resection of the small bowel, the increased load of nutrients arriving at the ileum is associated with mucosal hypertrophy and increased glucose absorption.[16] Intraluminal nutrients play a major role in the adaptation of the intestinal mucosa. The adaptation effects may be direct through chemical, physical, and mechanical actions of the food on the mucosa or indirect by stimulation and release of local and systemic hormones, alterations in intestinal flora, and changes in intestinal motility.

In a recent study, I have examined the small-bowel mucosa of developing rats for the effects of some components of dietary fiber on the morphology. I have confirmed the development of leaf-shaped ridging occurring in the mucosal pattern of rats as they mature while fed a normal laboratory diet.

A comparison was made of the jejunal and ileal mucosa in rats on three dietary regimes. The diets were a nutritionally complete fiber-free diet, the same diet with added cellulose, and the same basic diet with added pectin. The rats on a no-fiber diet and a no-fiber-plus-cellulose diet maintained a villous pattern similar to that seen in immature rats. The rats on a pectin diet developed distinct ridging and alterations in the appearance of the mucosa (Figs. 1 and 2). The number of villi present in samples from the jejunum and ileum of these animals was counted under standard conditions by dissection microscopy. There was no difference in the number of villi present between the no-fiber and the no-fiber-plus-cellulose diet, but there was significant reduction in the number of villi in the rats with a no-fiber-plus-pectin diet (Table 1). The removal of fiber from the diet delayed the normal changes seen in maturing rats. The addition of cellulose had no effect in producing these changes, but when pectin was added the usual "maturing" changes in villous shape were observed.[17]

The incomplete state of our knowledge makes it impossible to draw any firm conclusions on the effects of other components of dietary fiber or of the importance of these effects in the pathogenesis of the diseases thought to be due to dietary fiber deficiency.

III. DIETARY EFFECTS ON SMALL-BOWEL MICROBIOLOGY

The complex flora of the intestine is very effectively hidden from observation and sampling, so our understanding of it has remained sketchy and

Figure 1. Scanning electron microscopy appearance of the jejunum of rats after 12 weeks of fiber-free diet.

incomplete. Dramatic changes in diet do stimulate major changes in intestinal flora.[18] Therefore, it is not surprising that different racial groups have differing indigenous gut flora.[19,20]

The gut floral population is influenced by diet. As the breast-fed infant passes to supplementary feeding, the fecal flora changes from a predominantly lactobacillic type to a mixed floral growth. In considering the effects of diet on

Table 1. Number of Villi in Samples from Fixed Positions in the Jejunum and Ileum after 12 Weeks of Dietary Therapy

	Jejunal villi		Ileal villi	
Diet	*N*	SE	*N*	SE
Fiber-free	1769	28	3174	165
Fiber-free + cellulose	1789	49	3467	166
Fiber-free + pectin	1548	47	2802	156

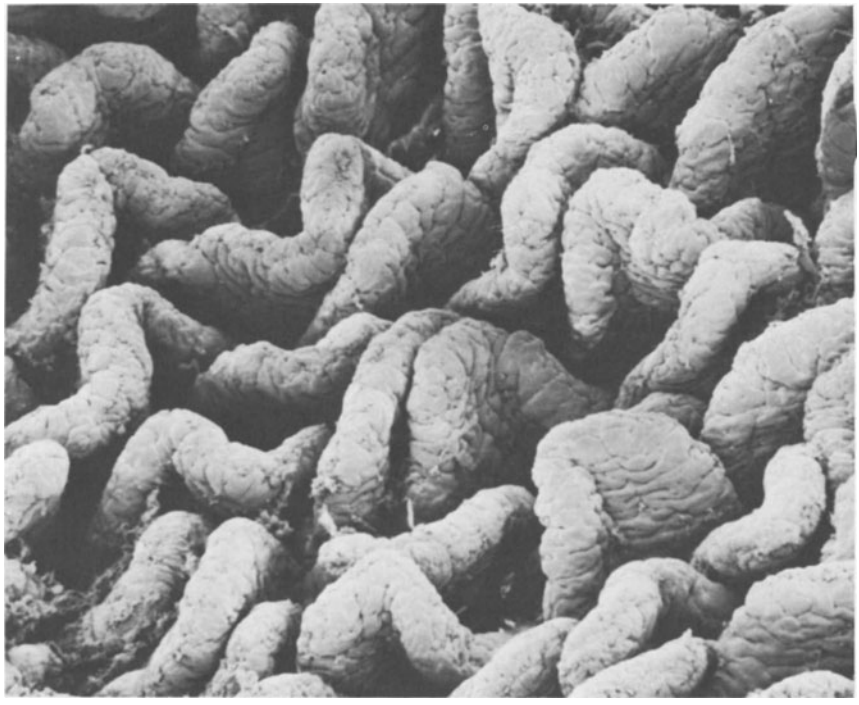

Figure 2. Scanning electron microscopy appearance of the jejunum of rat after 12 weeks of a fiber-free diet to which pectin had been added.

the flora, it is important to realize that each day the human adult secretes at least 100 g of endogenous protein from digestive juices, desquamating epithelial cells, and other intestinal secretions. Thus, irrespective of the diet, the intestinal microbes are never restricted to a purely vegetarian diet.

In an effort to better understand the factors involved in the growth of intestinal flora, mice have been studied in succeeding weeks from birth. In the first week, there is a dominant lactobacillus/streptococcus infestation, which changes to anaerobic spiral microbes, then to facultative anaerobes (coliform and enterococci) and, eventually, to populations of fusiform and spiral-shaped anaerobes. By the fourth week, segmented filamentous microbes appear in the lower small bowel.[21] The successive changes in microbial types parallel the changes in the diet, which indicates that diet is probably an important factor influencing the colonization of the gastrointestinal tract. If mice are starved for 48 hr, a drastic reduction occurs in the number of microbial organisms in all regions.[22]

By the 12th week of our study, the segmented filamentous microbes were

seen in profusion in those rats fed a normal laboratory diet. In spite of intensive search, none were seen in the rats on a fiber-free diet or a fiber-free-plus-cellulose diet. Small numbers were seen in rats on the pectin diet.

IV. RELATIONSHIP BETWEEN INTESTINAL FLORA AND MUCOSAL STRUCTURE AND FUNCTION

Intestinal microflora do affect the rapidly and continuously changing epithelium of the small intestine. If salmonella enteritis is introduced into the small bowel of the mouse, the villi of the duodenum become shorter and flatter than normal.[23]

Comparisons of the jejunal epithelium of germ-free and conventional mice show that germ-free animals have distinctly lower rates of epithelial renewal and a decrease in the number of epithelial cells as compared with the conventional rodents.[24]

Microorganisms adhere to the gut epithelium by three distinct methods. Some adhere by a sticky envelope of acidic mucopolysaccharides. In others, a modified terminal segment inserts into the brush-border membrane of cells. The third method of attachment is by a long filamentous thread.[21] This close association of organisms can affect the superficial brush-border area of the villi, but it is unlikely that these attachments can directly affect the grosser mucosal pattern.

The intestinal brush-border area, composed of microvilli and the associated glycocalyx, is an area important in digestion and absorption. The brush-border enzymes include disaccharidases, peptidases, and phosphatases. Some organisms produce toxic bile-salt deconjugation products which are injurious to the intestinal mucosa.[25] In the blind-loop syndrome, with an increased organism population, there is ultrastructural damage to the villi with reduced disaccharidase activity.[26,27] If chloramphenicol is given to animals with a blind-loop syndrome the disaccharidases return to normal or near normal in a few days.[27] Dietary substances influence intestinal organism composition, which, in turn, determines the chemical environment from bacterial metabolism of bile salts and other substances. Intensive and difficult research will be necessary to unravel these relationships and determine their significance.

Usually, it is thought that the organism concentration in the small bowel is too low and the transit time too short to produce a concentration of toxic substances within its lumen significant enough to cause structural damage. With improving techniques, this should be reviewed. If the current hypothesis that toxic chemicals are almost certainly the result of colonic organism activity, it is likely that these toxins are the cause of the small-bowel structural and functional changes.

The relationship of diet, intestinal flora, and intestinal hormones is com-

plex. In total parenteral nutrition, there is a reduction in microbial flora and a mucosal hypoplasia that is not prevented by cholecystokinin or secretin.[28,29] Dietary fiber may be of special importance in "binding" intestinally active enzymes.

V. SUMMARY

Dietary factors may influence structural and functional changes of the small bowel. Preliminary evidence suggests that components of dietary fiber have specific effects on small-bowel morphology. Further intensive studies, both in animals and in man, will be necessary to clarify the extent, the pattern, and the importance of the fiber-related structural and functional changes.

It seems unlikely that the main structural changes are due to direct contact injury. While it is tempting to relate structural changes in the small intestine to changes occurring in the intestinal flora, focal-induced changes, as in local and systemic hormone production and availability, may be important etiological factors.

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5

Colon Cancer: The Emergence of a Concept

Denis P. Burkitt

I. EPIDEMIOLOGICAL FEATURES

A. Worldwide Distribution

Incidence rates for cancer of the colon are more closely related to the extent of economic development in different countries than are those for any other form of cancer. Highest rates are found in Western countries. For example, age-adjusted yearly rates for men from 30 to 65 years old are, in Connecticut, 51.8 per 100,000; in Scotland, 51.5; and in New York, 45.3.[1] Lowest rates have been reported from Africa, those for Uganda being 3.5; Mozambique, 5.5; and Nigeria, 5.9. Between these extremes are rates for Bombay, India, 14.6; and for Eastern Europe, with Yugoslavia at 20.1 and Bulgaria at 21.0.

Although Japan is a highly industrialized society, incidence rates for colon cancer have been low[1] but they are now rising, particularly in urban communities.

Unlike many other forms of cancer, tumors of the colon are universally rare in Third World countries and do not show the contrasting prevalences in different communities that are observed in the case of tumors of other parts of the alimentary tract, for example, of the esophagus and stomach.[2] Not only do some less-developed countries have a high incidence of such tumors and others a low incidence, but these can vary greatly within individual countries. In con-

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trast, colon cancer uniformly accounts for approximately 2% of all cancer throughout Africa.[3] The lack of any direct or inverse relationship between the distribution of colon cancer and tumors of the upper gastrointestinal tract suggests that they result from entirely different environmental factors.

Although a worldwide view shows that the incidence of colon cancer relates directly to extent and duration of impact by the modern Western style of life, some marked contrasts exist between communities within the sphere of this culture. For example, the risk by Seventh Day Adventists[4] and Mormons[5] of developing colon cancer is approximately 30% less than that of Americans in general. Both Copenhagen Danes[6] and New Yorkers[7] are at approximately four times the risk of rural Finns. Rural communities in North America,[8] Scandinavia,[9] and Poland[1] have been shown to be less at risk than are urban communities.

Incidence changes have followed emigration or cultural changes within communities. The most striking example of the increasing prevalence of colon cancer associated with cultural change is that demonstrated by black Americans. It can be assumed that when their ancestors were brought to America, their patterns of noninfective disease were somewhat similar to those obtaining in rural Africa today. All available reports indicate that 40 and more years ago they suffered much less from colon cancer than did white Americans,[10] although much more than did Africans. At that time, their risk of developing other epidemiologically related diseases such as appendicitis[11] and diverticular disease of the colon[12] was, like the risk of colon cancer, intermediate between that of Africans and that of white Americans. Today black and white Americans are at similar risk of developing all of these diseases.

A particularly well-studied population are the Japanese who emigrated to Hawaii. Within a generation, their risk of developing both polyps and cancer of the colon has changed from a distinct rarity of the former and a relative rarity of the latter to prevalences comparable to those of other Americans.[4,13]

B. Pathological Relationships

1. Polyps

Many authorities[14] believe that in Western countries, most if not all malignant tumors of the colon arise in preexisting polyps. This, however, cannot be the case in developing countries, in which polyps are exceedingly rare and are observed much less frequently than is cancer.[15,16] In all communities studied having low colon-cancer rates, observation showed polyps to be rare, whereas in communities with high rates they are exceedingly common, being reported in up to 25% of adult autopsies.[17]

The epidemiological evidence suggests that the factors responsible for the occurrence of occasional colonic cancers, unassociated with polyps, in rural populations in the Third World differ from those responsible for the increase

in cancer and the massive increase in polyps that are associated with westernization.

2. Appendicitis

This disease is uncommon among populations who have had minimal contact with Western culture. It is one of the first of several diseases, including colon cancer, that emerge or increase in prevalence at varying periods of time after changes in life-style associated with Western culture.[18] The incidence of colon cancer has never been observed to rise significantly until several decades after appendicitis has become relatively common.

3. Diverticular Disease

This disease has always been rare in communities with low incidences of colon cancer. It emerges as a medical problem even later than do tumors of the colon.

4. Bowel Behavior

In all communities studied having high incidences of colon cancer, stool output is small, usually below 150 g/day in young adults and not uncommonly below 50 g in the elderly. In communities at minimum risk, daily stool output commonly exceeds 400 g.

In the former situation, mouth-to-anus intestinal transit times estimated by Hinton's method average about 3 days in young adults and frequently exceed 2 weeks in the elderly. Transit times in young adults in Third World communities is usually under 2 and not uncommonly under 1 day.[19]

5. Diet

The main features that characterize the diets in low-risk communities are high intakes of starchy staple foods retaining their natural fiber content and low consumption of fat, which is mainly vegetable derived. In contrast, not only do the diets in high-risk communities have a lower proportion of carbohydrates, but about half of it is composed of simple sugars rather than of complex carbohydrates (starches), and much of the fiber has been removed. Moreover, much more fat is consumed, mostly of animal origin.

The proportion of energy derived from proteins is similar in the two groups, but it is mainly from vegetable sources in poorer communities and mainly from animals in more affluent societies.

C. Conclusions from Epidemiological Evidence

The first two deductions that must be made from the epidemiological features of colonic cancer are that its incidence is determined more by environmental than by genetic factors, and that the responsible environment is closely

associated with modern Western culture and must consequently relate to man-made changes. The weight of evidence points to dietary habits as being of paramount importance.

II. THE HIGH-FAT, LOW-FIBER HYPOTHESIS

Any hypothesis to explain the causation of a disease is only tenable if it is consistent with the available evidence. The hypothesis outlined below fulfills this criterion. This does not of course confer proof of validity, but it does suggest mechanisms that can be tested and subsequently confirmed or discarded.

Contrasts between the environments characteristic of communities with high the low risks of developing colon cancer are numerous. The feces are, however, the predominant environment to which the site of neoplastic changes, the colonic mucosal lining, is exposed. The nature of feces is determined primarily by the food ingested, so it seems reasonable to search for causes of colon cancer in dietary patterns rather than in other environmental influences.

If, as is now generally accepted, food plays a dominant role in the pathogenesis of this disease, the question must be asked: Are active carcinogens swallowed or are they formed in the colon?

The mucosal surface of the small intestine is over 100 times as great as that of the colon, yet both benign and malignant tumors are over 100 times as frequent in the large as in the small bowel; thus tumor risk relative to mucosal area is more than 10,000 times greater in the large than in the small bowel. Allowing for the fact that large-bowel mucosa appears more likely to undergo neoplastic change, this observation must suggest that the agents responsible for colon cancer are either formed or activated in the gut rather than being consumed in food in an active form and traversing the small intestine without affecting it. The role of bacterial activity in colon carcinogenesis and the effect of diet in modifying both the numbers and activity of fecal bacteria are examined briefly in Chapter 6 of this volume.

Epidemiological evidence suggests that colon cancer risk is directly related to stool pH: the more acid the stool, the lower the risk.[20] Although bacteria are known to alter acidity through fermentation of the fiber that reaches the colon, the changes in diet that most influence the pH of stools have not yet been determined. On the other hand, fat increases the secretion of bile, which contains substrates on which bacteria may act.

Unfortunately, the hypothesis favored by Wynder and Shigematsu,[4] Reddy *et al.*,[7] Hill *et al.*,[14] and others, which postulates that diets rich in fat increase colon cancer risk, has been viewed as contrasting with the concept put forward by Malhotra,[21] Walker and Walker,[22] Burkitt,[3] and others suggesting that adequate dietary fiber may provide protection against development of colonic tumors. These should be viewed as complementary and not as conflict-

ing concepts, since fat may well be causative and fiber protective. Health or illness depends on the balance between factors causative of and those protective against the development of disease.

As previously emphasized, diets rich in fat are almost universally low in fiber and vice versa. Consequently, almost all epidemiological evidence relates such diets to high prevalences of colon cancer. High-risk communities also have a higher intake of animal protein, which must therefore be included as another possible causative factor. The tendency of both fiber-depleted carbohydrates and fat to promote obesity must also be considered, and there is evidence both in human studies and animal experiments that obesity predisposes to the development of cancer.[23]

A. *Consistency of the Hypothesis with Epidemiological Evidence*

The available evidence is consistent with the hypothesis that excessive fat intake may contribute to the cause of colon cancer and that fiber, and cereal fiber in particular, may exert a protective influence. Not only do fruits and leaf vegetables have a low fiber content, but their fiber is relatively low in pentoses, whereas the reverse is true of cereal foods.[24] The pentose fraction of fiber seems to exert the greatest influence in increasing stool bulk, a factor inversely related to cancer risk.

Some studies appear more consistent with the fiber aspect of the hypothesis than with the fat aspect. Copenhagen Danes, for example, have four times the colon cancer risk of rural Finns. They have similar fat intakes, but the Finns consume 80% more fiber, mostly of cereal origin, and consequently pass much larger stools.[6] The same applies to comparisons between New Yorkers and Finns.[7] Fat may well be injurious in all situations, but the protective influence of the Finns' cereal fiber intake may outweigh the deleterious influence of their high fat consumption.

The reduced incidence of colon cancer in vegetarian Seventh Day Adventists is understandable on both low-fat and high-fiber bases, but the similar reduction in Mormons, who are not vegetarians, cannot be related to low fat consumption. It has been suggested[25] that homemade whole-grain bread in their diet may be protective.

Much has been made of the increased fat consumption of Japanese emigrants to America, but less has been written of the comparable, if not greater, reduction in their fiber intake, which may be equally significant.

Numerous experimental studies have demonstrated that fat-rich diets can enhance and that fiber-rich diets can reduce the incidence both of polyps and of cancer of the colon.

It is, however, doubtful whether a demonstrated effect or lack of effect of dietary changes in altering proneness to cancer in rodents receiving subcutaneous injections of 1,2-dimethylhydrazine has relevance to the human situa-

tion. Quite unwarranted extrapolations have been made from such experiments and applied to the totally different human situation.

B. Practical Considerations

Bruce *et al.*[26] claim to have reduced by half the number of mutagens in the feces either by reducing fat intake by two-thirds or by supplementing average Canadian diets with one heaped tablespoonful of bran daily. If these or similar measures do have the same effect, the latter is very much easier to implement. In our present state of knowledge, it seems prudent both to curtail consumption of fat and to increase that of starchy staples retaining their fiber.

The attitude that decries change until a case is proven is both illogical and morally indefensible. Medical history is full of instances in which effective action was taken to reduce the incidence of a disease by avoiding situations known to be associated with it, long before the cause of the disease was known or the mechanisms involved in its causation understood. To retain their lead over other countries in colon cancer incidence, Western countries have only to make no changes in their present life-styles and in their dietary habits in particular.

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6

Experimental Animal Studies in Colonic Carcinogenesis and Dietary Fiber

Hugh James Freeman

I. INTRODUCTION

In many highly industrialized nations, colorectal cancer is the most commonly diagnosed internal malignancy when male and female rates of occurrence are combined.[1-3] In Canada and the United States, in particular, it has emerged as a major cause of cancer mortality and a leading cause of significant morbidity among all types of malignancy.[1,2] In 1977, over 100,000 individuals were diagnosed with large-bowel cancer in the United States alone, and about 50,000 persons died with this malignancy.[1] Clearly colon cancer is one of the most serious problems facing our society. Unfortunately, even fundamental mechanisms involved in its etiology, pathogenesis, natural history, and spread of metastases are not well understood.

While clinical methods of colon cancer detection have improved, the insidious onset of this disease makes early diagnosis very difficult. As a result, only 40% of all colorectal cancers are diagnosed before they spread to regional lymph nodes. Of this group, about 60% survive. With involvement of regional lymphoid tissue, however, the prognosis is more dismal. In this group, survival

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figures fall to less than 40%. Current methods of treatment appear to have provided little, if any, improvement in patient survival over the past 15 to 20 years.[4] Surgical techniques and methods of radiation delivery are admittedly better. However, in large part, improved understanding and management of the complications of this disease and its treatment are responsible. Advanced colon cancer remains exceptionally resistant to several modes of chemotherapy as well as adjuvant immunotherapy.[4] There remains room for optimism, and treatment for these patients should continue in controlled and well-designed clinical trials; however, overall results are far from satisfactory and only very rarely do patients with advanced colon cancer have complete and definitive remissions. Although improvements in treatment of patients with this disease are desperately required, a growing need exists to assess critically and further examine specific measures to prevent colon cancer.

In recent years, experimental animal models have been used to study some of these fundamental changes that characterize or accompany colonic neoplasia, the effects of various measures used in treatment, and the potential role of various dietary factors in its development. One of these, dietary plant fiber, continues under intense investigation in several laboratories. This chapter reviews the rationale for this particular experimental approach, the salient features of the experimental animal model of human colon cancer, and the specific results achieved thus far regarding dietary fiber in this experimental model system. Finally, future directions for investigation in this area are proposed based on the physiochemical properties and possible mechanism of action of dietary fiber in the mammalian intestine.

II. GENERAL CONCEPTS AND RATIONALE

A growing body of scientific literature suggests that colon cancer is largely environmental in origin and thus probably preventable.[3,5] Among several possible environmental agents, dietary factors may be particularly relevant. Plant fiber (or plantix)[6–10] is a key element in this dietary hypothesis, and diets rich in plant fiber are thought to play a preventive role in the development of human colon cancer.[11–17] While the potential importance of fiber is now widely recognized, it must be strongly emphasized that this substance may not be the only relevant dietary variable. Based on current information, no hypothesis can completely exclude the possible importance of other dietary factors.

Dietary fiber, itself, is an extremely complex substance composed of individual polysaccharide and nonpolysaccharide polymers of plant cell wall origin. These include cellulose, hemicelluloses, pectin, lignin, and several other components.[6–10] They share a common feature: apparent resistance to human intestinal hydrolytic enzymes, although digestion by enzymes of bacterial origin may occur.[9,10] Several hydrolytic products result from this digestion.[9] These byproducts may vary depending on the fiber component ingested and could, in themselves, alter the luminal environment within the colon or the colonic

mucosa. There are both similarities and differences among individual fiber polymers.[9,10,18] The type and amount of a specific fiber polymer ingested might produce varied results. To assume, therefore, that all forms of dietary fiber or its constituent polymers belong under the umbrella of the fiber hypothesis may be inaccurate.

Superficially, an examination of fiber might not seem to be difficult, but fiber polymers do not occur in nature in the purified form and therefore are not easily dissected. Foods that contain fiber, such as wheat bran, also contain substances that can be hydrolyzed by human alimentary tract enzymes, and these may undergo nutrient absorption.[8,19] These nonpurified, fiber-containing food substances[8] may be highly variable as to type and composition of individual fiber polymers, moisture content, and other nonfiber nutrients, depending on their source and mode of preparation.[19] These complexities regarding the very definition, nature, and analysis of dietary fiber have contributed to the controversy that has existed in this investigative area. In recent years, however, significant progress has been made. As the concept of dietary fiber has evolved, so the techniques for its analysis have improved.[20–23] These methods now permit more accurate and precise definition of the amounts and types of dietary fiber polymers in various human foodstuffs and of those that might be used for studies of experimental intestinal carcinogenesis.

When viewed from this perspective, the information available to support or refute the fiber hypothesis is limited. However, a recent study from Europe has provided some particularly interesting information.[17] The diet of the urban population of Copenhagen was compared with that of a rural area of Finland, Kuopio. The former has a high incidence of colon carcinoma and the latter a low incidence. In the diets of these two groups, the proportions of different dietary fiber polymers measured were similar. However, the mean intake of total dietary fiber, as well as the intake of the fiber components cellulose and lignin, was significantly less in Copenhagen. This study illustrated for the first time that measured fiber intakes differ in human populations with different incidence rates of colon carcinoma. Moreover, modern analytical methods of food fiber analysis were used in this study.

Since inherent difficulties remain in the prospective study of dietary variables and their long-term effects in humans, alternative measures have been used to explore their importance in colon cancer. One of these methods involves the induction of colonic neoplasia in experimental animals.

III. EXPERIMENTAL COLONIC NEOPLASIA: THE MODEL

A. Background

The critical assumption made in experimental colon carcinogenesis, regardless of the agent used, is that the fundamental mechanisms involved in neoplasia development are similar, though not identical, to some of those occur-

ring in human colon cancer. Based on this assumption, several chemical and physical agents have been used to induce colonic neoplasia.[24–37] None is ideal in these three essentials: exclusive and specific action only on colonic epithelium, completely reproducible effects in different animals, and definitive safety for the investigator. The colonic mucosa of several animal strains including rats,[38] hamsters,[39] and mice[40] is highly sensitive to tumor induction with certain chemicals such as 1,2-dimethylhydrazine,[30] whereas other agents produce tumors in the colon only incidentally.[32–35] In general, the effects of many carcinogens are relatively site-specific. However, neoplastic change is observed in other tissues, and this may vary depending on the specific agent used, dosage, route of administration, and time of autopsy following injection.[41–43] In addition, the species, strain, degree of inbreeding, and sex of the animals are important variables.[44–48] These factors require consideration in comparing results achieved in different animal studies. In addition to chemical carcinogens, other modalities can induce colonic neoplasia in experimental animals, such as ionizing radiation administered in different forms.[36,37] Since only chemical methods have been used thus far to examine the plant-fiber hypothesis, this discussion will focus only on these agents.

B. *Chemically Induced and Spontaneous Neoplasia*

The chemical induction of colon carcinoma in experimental animals was initially reported in 1941 by Lorenz and Stewart[24] using a cholanthrene derivative. Similar results have since been achieved using several other structurally different compounds, classified[49] into various categories including:

1. Cholanthrenes: 3-methylcholanthrene
2. Aromatic amines: 2,3-dimethyl-4-aminobiphenyl compounds
3. Alkylnitrosamides and nitrosourea compounds: *N*-methyl-*N'*-nitro-*N*-nitrosoguanidine
4. Aflatoxins: aflatoxin B_1
5. Cycasin and hydrazine derivatives: 1,2-dimethylhydrazine and azoxymethane

At present, the last category is the best studied and most popular. These compounds are also the most potent and most specific agents available.[49]

Small laboratory rodents generally have a very low rate of "spontaneous colon tumor" occurrence.[38] One report, for example, recorded an incidence rate of 28 in 3000 animals.[50] These colonic tumors occur most often in the cecum[51] as both epithelial and nonepithelial types.[51] For most strains, however, the precise frequency of these tumors is unknown; occasionally, an unusually high number of tumors is observed in some groups of animals.[52] Many studies examining dietary variables include control groups not receiving carcinogens, but such groups are usually small. Since the maintenance of large groups of con-

trols is costly, it is further assumed that the rate of tumor occurrence in untreated animals is negligible.

C. Metabolism and Action of Hydrazines

In 1963, Laqueur and his co-workers[28] induced colorectal adenocarcinoma in experimental animals with cycad meal derived from a tropical plant, *Cycas circinales*. Subsequently, cycasin, the glucoside derivative of methylazoxymethanol, was observed to be a critical carcinogenic agent in cycad meal.[29] In 1967, Druckrey *et al.*[30] described the induction of intestinal tumors in rats with a symmetrical hydrazine derivative, 1,2-dimethylhydrazine. For effective tumor induction, best results appeared to be achieved following parenteral administration. However, variable success has also been reported using oral, intragastric, and intrarectal routes of carcinogen delivery. It is thought that dimethylhydrazine first requires metabolic activation within the host to become an active carcinogen,[53] and therefore, it may be termed a procarcinogen[49] (Fig. 1). It is thought to undergo two hepatic oxidation reactions, although other tissues may be involved.[49,54,55] The first oxidation step produces azomethane, which may be expired by the host animal in its respiratory gases.[56] The second oxidation step converts azomethane to azoxymethane, another compound commonly used in experimental colon carcinogenesis. Azoxymethane is then *N*-hydroxylated to methylazoxymethanonl. The precise pathway that this agent subsequently follows *in vivo* is not known, although it may decompose spontaneously[57] or be altered by certain tissues enzymatically. Some of these enzymes, for example, the dehydrogenases, are present in several rat tissues, with high activities detectable in liver and colon.[58] Studies *in vitro* indicate that formaldehyde, water, and nitrogen are eventual by-products.[57] An alkylating intermediate, methyldiazonium, is formed during this decomposition. This agent, or a subsequent derivative, is capable of methylating cellular nucleic acids.[59] While this suggests a possible explanation for the mutagenicity of these

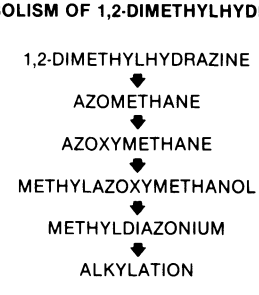

Figure 1. Metabolism of 1,2-dimethylhydrazine; probable pathway *in vivo*. Modified from others.[49,54]

agents, the precise mechanism leading to the actual production of neoplasia, especially in the colon, remains unknown. Alkylation may occur at other sites where tumors are rarely, if ever, detected.[60] Intraluminal factors appear to play some role, perhaps following biliary excretion of the carcinogen.[49,61] Luminal bacteria may be involved, since tumor production is decreased in germ-free rats treated with dimethylhydrazine but increased in those administered azoxymethane.[62,63] However, some evidence indicates other routes of carcinogen delivery, including the bloodstream.[49,64]

D. Potential Relevance of Hydrazines to Humans

While the carcinogenicity of these agents is not specifically known for human colonic mucosa, both synthetic and natural hydrazines exist in the environment as industrial and food contaminants.[65,66] 1,1-Dimethylhydrazine has been detected in significant quantities in tobacco plants, although a definite correlation between colon cancer incidence and smoking in humans is not evident.[65,67] Hydrazines are also found in wild and cultivated mushrooms including *Gyromitra esculenta* and possibly some *Helvella* species, both sometimes eaten by humans.[65,68] *N*-Methyl-*N*-formylhydrazine may be converted to methylhydrazine apparently under conditions similar to those in the human stomach.[69] Many of these compounds are found in rocket propellants, while hydroxyethylhydrazine is used as a ripener for certain plants.[70,71] Hydrazine and its many derivatives are also commercially used in pesticides, herbicides, blowing agents for plastics, and water treatment. Several of these hydrazine analogues can produce tumors in experimental animals.[65] While 1,2-dimethylhydrazine and azoxymethane are generally not found in nature, their use must be considered a serious risk to laboratory workers, especially since these agents and their derivatives may be excreted by test animals in the respiratory gases and urine as precursors or as potentially active carcinogens.[55,56]

E. Biological Aspects of Experimental Intestinal Neoplasia

1. General Principles

Dimethylhydrazine or its derivatives can produce tumors at any site within the intestine of the experimental animal.[72–75] However, in the small intestine the vast majority are usually found within the first few centimeters near the major bile-duct opening, providing additional evidence that either bile itself or some component excreted into bile or pancreatic juice is important. Tumors occur uncommonly in the jejunum and are extremely rare in the ileum. Tumors in the small intestine appear as polypoid or sessile lesions, and the latter can be confused macroscopically with mucosal lymphoid aggregates. The majority of small-bowel tumors appear to be adenocarcinomas. They tend to be locally invasive, although metastasis can occur to distant sites. Paradoxically, these tumors (and some tumors originating outside the intestine) pose

several problems in long-term dietary studies of colon carcinogenesis. First, they may cause the premature death of experimental animals, which may result from intussception and obstruction in the small bowel. Small-intestinal tumors may occur with or without colonic neoplasia in the same animal. Therefore, studies that compare duration of animal survival or occurrence of animal death may provide limited information. Second, the presence of a neoplasm at a site other than the colon may obscure the precise origin of a tumor metastasis. Reports of apparent colon metastases without evidence of careful examination of the small intestine, in particular, are likely to be inaccurate. Finally, the ratio of small-intestinal to large-intestinal tumors in this model differs from the observed ratio seen in humans. In both species, small-intestinal adenocarcinoma usually occurs proximally but at a lower rate of occurrence than in the large intestine. However, the relative ratio of tumors at these two sites is higher in the experimental animal following parenteral dimethylhydrazine.[75]

2. *Comparative Aspects of the Normal Colon*

Grossly, the normal colon of the rat may be divided into proximal and distal regions (Fig. 2). The cecum and the proximal or ascending portion of the colon are mobile and are attached by a long mesentery to the dorsal aspect of the abdominal wall. The cecum is generally found on the left side of the abdominal cavity, while the proximal colon traverses from left to right to become fixed cranially at the major flexure. No true transverse segment is present as in the human colon; the distal colon or descending colorectum traverses from the major flexure caudally in the median line to the anus. The entire distal colon is attached to the posterior abdominal wall by a short mesentery.

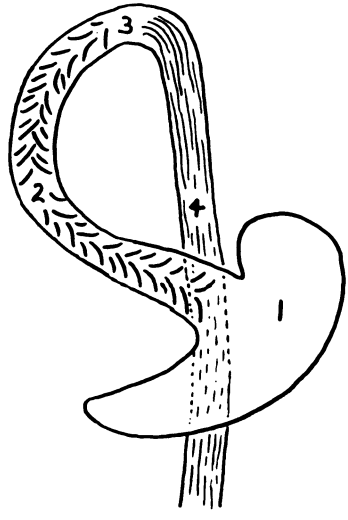

Figure 2. Normal rat colon anatomy: 1, cecum; 2, proximal colon; 3, major flexure; 4, distal colon. Proximal mucosal folds are oblique in orientation while distal mucosal folds are longitudinal.

The proximal colon may be distinguished from the distal colon by careful examination of the arrangement of mucosal folds. In the proximal colon these folds appear oblique in orientation, while in the distal colon they are longitudinal.[73,76]

On histological examination at light microscopy (Figs. 3–5), the colonic wall is composed of an innermost layer with lining epithelium, lamina propria, and the muscularis mucosa; then submucosa, an inner circular and outer longitudinal smooth muscle cell layer, subserosa, and serosa. Histologically, the mucosa varies along the length of the rat colon.[76,77] In the cecum and proximal colon, the colonic crypts consist primarily of columnar epithelial cells and goblet cells. In this region, goblet cells are distributed unevenly, being more numerous in the basal mucosa. Histochemically, these goblet cells stain with periodic acid–Schiff reagent, alcian blue, and iron diamine. Sulfomucins predominate in the goblet cells of superficial mucosa, and sialomucins are localized more in the basal mucosa.[77] In the distal colon, the colonic crypts contain

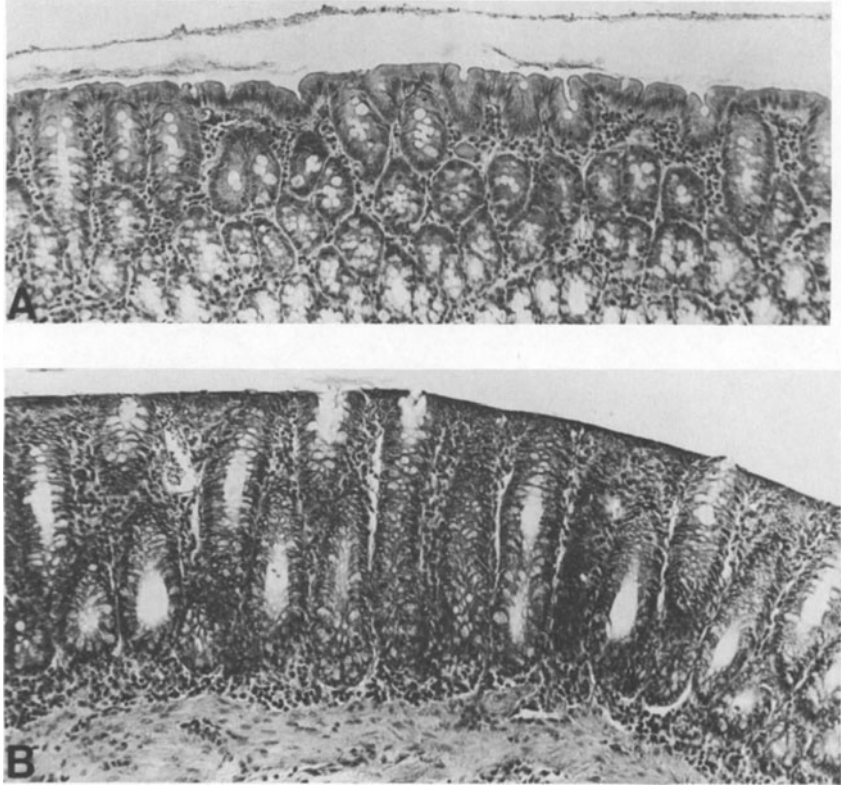

Figure 3. Normal rat colon histology (low power): A, proximal mucosa; B, distal mucosa.

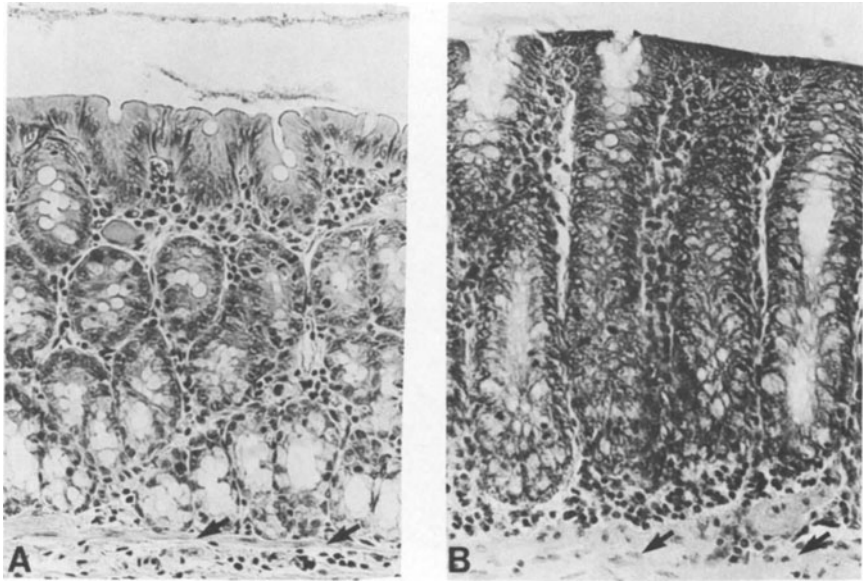

Figure 4. Normal rat colon histology (high power): A, proximal mucosa; B, distal mucosa. Arrows indicate muscularis mucosa.

similar cell types in the epithelium, but goblet cells are distributed evenly from superficial to basal mucosa. Strongly positive staining reactions for sulfomucins are found in these goblet cells.[77] Differential labeling with fluorescent histochemical probes are also found in both proximal and distal colonic mucosa, similar to regional differences observed in the small intestine.[78–80]

Regional differences in carbohydrate content and levels of different synthetic and degradative enzymes of glycoprotein metabolism have also been reported in normal colon of rats.[76] These regional morphological and biochemical differences provide evidence that the colonic mucosa differs biologically along its length. Lymphoid plaques are also visualized in both regions. The question that immediately arises is the precise relationship of these lymphoid aggregates, if any, to cancer development. A high concentration is found in the small intestine, particularly the ileum, where neoplasia is distinctly rare following administration of these agents. Less lymphoid tissue is seen in the proximal small intestine and colon, the two regions where carcinoma occurs most commonly.

3. *Pathology of Experimental Colon Carcinogenesis*

In the large intestine, rat epithelial tumors are markedly similar to human neoplasms in both histological type (Table 1) and overall site distribution (Figs. 6 and 7). Both epithelial and nonepithelial neoplasms occur (Figs. 8–14).

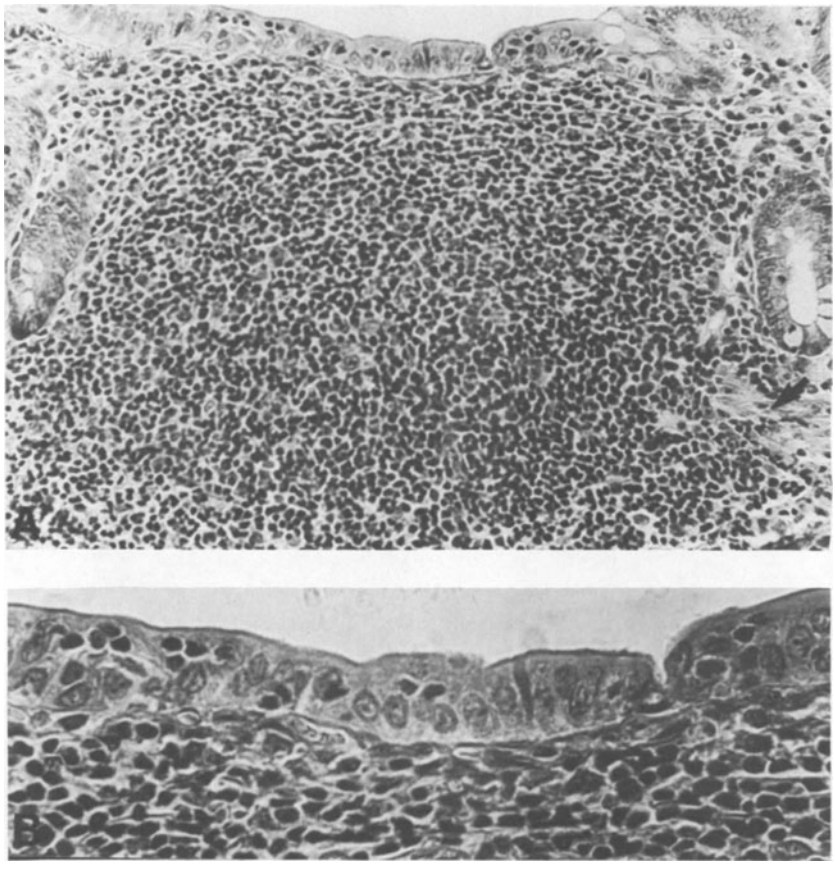

Figure 5. Lymphoid follicle in the distal colon: A, at low power, localized to the mucosa and extending across the muscularis mucosa (arrow) into the submucosa; B, at high power, surface epithelium overlying the lymphoid aggregate with intraepithelial lymphocytes.

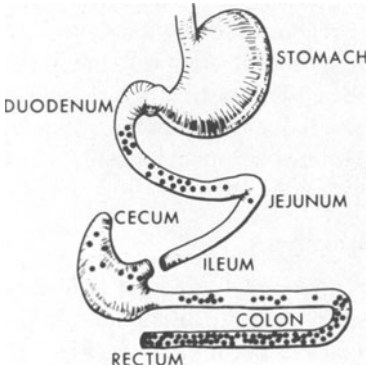

Figure 6. Representative distribution of intestinal epithelial neoplasia in male Wistar rats treated with a course of parenteral 1,2- dimethylhydrazine. Most small-bowel tumors are found proximally and most colon tumors distally.

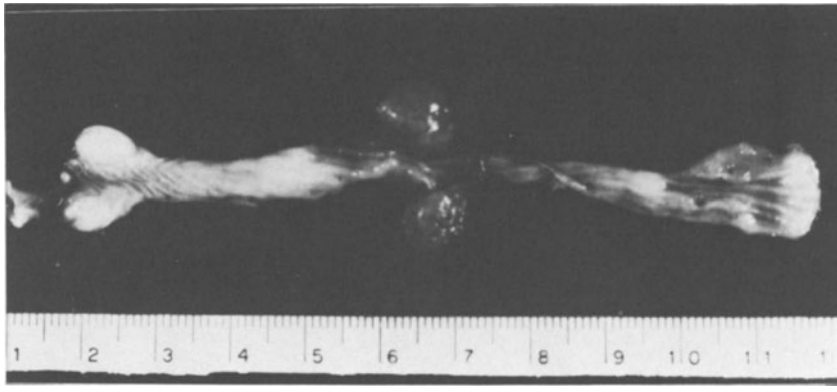

Figure 7. Colon of a dimethylhydrazine-treated rat with the cecum removed from the proximal end on the left. Multiple epithelial neoplasms are present and variable in size.

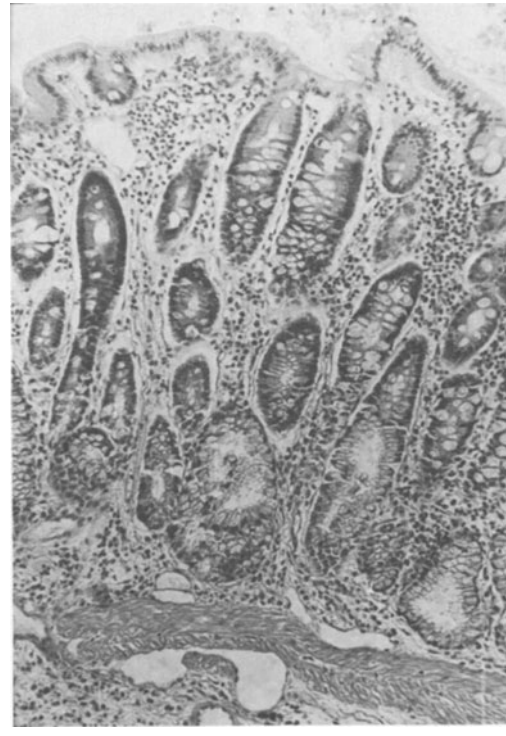

Figure 8. Proximal colonic mucosa from carcinogen-treated rat with a carcinoma of the distal colon. Crypts are branched and dilated with increased numbers of goblet cells containing abundant mucus. Foci of metaplasia are seen along with an apparent increase in lamina propria lymphoid cells.

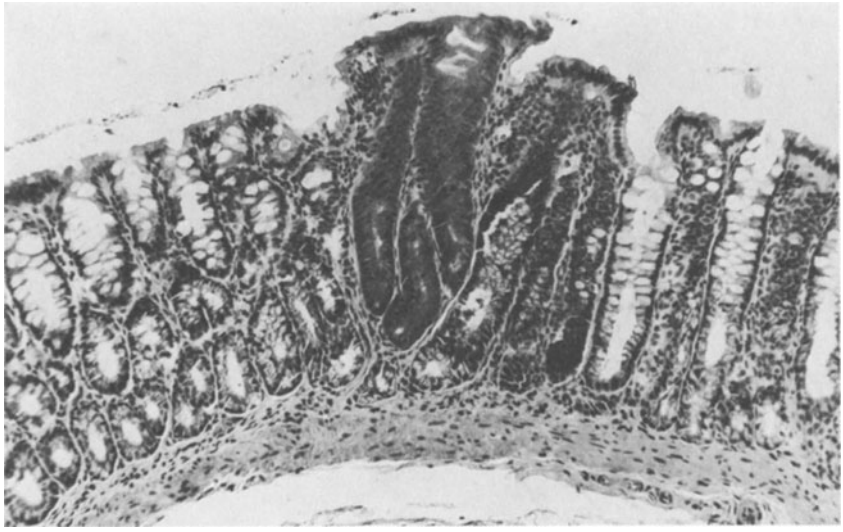

Figure 9. Distal colonic mucosa from a carcinogen-treated rat showing a microscopic polypoid-appearing lesion without detectable invasion of the muscularis mucosa.

In the experimental rat, benign epithelial neoplasms or adenomas are reported and are pedunculated or polypoid as well as sessile. They exhibit varying degrees of cellular atypia and mucus content, although mucus is usually reduced. Most are found in the distal colon, although they can develop in the proximal colon. More than one may be present in the same animal. Their size may vary considerably, although they tend to be smaller in comparison to obviously invasive lesions. Neoplasms of different types, which also occur in humans, may be observed in the rat, but they are usually composed of tubular or tubulovillus elements. The pure villus adenoma rarely develops. Disordered glandular proliferation and extreme cellular atypia may be observed. For this reason, serial sections rather than single or step sections of well-oriented tumors are preferred to exclude evidence of invasion of the underlying muscularis mucosa. Sectioning through the pedicle or base of the tumor is important to ensure that carcinoma is not present, and correct orientation will prevent erroneous conclusions due to apparent or pseudocarcinomatous invasion. Tumors without neoplastic cellular invasion into or beyond the muscularis mucosa may be inclusively labeled polypoid neoplasms.[73] By definition, this term is not precisely equivalent to the adenomatous polyp.

Epithelial neoplasms with demonstrable invasion are defined as carcinoma. These may occur in association with small- or large-intestinal tumors, including other metachronous carcinomas of similar or different histopathological type. Macroscopically, these invasive adenocarcinomas can appear as sessile plaques or erythematous polyps extending into the colonic lumen. Some may differ in appearance from polypoid neoplasms only because of invasion.

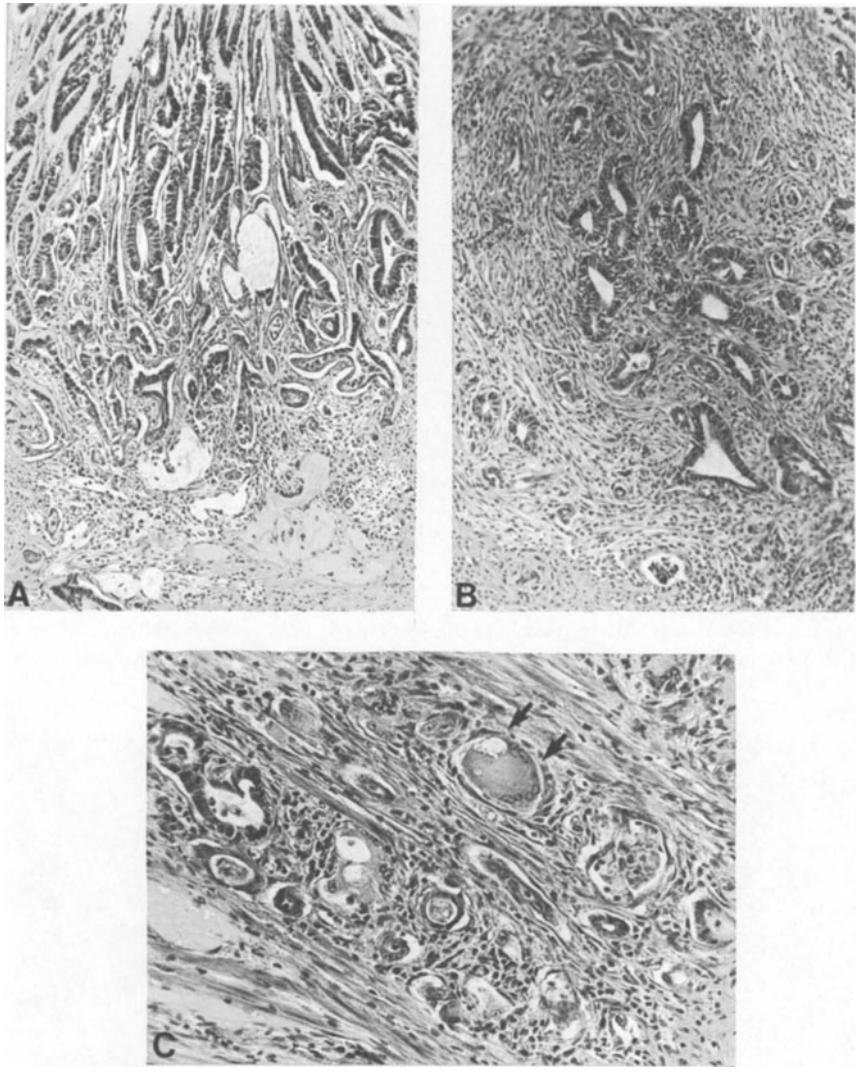

Figure 10. Distal colonic polyp: A, invasive adenocarcinoma showing a predominantly epithelial cell pattern although collections of extracellular mucus are present; B, invasive epithelial cells at higher power evoking a scirrhous reaction; C, invasive epithelial cells between muscle fibers and a multinucleated giant cell (arrows).

These invasive tumors vary considerably in size but, in general, tend to be larger than polypoid neoplasms. Small microulcerations may occur on the surface of these tumors, but this is not a distinguishing feature. Large, frank ulceration may occur, consisting of malignant epithelial cells, connective tissue elements, inflammatory exudate, and variable amounts of necrotic debris.

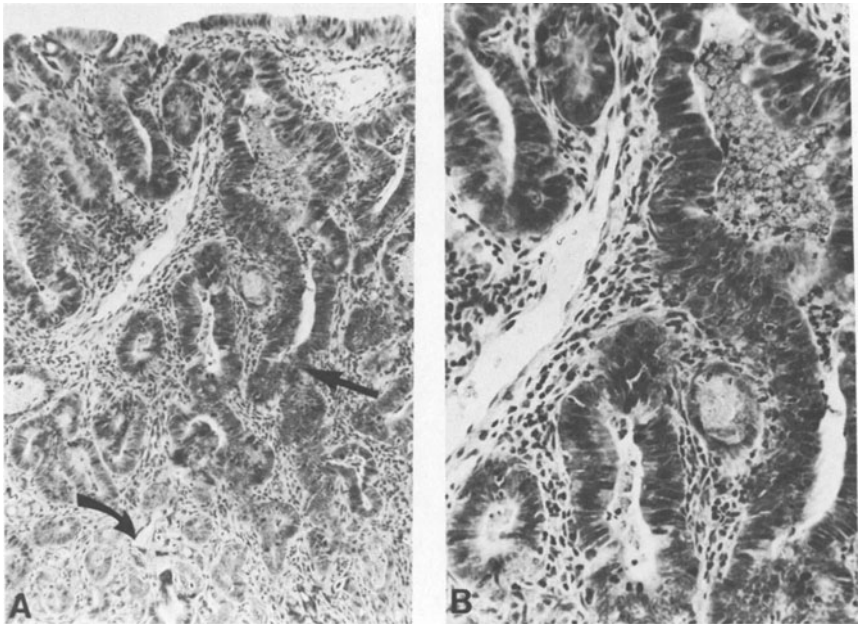

Figure 11. Sessile plaque from the distal colon: A, invasive adenocarcinoma shows marked atypia of epithelial cells with increased nuclear: cytoplasmic ratio and apparent loss of normal polarity (straight arrow) as well as frankly malignant cells below (curved arrow); B, high magnification of area indicated by straight arrow.

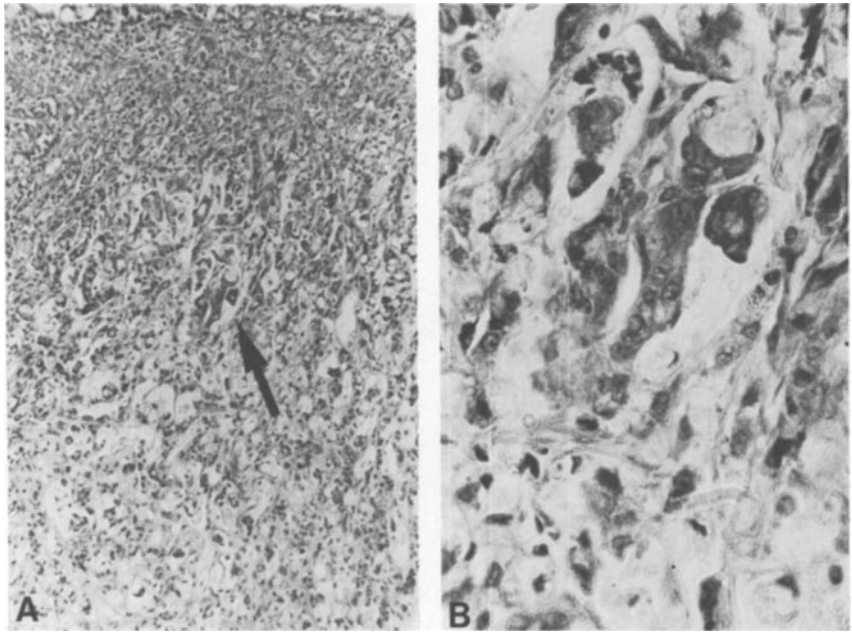

Figure 12. Ulcerating adenocarcinoma with poorly differentiated epithelial cells: A, lower power (arrow); B, higher power.

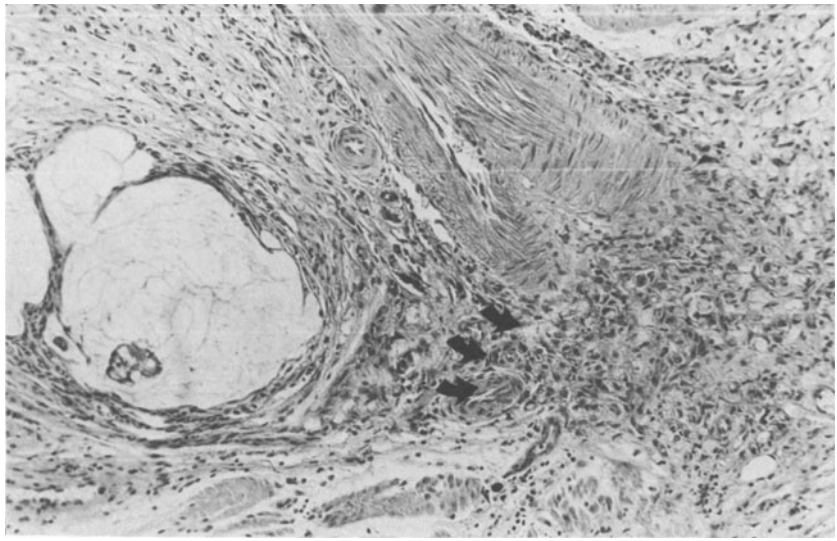

Figure 13. Mucinous-cystic adenocarcinoma invading the muscle wall of the proximal colon (arrows).

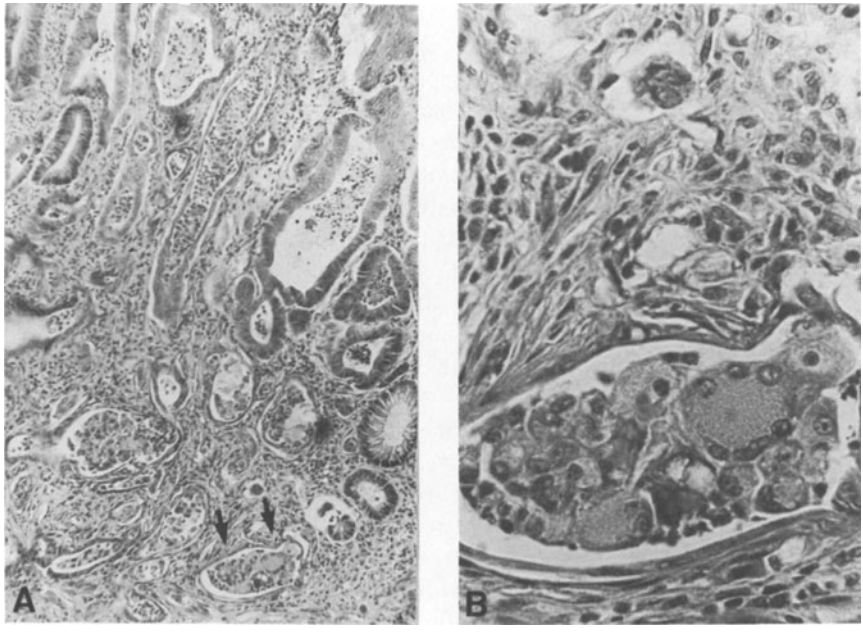

Figure 14. Adenocarcinoma showing: A, invasion with marked inflammatory reaction (arrow) characterized by, B, aggregates of tumor cells, multinucleated giant cells, and lymphoid cell elements.

Table 1. Experimental Colonic Neoplasia: Histopathologic Classification

I. Epithelial Neoplasms
A. Polypoid Neoplasms (noninvasive)
1. Tubular "adenoma"
2. Tubulovillus "adenoma"
3. Villus "adenoma"[a]
4. Other noninvasive neoplasms
B. Carcinoma (invasive)
1. Invasive adenocarcinoma
2. Mucinous adenocarcinoma
3. Signet-ring-cell adenocarcinoma[a]
4. Undifferentiated carcinoma[a]
II. Nonepithelial Neoplasia[a]

[a]Uncommon or rare.

Occult luminal blood loss may be detected and occasional frank rectal bleeding occurs.

Several histological varieties of carcinoma occur, but the vast majority are well-differentiated invasive adenocarcinomas, particularly in the more distal colon. Epithelial cells in these neoplasms form tubular, acinar, or papillary structures. Often tumors are nonuniform in structure, with occasional foci of poorly differentiated cells. Some epithelial cells may contain mucus. While most carcinomas occur in the distal colon, administration of lower dosages of carcinogen reportedly produces an apparent shift in distribution to the proximal colon.[72] Even with large dosage schedules, however, tumors of all types, including the well-differentiated variety, can be found in the proximal colon. These tumors may produce serosal umbilication in addition to mucosal ulceration. They may appear as pedunculated masses leading to intussception and obstruction. Protrusion through the anal verge is recorded but is uncommon.[49] In general, invasiveness appears to be related to size, but exceptions occur; very small lesions may be clearly invasive carcinomas. The well-differentiated form may involve local lymph nodes, pericolonic fat, and mesentery; but involvement of more distant sites, i.e., liver and lungs, is less common compared with other histological types.

In mucosa adjacent to these tumors, epithelial cells may appear hyperplastic with longer, often branched, crypts. Goblet cells may appear distended with mucus. Focal crypt abscesses, collections of inflammatory cells along with granulomas containing multinucleated giant cells, may be seen far from or close to the tumors. In other areas, the colonic mucosa may appear entirely normal on light microscopy, although ultrastructural changes may be observed. These alterations in mucosa adjacent to colonic tumors are similar to the transitional mucosa seen in association with human colon cancer. Histochemically, increased sialomucins and decreased sulfomucins are seen.[80,81] These changes in mucins may reflect an early feature of carcinogenesis.[80]

In this model, nonmucinous adenocarcinomas occur more often than the mucinous types.[73–75] Mucinous adenocarcinomas in the rat are found more commonly in the proximal colon paralleling the distribution of mucinous or colloid-type adenocarcinoma in humans.[73] However, their comparative frequency appears to be greater in the carcinogen-treated animal. Usually these tumors are sessile masses, often ulcerated, and may be associated with mucosal and/or submucosal lymphoid aggregates. In these tumors, clusters of epithelial cells tend to form glandular structures. Large ductular spaces and varying amounts of nonepithelial stromal elements and inflammatory cells may be present. The most prominent feature of these tumors is the considerable amounts of extracellular mucus, which may appear to distend glandular structures. This material stains with conventional histochemical reagents. Osteoid metaplasia has also been described.[73] Isolated groups of tumor cells may occur at variable distances away from the major tumor mass. All muscle coats and serosa may be involved. In general, they are less well-differentiated tumors and more invasive; they more often metastasize to distant sites including the liver, lungs, and abdominal and thoracic lymph nodes. Tumors of this type in the proximal colon are thought to arise from the base of the mucosal epithelium, where mucus-producing cells are more prevalent.

Other histological varieties of colon carcinoma may occur in this model that parallel the different types found in humans.[82] Neoplasms with high mucus content may be the signet-ring type, where isolated cells appear to be distended with mucus localized intracellularly. Undifferentiated carcinomas may be defined in the absence of glandular structures or mucus but, however, are uncommon. Nonepithelial cell tumors occur, including sarcomas. Carcinoid tumors have not been reported in this model of human neoplasia.

4. *Morphogenesis of Experimental Colon Cancer*

As in humans, the controversy surrounding the polyp–cancer hypothesis remains unresolved.[83,84] In this animal model, both invasive and noninvasive tumors occur. Some may differ in only one histological feature: the presence of cells beyond the confines of the mucosa. While proof that these tumors originate from the noninvasive lesion is not yet definitive, it is the opinion of this author that invasive carcinoma can arise from some noninvasive neoplasms, particularly in those macroscopically appearing polypoid. On the other hand, very small invasive tumors can be detected, suggesting that some tumors could arise *de novo*. In these, rapid transition from one phase to the next could possibly occur, especially in the proximal colon, where neoplasms often appear less well-differentiated and larger in size compared with those in the distal colon. Interestingly, the ratio of invasive to noninvasive neoplasms appears higher in most reports using experimental animals than the ratio of malignant to benign lesions in humans. In addition, detection of adenocarcinoma alone in hamsters treated with dimethylhydrazine has been reported.[39] The available evidence, therefore, fails to support or refute the polyp–cancer sequence as the only mechanism in the genesis of experimental colon cancer.

5. Ultrastructural and Correlative Biochemical Aspects

Scanning and transmission electron microscopy and freeze-fracture techniques have provided more refined ultrastructural definition of these colonic tumors induced with hydrazine compounds. Tumor cells, although highly variable in size and shape, tend to be smaller and more rounded than normal colonic epithelial cells. Microvilli are fewer, blunted, and smaller. In addition, fewer apical surface membrane particles are found than particles associated with the microvilli of surface membranes of normal colonic epithelial cells.[85,86] As judged by ruthenium red staining, fewer tumor cell-surface mucopolysaccharides are present than is normal.[85] While the appearance of this ruthenium red reaction product is uniform on the external surface microvilli of normal luminal colonic cells, it varies considerably from cell to cell in neoplastic epithelium. These findings generally correlate with reportedly lower cell-surface glycosyl-transferase activities of rodent colon cancer cells,[87] thought by some investigators to be important in the biosynthesis of the carbohydrate-containing components of some cell-surface membrane glycoproteins.[88] In addition, other histochemical studies have revealed reductions in total mucus content of tumors and altered staining reactions of uninvolved adjacent or transitional colonic mucosa, similar to observations reported in humans.[80,81] These microscopic findings correlate with several chemical and biochemical observations in dimethylhydrazine-treated animals. First, the carbohydrate content of colonic tumors is significantly reduced compared with noncancerous colonic mucosa from both normal and carcinogen-treated animals. Second, reduced activities of glycosyltransferases, i.e., enzymes involved in cellular glycoprotein biosynthesis, occur in these tumors. Third, the activities of glycosidases, i.e., enzymes thought to be involved in glycoconjugate degradation, are reduced or remain unaltered in colonic tumors. Fourth, differences are detectable between noncancerous colonic mucosa of carcinogen-treated animals and colonic mucosa from untreated animals.[76] Similar observations have been made in comparing human colon cancer tissues with uninvolved colonic mucosa.[89,90] These changes probably reflect the less differentiated state of colon cancer cells as well as alterations occurring during colon carcinogenesis.

F. Summary of the Model System

It can be concluded that chemical carcinogens, particularly parenterally administered hydrazines, produce neoplasia reliably in many strains of laboratory animals. Several of these agents are relatively specific and selective for the intestinal mucosa, especially the colon. The latency period to tumor induction is short and relatively predictable. In general, these are considered essential features for the creation of a useful experimental animal model. The most important question, however, relates to its applicability to human disease. Several morphological and biological characteristics of experimental colon cancer

appear similar, even identical, to observations reported in human colonic neoplasia (Table 2). However, differences, as well as several basic assumptions made by the investigator, warrant caution in extrapolating results directly to human disease.

IV. STUDIES WITH DIETARY FIBER IN EXPERIMENTAL COLONIC NEOPLASIA

A. Background

Several animal studies are now available that report in detail[75,91–97] and/or in abstract form[98–103] the effects of fiber-containing foods or individual fiber polymer components on colonic neoplasia induced with various carcinogens. These studies indicate the potential for examination of the fiber hypothesis using this experimental approach under carefully controlled conditions, which are advantageous compared to difficulties possible in long-term human studies.

B. Studies with Mixtures of Individual Fiber Polymers

In most reported studies to date of experimental animals (Table 3), the major, although not exclusive, source of dietary fiber has been bran.[91–95] Bran contains a relatively high proportion of measurable fiber[9,104]; however, it also contains substances that are not dietary fiber. Wheat bran, for example, contains about 70% carbohydrates, including 12% starch, 8% sugar, 45% hemicelluloses, and 35% cellulose. Other (noncarbohydrate) substances are also present, including the fiber polymer lignin and protein, fat, several vitamins, and various minerals. These elements may vary in the different types of wheat bran depending upon source and milling procedure.[104] Wilson *et al.*[91] and, later, Barbolt and Abraham[92] provided some evidence to suggest that bran-containing foods could protect against colon-tumor induction in the experimental animal. In both studies, prolonged bran ingestion lowered the percentage of dimethylhydrazine-treated rats developing colonic neoplasia. The protective role of a bran-containing diet for the colon was also reported by Chen *et al.*[93] in mice. Subsequently, Fleiszer *et al.*[94] found a significantly reduced incidence of colon cancer in rats that were fed bran compared with a group receiving a fiber-free elemental diet. No statistically significant effect was observed, however, with other fiber-containing chow diets, at least in the amounts administered to the animals in their study. Later, Cruse *et al.*[95] reported that ingestion of fiber-containing diets (one containing bran) had no effect on overall mortality in rats treated with dimethylhydrazine. Since other tumors occur in this model, it is difficult to be certain whether all animal deaths could be attributed directly to the presence of colon cancer. Interestingly, despite the high level of

Table 2. Colonic Neoplasia in Rats and Humans

Parameter	Rat	Human
Etiology	Vast majority induced by chemicals or radiation in laboratory species. Occasional tumors of unknown etiology (i.e., spontaneous tumors). Rare strains with high tumor rates.	Unknown but probably environmental factors involved. Predisposition in patients with multiple colonic polyposis syndromes, inflammatory bowel disease and familial cancer syndrome.
Dietary factors	Good evidence for effect of both fiber and some nonfiber dietary components.	Suggestible evidence in some studies for effect of fiber and/or nonfiber dietary components.
Incidence	Normally, very rare.	Common, relative to other malignancies, in most industrialized nations. Geographic differences.
Normal colon anatomy	Proximal or ascending (including large cecum) and distal or descending portions. Single major flexure. No transverse colon. Proximal colon mobile.	Ascending (including small cecum and appendix), transverse, and descending colon and rectum. Two major flexures. Mobile and redundant sigmoid portion of descending colon.
Mucosa	Regional histological and functional differences. Major epithelial cells are columnar and goblet cell in type with regional differences in histochemical straining reactions.	Regional histological and functional differences. Major epithelial cells are columnar and goblet cell in type with regional differences in histochemical staining reactions.
Colonic neoplasia site	Majority distal if chemically induced, but more often proximal if spontaneous tumor. Mucinous adenocarcinoma most common in proximal colon.	Majority distal. Usually proximal in family cancer syndrome. Mucinous (colloid) adenocarcinoma more common proximally.

Size	Variable. Small tumors may be invasive.	Variable. Larger tumors (over 2cm) often carcinoma.
Number	Frequently multiple carcinomas of similar or different histologic type often associated with one or more noninvasive neoplasms.	Occasional metachronous carcinomas or adenomas. Multiple tumors (more than 50) in multiple colonic polyposis syndromes.
Histology	Polypoid neoplasms, usually tubular or tubulo villus types. More common distally. Carcinoma, invasive, well differentiated most common. More common distally. Carcinoid not reported. Nonneoplastic lesions occur.	Adenomas, tubular, tubulo villus, and villus types. More common distally. Several histologic varieties of carcinoma. Nonneoplastic lesions occur.
Cancer cells	Ultrastructural features similar to humans.	Ultrastructural features similar to rats.
Other features	Reduced mucus content of epithelial cells in neoplasia histochemically. Sugar content of tumors reduced compared with noncancerous mucosa of normal and carcinogen-treated rats. Reductions in glycosyltransferase activities in tumors and reduced or unaltered glycosidase activities in tumors compared to noncancerous mucosa of normal and carcinogen-treated rats.	Reduced mucus content of epithelial cells in neoplasia histochemically. Sugar content of tumors reduced compared with noncancerous colonic mucosa of colon cancer patients. Similar observations in enzymes thought to be involved in glycoprotein metabolism compared to rat.
Associated tumors	Common in experimental neoplasia. Usually small intestine and/or external auditory canal.	Rare except in some polyposis syndromes, e.g., Gardner's (bond, skin, soft tissues), Turcot's (brain).

Table 3. Summary of Published Papers on Experimental Colonic Neoplasia and Dietary Fiber[a]

Reference	Animals	Carcinogen[b]	Diets	Effect of bran diet on colon
		Studies with mixtures of individual fiber polymers		
1. Wilson *et al.*[91]	Male Sprague–Dawley rats	DMH, 30 mg/kg, i.g., 4 or 8 doses	With and without 20% wheat bran	Protective
2. Barbolt and Abraham[92]	Male Sprague–Dawley rats	DMH, 30 mg/kg, i.g., 10 doses	With and without 20% wheat bran	Protective
3. Chen *et al.*[93]	Female CF_1 mice	DMH, 20 mg/kg, s.c., 26 doses	With and without 40% wheat bran	Protective
4. Fleiszer *et al.*[94]	Male Chester–Beatty rats	DMH 20 mg/kg, s.c., 13 doses	With and without 28% "fiber" as wheat bran[c]	Protective
5. Cruse *et al.*[95]	Female Wistar rats	DMH, 40 mg/kg, s.c., 13 doses	With and without 20% "fiber" as wheat bran[d]	Not reported[e]
		Studies with single-fiber polymers		
6. Ward *et al.*[96]	Male Fischer rats	AOM, 14.8 mg/kg, s.c., 10 doses	With and without 20% and 40% cellulose	Not protective[f]
7. Freeman *et al.*[76]	Male Wistar rats	DMH, 25 mg/kg, s.c., 16 doses	With and without 4.5% microcrystalline cellulose	Protective
8. Watanabe *et al.*[97]	Female F344 rats	AOM, 8 mg/kg, s.c., 10 doses; MNU, 2 mg/rat, rectal, 6 doses	With and without 15% undegraded carrageenan in 5% cellulose diet	Not protective[g]

[a]Chemical carcinogenesis studies published to January 1980, excluding abstracts.[98–103]
[b]DMH Abbreviations: 1,2-Dimethylhydrazine; AOM, azoxymethane; MNU, methylnitrosourea; i.g., intragastric; s.c., subcutaneous.
[c]Comparisons made with fiber-free, elemental diet and two fiber-containing (5 and 15%) nonbran diets.
[d]Comparisons made with fiber-free and a fiber containing (4.8%) nonbran diet.
[e]All animals dead by 52 weeks, but survival greater in both fiber groups before 46 weeks. One colon cancer found in each treated animal, but more detailed pathological information not reported.
[f]Protective effect, small intestine only.
[g]Enhancing effect of carrageenan in chemical carcinogenesis.

carcinogen administered, survival was greater in both fiber-diet groups for most of the study (i.e., 44 of 52 weeks following the initial injection).

While all of these studies have stimulated great interest in the role of dietary fiber in this model, it cannot be determined whether the bran component or the specific fiber components found in bran were important. Precise conclusions based on comparisons of bran and bran-free diets are difficult for several reasons. In general, the addition of dietary fiber in the form of a fiber-containing food source requires the displacement of other nonfiber components in these diets. The level of bran administered in each of these studies ranged from 20 to 40%, effectively reducing other elements by a similar percentage. Thus, quantitative and/or qualitative differences in the intake of specific fiber polymers as well as nonfiber polymer components may have been important.

The last study did serve to emphasize, however, one very important observation made in each of the previous investigations: ingestion of fiber-containing diets does not ensure complete and lifelong protection for experimental animals from the effects of carcinogen administration. Unfortunately, detailed pathological information was not provided, making it impossible to determine if this apparently time-dependent effect on animal mortality had any direct relationship to actual colon cancer development.

To explore the effects of different fiber-containing foods, differences in caloric intake and resultant animal nutritional status must be considered. Caloric restriction, for example, may inhibit the formation, delay the appearance, and decrease the incidence of some tumors. Furthermore, other forms of neoplasia may be enhanced with reduced caloric intake.[105]

As an initial step,[106] groups of male Wistar rats receiving dimethylhydrazine and chemically defined diets with essentially equivalent ratios of fat, protein, and carbohydrate calories were compared. These diets contained 4.5% fiber-containing food substance. The precise fiber polymer composition and content of each diet was determined by analytic measurement as described by Southgate.[20,21] Two of these diets contained either alfalfa leaf or slippery elm bark, sources of dietary fiber. On analysis, the effective total dietary fiber polymer content was 2.70% and 0.94%, respectively. The composition determined in the 4.5% fraction for alfalfa was 8% cellulose, 7% hemicelluloses, 2% lignin, 4% pectins, and traces of gums and mucilages; that for slippery elm was 30% cellulose, 5% hemicelluloses, 9% lignin, traces of pectins, and 16% mucilages.

As expected at this 4.5% level of fiber ingestion, weight gains and intakes measured in metabolic scales were similar during carcinogenesis. The number, distribution, size, and histopathology of both small- and large-intestinal epithelial neoplasms was recorded up to 44 weeks after the initial carcinogen injection. Except for fecal weights, which were higher in both fiber groups, statistical differences were not seen, although the total number of tumors in the slippery elm group was 12% lower and in the alfalfa group, 19% higher. Thus, two different fiber-containing diets at the 4.5% level had no discernible effect on colon cancer occurrence in this experimental model.

Several conclusions resulted from the studies of different fiber-containing food sources.

1. In some experimental animal species treated with chemical carcinogens in different dosages, the ingestion of foods containing fiber polymers may be associated with a reduction in the number of detectable colonic neoplasms and/or the number of animals involved with colonic neoplasia.

2. The possible mechanisms for the results observed in these studies are obscure, and it is difficult to determine if dietary fiber, itself, was responsible because of possible nutritional alterations imposed by different diets.

3. Complete protection from colon cancer in these studies was never achieved.

4. The interrelationship between the dosage of administered carcinogen, the amount of dietary fiber, and the time of autopsy of animals after carcinogen administration is complex.

5. The long-term effects, particularly on colonic morphology, of fiber-containing foods (i.e., bran) in untreated experimental animals has not been satisfactorily studied.

6. Some fiber-containing foods have no effect or may possibly enhance the development of colon cancer in this model. Since the administration of different diets permits comparisons of animals that appear nutritionally equivalent, studies with highly purified single-fiber polymers as the only experimental variable would appear feasible and might begin to answer the questions that these other studies have raised.

C. *Studies Examining Single Fibers*

Ward *et al.*[96] reported the effect of a single fiber, cellulose, added in considerable excess to a semisynthetic diet and fed to azoxymethane-treated rats. The occurrence of small-intestinal tumors was significantly reduced without an observable effect on colonic neoplasia. Because of the very high percentage of cullulose fiber (20% and 40%), however, the food intakes of animals on these diets were altered substantially compared with a control group not receiving cellulose. In recent years, tables have been published giving the approximate amounts of total dietary fiber and of individual fiber polymers in various human and animal foods. Some high-fiber foods such as All Bran® are reported to contain 26.7% total dietary fiber including about 6% measurable cellulose.[9] In a double-blind study to eliminate observer bias, the effect of a highly purified form of microcrystalline cellulose on experimental colonic neoplasia was examined[75]; cellulose was provided at the 4.5% level. The cellulose group had fewer colonic neoplasms than a group ingesting a diet free of fiber polymers (Fig. 15). No effect was observed for tumors occurring at other sites. Although the number of animals was limited, the distribution of tumors appeared to shift

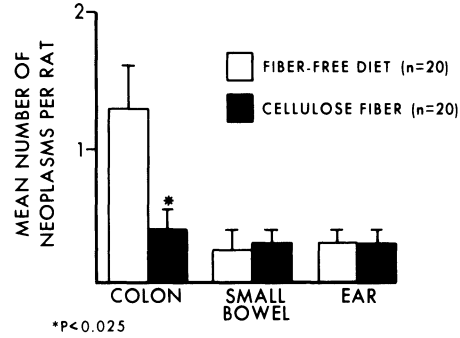

Figure 15. Mean number of neoplasms detected in rats treated with 1,2-dimethylhydrazine after fiber-feeding program. A significant reduction in colon tumors occurred while the number of tumors at other sites was not altered. Fiber component was highly purified microcrystalline cellulose (see Section IV.C). Adapted from Freeman *et al.*[75]

from a proximal to a more distal location with fiber ingestion. No effect on size or histopathology of the tumors was observed, differing somewhat from the preliminary observations on dimethylhydrazine-induced carcinoma reported by others.[98] The precise importance of other fiber polymers could not be excluded. Future studies may need to consider possible interactions of different fiber polymers in food, since these may not be strictly additive.

In a recent study,[97] undegraded carrageenan fed at the 15% level appeared to enhance the development of colonic neoplasia in rats treated with either azoxymethane or methylnitrosourea. While the caloric contents of the diets and the resultant growth curves of the animals were not strictly comparable, the apparent promoting effect of this agent may relate to its ability to cause colonic mucosal injury.[107–109] Similar results have been reported following surgically induced colonic mucosal injury in experimental animals receiving carcinogens.[110] In addition, it had been shown earlier that degraded carrageenan from the red seaweed *Eucheuma spinosum* was carcinogenic to the colorectum of experimental animals if administered orally for long periods. Squamous-cell carcinomas, adenomas, and adenocarcinomas could be detected.[111,112]

These observations with single fibers indicate several conclusions. First, some polymers, such as cellulose, can reduce the incidence of intestinal neoplasia in experimental animals administered chemical carcinogens; however, the mechanism for this observed effect is obscure. Second, some fibers, specifically carrageenan, appear to be actually carcinogenic and can enhance the development of colon cancer in animals given carcinogens. Finally, the actions of other polymers alone,[75] their interactions with other polymers and nonfiber constituents in various foods,[113] and possible mechanisms that might be involved in carcinoma development remain to be elucidated.

V. FUTURE DIRECTIONS AND MECHANISMS OF FIBER ACTION

A. Background and Physiochemical Properties of Fiber Polymers

Several changes appear to occur within the gastrointestinal tract following the ingestion of fiber. As fiber passes through the length of the small and large bowel, some hydrolysis of polymer components can occur, primarily through the action of bacterial enzymes.[9,114] The susceptibility of each polymer to hydrolysis may vary considerably.[115] This hydrolysis appears to depend on apparent substrate preferences of a complex array of microflora, regional differences in microbe ecology within the gut, and variations in microbe populations in different human populations eating different diets.[9,114,116,117] In addition, fiber may alter some characteristics of the intraluminal flora or their metabolic activities.[118–120] Several by-products can result from this bacterial hydrolysis. These include hydrogen, carbon dioxide, water, methane, and several short-chain fatty acids.[9] These by-products could conceivably alter the mucosa or intraluminal content of the intestine in different ways. Therefore, changes attributable to fiber that follow ingestion of a fiber-containing food may reflect a composite of actions of individual fiber polymers, each polymer with several different physiochemical properties and the fiber's interaction with other dietary components and with the luminal environment, as well as the hydrolytic by-products of fiber that may result. The observed physiochemical properties of individual fiber polymers may be particularly relevant in considering possible roles of dietary fiber in the pathogenesis of colonic neoplasia. Some of these properties are water-holding capacities; ability to bind various organic and inorganic compounds; and effects on intestinal transit, bile secretions, and intestinal microflora.

B. Water-Holding Capacities of Fiber

The different water-holding capacities of various foods depend to a great extent on the quantity and quality of different fiber polymers in the food.[121,122] Foods with a high polysaccharide content generally produce stools with high amounts of moisture, whereas lignin-containing diets seem not to change the fecal water content significantly. Water-adsorbing capacities of individual fiber polymers differ. Hemicellulose has a greater capacity than cellulose, while both these components adsorb more water than the phenylpropane polymer lignin. During induction of neoplasia in the experimental animal, certain fiber polymers in the lumen could increase the water content and effectively dilute the concentration of an ultimate carcinogen or cocarcinogen.

C. Fiber Adsorption of Organic and Inorganic Compounds

Organic and inorganic compounds may also be adsorbed to dietary fiber, and increased intake of fiber polymers may enhance the fecal excretion of some of these.[123–132] Bile acids, for example, may be adsorbed to the surface of certain fiber polymers, particularly lignin. This lignin effect appears to be most significant for bile acids that are deconjugated.[125–127] The fecal excretion of certain sterols and lipids is enhanced by pectins, whereas cellulose has a variable effect.[128] Fecal fat and nitrogen are greater with increased fiber intake.[129] Mutagens (presumptive carcinogens) detected in human stool[132] and possibly derived from endogenously generated nitrites and amines,[133] are reportedly reduced by increased bran intake.[132] Although conclusive information is still required, some components of fiber might differentially adsorb a carcinogen or cocarcinogen, effectively reducing its possible deleterious effects by preventing interaction with the intestinal mucosa.

D. Fiber and Intestinal Transit

The role of intestinal transit in the pathogenesis of experimental colon cancer requires study. It has been hypothesized that increased time of intestinal transit of luminal content may result in increased time for contact of a luminally active carcinogen with the intestinal lining epithelium. The current methods used to measure intestinal transit, however, may not accurately reflect the transit time of a specific carcinogenic agent or its time of contact with the intestinal mucosa. Furthermore, there may be regional differences in transit through the intestine in response to various fiber components.[134] Interestingly, laxatives fed to rodents had no observable effect on the chemical induction of colonic tumors.[135]

E. Fiber and Bile-Acid Metabolism

The precise effects of different fiber polymers on the luminal metabolism of individual bile acids requires further clarification in relation to colon carcinogenesis. In addition to the role of various types of fiber and some fiber components in binding various bile acids, studies of experimental animals suggest that certain fibers can increase the excretion as well as alter the pool size and turnover of these compounds, although in humans the results have not been consistent.[136–142] In humans, the excretion of fecal bile acids is generally greater in individuals living in areas of high colon-cancer incidence compared with that of people in low-incidence areas where fiber ingestion differs.[143] The stools of individuals from areas of low colon-cancer incidence show reduced activities of

7-α-dehydroxylase, an enzyme important in the converting of primary bile acids to secondary forms and possibly in forming some polycyclic aromatic compounds.[144] Studies *in vitro* indicate that some bile acids may be converted to potentially carcinogenic polycyclic aromatic compounds.[145] Similar observations are reported for certain bacterial species present in stool,[146] particularly a group of lecithinase-negative clostridia. Further investigations are needed to assess the effects of various fiber polymers *in vivo* on mammalian bile acids and their possible role in colon carcinogenesis. The model described in this chapter might be used, although rats are generally not considered the optimal animal for such a study.

F. Fiber and Intestinal Microflora

The possible role of intestinal microflora in colonic cancer is also of great interest.[147] Intestinal bacteria are postulated to have the metabolic potential for transforming precursor exogenous or endogenous agents into active carcinogens or cocarcinogens.[148] Dietary factors, including plant fiber, may influence this microflora and the substrate available for carcinogen or cocarcinogen production. On the basis of stool collections, several studies have reported differences in both quantity and quality of fecal microbes in populations ingesting different diets and having different risks for large-bowel cancer. It is not clear, however, whether these observations on collected stool accurately reflect alterations in microbe populations within the intestine. Furthermore, the present methods for taxonomic grouping of intestinal bacteria may be inadequate for an examination of this question.[149] Recent studies also suggest that the activities of several fecal enzymes including nitroreductase, azoreductase, and β-glucuronidase are dependent, in part, on the diet ingested by experimental animals.[148] Some of these enzymes may have a pivotal function in the metabolism of some environmental carcinogens. In addition, 1,2-dimethylhydrazine administered to experimental animals alters the activities of some fecal enzymes, such as β-glucuronidase.[150] While a definite relationship, if any, to neoplasia remains to be established, the role that each specific fiber polymer might play in the induction or repression of bacterial enzymes requires further difinition.

G. Fiber in Anticarcinogenesis

It has also been hypothesized that some components of dietary fiber may function as antioxidants or free-radical scavengers within the intestine,[9] in a way similar to the activity of agents such as disulfiram. This compound appears to inhibit the *in vivo* oxidation of several agents commonly used for the induction of colonic neoplasia including dimethylhydrazine and azoxymethane and to inhibit experimental animal intestinal tumors induced by either agent. Certain phenolic antioxidants also inhibit colon carcinogenesis in rats treated with

azoxymethane.[151] Whether lignin, which contains phenolic groups,[9] acts through a mechanism similar to these known anticarcinogens remains to be elucidated.

VI. CONCLUSION

While more detailed studies of the role of dietary fiber in the development of colon cancer in humans are certainly required, the experimental animal can provide a useful alternative as a model system for the study of this disease and the fundamental mechanisms involved in its etiology and pathogenesis. With more precise definition of various dietary constituents, including fiber, the relevance of each, if any, to the development of colon cancer may be better understood.

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7

Epidemiology of Colon Cancer: Fiber, Fats, Fallacies, and Facts

Baruch Modan and Flora Lubin

I. INTRODUCTION

Epidemiology is defined as the study of disease distribution in a population. During the past 30 years, this tool has served as a major vehicle for the identification of risk factors in neoplastic disorders.

The epidemiologic approach is usually multistaged. First, one explores the disease distribution in various population strata to define high-risk groups. When these groups have been defined, one looks for distinguishing characteristics of high- or low-risk groups. This can be done either by a correlation of disease incidence with various environmental characteristics such as smoking, income, and diet and/or by more refined analytic case-control studies. Once a differential incidence of a disease in distinct population groups has been determined, the inquiry focuses on the relative importance of genetic and environmental components.

While genetic factors enter the equation, cancer of the colon has been repeatedly considered an example of an environmentally determined disease. This hypothesis stems from the extreme variability in incidence among worldwide population groups, the rapid change in incidence over time and migration, and the distinct demarcation between affluent and developing societies.

Cancer of the colon has also been the most frequently cited example for attributing a causal role to diet. However, dietary findings of epidemiologic

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studies can only be indicative of etiology because of the potentially multifactorial nature of neoplastic disorders. One cannot rule out the involvement of either multiple dietary factors or a single dietary factor acting synergistically with a completely different etiological component.

II. DISEASE DISTRIBUTION

Like most other malignant neoplasms, cancer of the colon is a disease of advanced age. Its incidence in U.S. whites rises continuously from 3 to 4 per 100,000 in the 30–34 age group to more than 3 per 100 of those aged 75 and over.[1] In contrast to many other malignant disorders, the incidence in most populations is approximately equal in men and women.

The highest annual incidence rates for colon cancer have been reported in Scotland, among U.S. and Canadian whites, and in New Zealand. The lowest rates occur most in African countries and especially in Nigeria. The difference between incidence rates in high- and low-risk countries is more than 10-fold (Table 1). Despite the wide geographic variability in its incidence,[1–3] certain consistent patterns appear[1]: relatively high rates of colon cancer are found in populations of highly developed countries and extremely low rates in the developing ones[2]; relatively higher incidences occur among subgroups of higher socioeconomic status, as has been demonstrated by intracountry, interethnic comparisons (for example, between whites and blacks in the U.S.[4] and South Africa,[5] and between Jews of European and Oriental origin in Israel.[6]) Low incidence rates have also been found among American Indians,[7] where the gallbladder and biliary tract, rather than the colon, are the most frequent sites of gastrointestinal malignancies.

On the other hand, the Seventh Day Adventists,[8] who adhere to a strict vegetarian diet, are also at a low risk of the disease that is independent of their socioeconomic status.

Significantly, low rates of colon cancer are also noted in Utah, where over 70% of the population are Mormons. Although the latter observation is consistent with the generally low incidence of cancer at many other sites among Mormons,[9] the low rate of colon cancer may actually be shared by Mormons and non-Mormons in Utah.[10]

Observations indicate similar differences between urban and rural populations in various countries. As a rule, incidence rates are higher in urban populations; for instance, a 5-fold difference in Denmark, 4-fold in Hungary, 2.5-fold in Poland and 1.5-fold in Norway.[1] The low incidence in rural areas is probably related to a lower income and socioeconomic status[5,11,12] rather than to lack of industrial pollutants. Thus, the incidence of colon cancer in Iowa, an affluent but typically corn-belt state in the U.S., is almost identical with that of Alameda County, California, or with that of the state of Connecticut.

Table 1. Mean Annual Age-Adjusted Incidence Rates of Colon Cancer in Selected Countries (circa 1970)[a,b]

Country	Males	Females
U.S. (Connecticut), white	30.1	26.1
U.S. (San Francisco Bay Area)		
White	28.3	24.0
Black	24.0	21.2
Chinese	23.5	13.8
Hawaii		
White	23.9	22.9
Japanese	22.4	18.8
Hawaiian	14.1	16.9
Canada (British Columbia)	23.5	24.1
New Zealand		
White	23.0	23.2
Maori	7.4	14.2
Switzerland (Geneva)	18.9	13.5
Scotland	16.6	18.9
U.K. (Birmingham)	16.5	15.0
Denmark	16.2	17.5
Sweden	15.8	14.7
West Germany (Hamburg)	13.6	13.6
Norway	12.7	13.0
Iceland	12.3	13.8
Singapore		
Chinese	11.9	9.5
Malay	3.4	3.6
Poland (Warsaw)	10.9	8.6
G. D. R.	9.6	9.6
Jamaica	9.1	7.9
Yugoslavia	6.0	6.0
Brazil (São Paulo)	8.7	10.8
Finland	7.9	8.0
Malta	7.0	5.3
Cuba	6.9	8.7
Spain (Zaragoza)	6.5	5.5
Puerto Rico	6.0	6.7
Japan (Miyagi)	5.6	5.4
India	4.6	3.3
Columbia (Cali)	3.2	3.4
Hungary (Szabules-Szatmar)	3.1	2.8
Rumania	3.0	3.6
Nigeria	1.3	1.2

[a]Adapted from Waterhouse *et al.*[1]
[b]Values are given per 100,000.

One other point of interest is the differential incidence of anatomic subcategories of colon cancer. Cancer of the right colon is more prevalent in low-risk groups such as those in Africa or the Seventh Day Adventists, while in high-risk populations, cancer of the left colon is more common.[13–15] This may indicate different etiological factors for distinct colon locations. Recently, a shift has been observed in the anatomic distribution of colon cancer in the U.S. towards relatively more cases in the right, ascending, colon and fewer on the left side.[16–18] The shift may reflect changes in the etiological contribution of specific nutritional patterns, i.e., a decreased exposure to the causal factors that have been associated with affluence. If this trend persists, the change in the relative site distribution should be followed by a decrease in incidence.

A. *Migrant Populations*

The most efficient way to distinguish between genetic predisposition and environmental influence is through studies of migrant populations. A rapid change in disease incidence indicates an environmental role, because of adaptation to newly acquired life habits, some of which are unavoidable. Our transitional society enables us to study this phenomenon in many parts of the world as well as within set societies. Population groups that served as models for such studies include primarily Japanese who moved to Hawaii and the U.S. mainland,[19–20] Poles and Scandinavians who migrated to the U.S.[21,22] and Australia,[23] Indians who moved to South Africa,[24] and Middle Eastern and North African Jews who settled in Israel.[25]

Almost by definition, in the vast majority of cases, the direction of migration is toward a more affluent society. Since colon cancer is a disease of industrialized society, the shift in incidence is, as would be expected, toward the absorbing society.

The consistently reported increase over time in the incidence of colon cancer[26] is compatible with worldwide improvement in the standard of living. So, probably, is the recent equalization of rates between blacks and whites in the U.S.

B. *Etiology*

Diet is the most frequently investigated causal factor in the etiology of colon cancer. The diet hypothesis presumes an interplay of either an ingested or metabolically produced carcinogen and/or a cocarcinogenic factor of certain dietary components. Accordingly, the carcinogenic process would involve one or more of the following pathways:

1. Ingestion of a carcinogen.
2. Enhanced contact with, concentration of, or absorption of a carcinogenic substance.

3. An *in vivo* synthesis of a carcinogen or a metabolic by-product.
4. Facilitation of a carcinogenic activity through the modification of the intestinal flora.
5. Provision of a more favorable milieu for carcinogenesis by either a mechanical or a biochemical tissue change.
6. Lack or disappearance of a protective factor.
7. Modification of the host's immune mechanism.

The implication of specific food components in cancer etiology was first proposed at the beginning of the 20th century.[27] Numerous experiments followed, usually involving such substances as fats, carbohydrates, and total caloric intake. Today most investigative effort centers around high-fat and/or low-fiber intake, focused on the pathogenic mechanisms stated.

The possibility that fiber* may be a protective agent against colon cancer was first presented by Walker and Arvidsson[28] as far back as 1954, other investigations followed[29–31] The recent resurgence of medical interest in this substance, once considered inert, may be credited to Burkitt,[32] who contributed significantly to the popularization and practical implications of the concept.

Current epidemiological inferences about the role of diet in the etiology of colon cancer are based mainly on two types of observations:

1. Correlations between disease incidence and consumption patterns.
2. Case-control dietary studies.

III. CORRELATIONAL STUDIES

Controlled dietary studies and investigations of disease incidence and consumption patterns have been repeatedly employed to indicate a relationship between the consumption of specific food components and disease incidence.

The most consistently cited correlation is that between worldwide colon cancer incidence and the consumption of fat or high-fat food items.[33–36] Other sporadic reports correlated the disease incidence with animal protein,[36,37] tea,[36,38] and sugar,[34–36] while an inverse correlation has been occasionally reported with cereals.[34,36,39]

Changes in disease risk with migration have provided some additional leads. One good example for a process of this kind has been demonstrated recently in a study of Hawaiian-Japanese, a population undergoing displacement from low to high colon-cancer risk, where transition from Japanese- to Western-style diet[40] has simultaneously occurred. Similarly, a significantly higher consumption of such typical American nutrients as beef, lamb, and sau-

*The term "fiber" is used in this chapter to represent the sum of cellulose, water-insoluble hemicelluloses, lignin, pectin substances, gums, and mucilages, i.e., the carbohydrate polymers undigested by human enzyme, plus lignin.

sage was reported among Japanese migrants with bowel cancer in Hawaii than among matched controls.[41]

More general observations show that bowel cancer is extremely rare in developing countries, where much fiber is consumed, and that people residing in such societies and other individuals on high-fiber diets tend to differ in certain bowel characteristics that have been related to the pathogenesis of colon cancer. Thus, their intestinal transit time is shorter, their stools are bulkier, and they have a smaller amount of bile degradation products and a lower anaerobic : aerobic ratio in the intestinal flora.[5,42–44]

Recently, Manousos *et al.*[45] compared intestinal transit times and stool weights of residents of Athens and inhabitants of a small Greek village. The rural group, who conformed to a relatively higher-residue diet, had a shorter transit time and heavier stools. Also, the transit-time values were intermediate between those found in British and Ugandan inquiries, in line with the incidence pattern of colon cancer in the three countries.

An international collaborative group led by McLennan[46] has demonstrated a higher fiber intake in rural Finland, where colon cancer is relatively rare, than in Copenhagen, where its incidence is quite high. Specifically, the fiber intake was 30.9 g/day in the rural area versus 17.2 g in Copenhagen, in the presence of a fourfold differential in colon cancer incidence.

Conclusions from these correlational observations are, however, hampered by two facts. First, the human individual's diet consists of a large variety of components, which are not consumed independently; e.g., people having a high intake of one group of foods have a low intake of another group.[47] Second, food consumption patterns are highly correlated with other life habits that differ markedly between industrial and developing societies. Therefore, such correlations can be misleading.

IV. CASE-CONTROL STUDIES

It appears that a more refined approach to the determination of the etiology of colon cancer consists of interview studies of dietary intake, even though the number of such studies is surprisingly small. The first case-control dietary study of "cancer patients" was started about 50 years ago in London under the guidance of Percy Stocks.[48] However, the conglomerate of "cancer" was not split into site categories. Following the initial effort, this approach was left dormant until the 1950s when an upsurge of dietary studies started, increasing in momentum in the current decade. Early studies by Boyd and Doll,[49] Pernu,[50] Higginson,[51] Wynder and Shigamatsu,[52] and Wynder *et al.*[53] yielded very limited information. In contrast, more recent investigations formed two consistent patterns, which are compatible with previously obtained noncontrolled observations.

The main findings are summarized in Table 2 under four major categories: fiber, vegetables, fats, and meat. Thus far, high-fiber items, particularly vegetables, have emerged as protective agents for colon cancer in four such studies.[54–58] Fat and beef have been directly incriminated in two.[8,62]

A study conducted by our group in Israel,[54] based on 198 histopathologically confirmed colon-cancer patients and two matched control groups, may serve as an illustrative example. Each individual was interviewed with regard to consumption of 243 food items up to 1 year prior to diagnosis. Indirect quan-

Table 2. Summary of Dietary and Related Findings of Case-Control Studies

Author	Food item/group	Place	Year	Remarks
		Dietary Findings:		
Dales *et al.*[58]	Fats, vegetables,[a]fiber[a]	San Francisco	1979	Black patients only, statistically significant differences noted only for combination of high fat–low fiber; in the rest, just a trend.
Graham *et al.*[57]	Vegetables[a]	Buffalo	1978	Reliability of interview through reinterview; separate analysis for males and females; findings present also for rectum but females only.
Modan *et al.*[54]	Fiber; vegetables,[a] fruits[a]	Israel	1975	Separate item and frequency analysis; no separate analysis by sex; reinterview; present and past diet.
Phillips[8]	Fats, meat, fish, white bread, fresh fruits[a]	Utah	1975	Separate analysis for current and previous data; preliminary report; small sample size.
Bjelki[55,56]	Meat, vegetables[a]	Norway and Minnesota	1974	Dietary information obtained by mail; age match within 10 years; pooled controls; information up to 1 year prior to illness; earlier food frequency asked for; reinterview.
Haenszel *et al.*[62]	Fats, meat, starches	Hawaii	1973	Colon and rectum analyzed together; cases not matched on nativity; analyzed separately.
Wynder *et al.*[53]	Fresh fruits, milk, rice[a]	Japan	1969	Summary emphasized meat consumption as risk factor for colon cancer but data do not show it.

[a]Eaten less often.

(continued)

Table 2. (Continued)

Author	Food item/group	Place	Year	Remarks
		Related Findings:		
Higginson[51]	Laxatives	Kansas	1966	Small sample; reinterview of 37 patients; composition of control groups not entirely clear; hospital only; group analysis for colon and rectum.
Pernu[50]	Food temperature	Finland	1960	Main questionnaire only to surviving patients; 30% nonresponse in cases, 60% in controls; selective control group; inconsistent findings in males and females for fats and sugar; group analysis for colon and rectum.
Boyd and Doll[49]	Laxatives	U.K.	1954	Secondary evaluation of lung cancer study; some differences in residue between cases and controls; cannot be considered as a diet study; group analysis for colon and rectum.

tification was based on frequencies ranging from at least once daily to several times a week, several times a month, rarely, and never. Any major changes in frequencies during the past 10 years were also recorded. Various food groups were analyzed by comparing intrapair frequencies between case and each control.

Fiber turned out to be the only food group where significant differences were noted in comparison with both controls (Table 3). These observations are strengthened by two additional findings. First, no such differences were found in other sites of gastrointestinal cancer, simultaneously studied by us, where such an association seems less plausible.[54,59] Second, the higher frequency of fiber consumption among controls was not limited to a few food items but was present in most of them. Thus, out of 73 items originally labeled as having a relatively high fiber content, 61 and 57, respectively, were consumed less frequently by the cancer patients than by the neighborhood and surgical controls. Again, no such effect was noted for other gastrointestinal sites; for instance, the respective numbers for rectal cancer were 37 and 38 (Table 4).

Compatible results were obtained in three other studies,[55–57] conducted

with a methodology fairly similar, in three entirely different settings. Bjelke[55,56] found a decreased consumption of vegetables and a "low fiber index" in 162 colon cancer patients in Norway and in 259 patients in Minnesota as compared with two large control groups.

More recently, Graham *et al.*[57] demonstrated a lower frequency of vegetable consumption among 470 patients with colon cancer in Buffalo as compared with 783 controls. The study included both males and females. Similar information comes from a most recent study conducted in San Francisco among blacks by Dales *et al.*,[58] where low intake of foods with at least 0.5% fiber was reported in 72 colon cancer cases.

All these studies can also be construed as consistent with a protective effect of certain vegetables' compounds rather than fiber. Such an interpretation was favored by Graham and is supported by Wattenberg's laboratory findings[60,61] of an inhibition of tumor carcinogenesis in animals when they were fed certain specific vegetables, either raw or cooked.

In contrast, Haenszel *et al.*,[62] in a study based on 179 Japanese large-bowel cancer patients in Hawaii and 357 hospital controls, found a higher consumption of beef and certain legumes among cancer patients. Similar findings

Table 3. Summary of the Comparison of the Consumption Patterns of Major Food Groups between Cancer Cases and Controls[a]

Food group	Number of items in list	*p* Value: Colon cancer patients compared with neighborhood controls	*p* Value: Colon cancer patients compared with surgical controls
Fiber	73	0.001	0.05
Fats	12	0.68	0.89
High-fat items	43	0.98	0.46
Starches	50	0.49	0.85
Sugars	23	0.37	0.78
Animal protein	56	0.16	0.85
Vegetable protein	12	0.18	0.04
Salted foods	23	0.60	0.10
Artificial additives	22	0.95	0.90
Fat antioxidants	25	0.53	0.70
Alcoholic beverages	9	0.01	0.23
Carbonated drinks	8	0.57	0.42
Pepperin spices	5	0.92	0.98
Aromatic spices	6	0.04	0.14

[a]Modan *et al.*[54]

Table 4. Distribution of Fiber Items According to Direction of Mean Difference in Consumption Frequency of Each Item between Colon and Rectal Cancer Patients and Their Matched Controls[a,b]

Direction of mean intrapair item difference in consumption frequency[b]	Cancer patient to neighborhood control		Cancer patient to surgical control	
	Colon	Rectum	Colon	Rectum
Lower	61	37	57	38
Higher	12	33	16	35
Equal	—	3	—	—
Total number of items	73	73	73	73
p (Sign test)	0.001	0.56	0.001	0.70

[a]Adapted from Modan *et al.*[54]

[b]Items consumed less frequently by colon cancer patients than by both control groups: apples, apricots, artichokes, avocados, dried black beans, dried fava beans, fresh fava beans, fresh lubia beans, dried white beans, beets, cabbage, red cabbage, carrots, chick peas, chick-pea salad, "cholent," corn, cucumbers, dates, eggplant, grapefruit, grapes, groats, guavas, kohlrabi, lentils, melon, green olives, stuffed olives, olives, oranges, parsley, peaches, dried peas, fresh green peas, pears, green peppers, red peppers, pickles, plums, pomegranates, radishes, sabras (prickly pears), sauerkraut, seed (sunflower etc.), tangerines, tomato sauce, turnips, watermelon.

Items eaten less often by colon cancer patients than by neighborhood controls but more frequently than by surgical controls: bananas, string beans, yellow fresh beans, cauliflower, halva, halva spread, lettuce, mushrooms, potatoes, squash, strawberries, tomatoes.

Items consumed less frequently by colon cancer patients than by surgical controls but more often than by neighborhood controls: almonds, celery, figs, dried fruits, leeks, okra, black olives, peanuts.

Items eaten more often by colon cancer patients than by both control groups: bourghyl, oats, spinach, walnuts.

[c]As determined by direction of the mean difference in consumption frequency of each item over all case-control pairs.

were given in a preliminary report of a study by Phillips[8] of 41 Seventh Day Adventists and 126 controls. A study by Dales *et al.*[58] indicated a higher consumption of saturated fat, though a lower one for beef, among the colon cancer patients.

Dietary studies can be criticized because of deficient recall, inaccurate quantification, food interaction, and inability to determine the time of onset of the carcinogenic process and so the relevant diet at that time. Long-term prospective studies may not provide a practical alternative. If recent diet does not represent the individual's long-term nutritional patterns, obtaining dietary information at one particular point in time does not ensure against future changes. Consequently, the nutritional pattern involved in the carcinogenic process may not be the one obtained. On the other hand, consistently observed results of well-validated retrospective dietary studies[63] may be valuable in providing leads if they can be fitted into a working model.

A. The Working Model—A "Jigsaw Puzzle"

The expression, "working model—a 'jigsaw puzzle,' " part of which was borrowed from Burkitt,[64] demonstrates the complexity of the problem: the evaluation of observed relationships between certain nutritional patterns and colon cancer in the light of descriptive data on cancer incidence in distinct population groups and experimental evidence on gut metabolism under differential dietary intake. The descriptive data indicate an environmental factor with a roughly similar exposure in both sexes, which is more prevalent in developed societies, and which is rapidly acquired once the individual is absorbed into a new high-incidence surrounding. Low-fiber intake and/or high-fat consumption do seem to provide the most obvious leads.[65,66] However, the delineation of one specific dietary factor may be an almost impossible mission.

The descriptive data are consistent with correlational observations and dietary case-control studies pointing towards a dietary factor that is either more or less frequently consumed in affluent populations. The findings are further supported by animal experimentation.[67–70]

To date, the following effects of fiber have been suggested as being protective[71–80] (see Fig. 1):

1. Shortening of intestinal transit time.
2. Bulkier stool.
3. Lowering of absorption of potential carcinogens.
4. Reduction of conversion of bile salts to potentially carcinogenic sterols.
5. Reduction of available cholesterol through binding.
6. Influence toward a lower anaerobic : aerobic ratio in intestinal flora, which in turn affects bile-salt degradation.

With the exception of intestinal transit time and bulkier stools, deleterious effects of a high-fat diet could be easily construed along simililar lines.[2,81–85] In either case, the potential pathogenetic pathway [11] for the carcinogenic process implies a longer or a closer contact with the gut mucosa as well as an increased conversion of sterols and a higher availability of potentially carcinogenic metabolities.

B. Prospects

One of the most intriguing recent epidemiologic observations has been the correlation between the risk of breast cancer, colonic cancer, and arteriosclerotic heart disease in many countries and population groups.[86,87] The reason for this odd triad is unclear. High-fat diet has been claimed as a common denominator for all three diseases. On the other hand, an unexpected result of a 20-year prospective study conducted by Morris and his associates[88] revealed that fiber rather than fat was the only food group of influence in the development

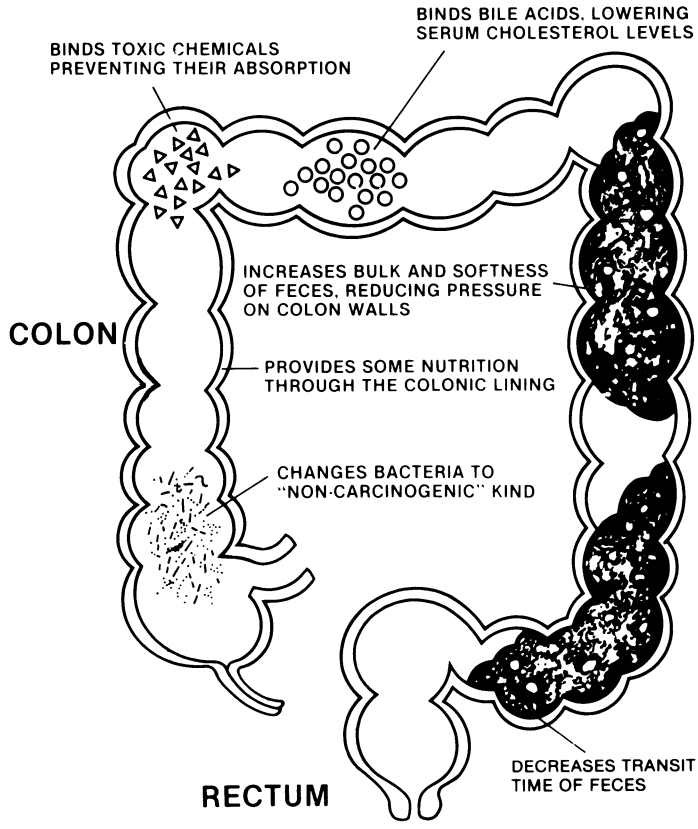

Figure 1. Protective properties of fiber. Reprinted with permission, from: Smith, R. D. *The Sciences* **16**:25–29, 1976.

of subsequent coronary events. This is thought compatible with the lowering effect of fiber on blood lipids[89–92] and suggests similar pathways towards protection in the three disorders.

The crux of the issue is the real identity of "fiber," and how we define high-fiber food. The questions become especially pertinent in view of the fact that by now we know that, despite certain common properties, fiber does not constitute a homogeneous group from the standpoint either of chemistry and biology or of disease etiology.[93–96] To the contrary, this broad category, also called "plantix"[97] to underline the plant origin, encompasses a variety of substances differing in their biochemical composition and their potentially physiologic action.[98–100] Therefore, one cannot rule out the possibility that a specific component,[101] e.g., cellulose or hemicellulose, is protecting against colon cancer through its effect on bowel contents, while another, pectin or lignin, for example, is most influential in protecting against arteriosclerotic heart disease or breast cancer through its cholesterol-binding capability.

One may also wonder to what extent the decisive etiological factor can be pinpointed. According to an approach of this kind, once it has been established that certain compounds, whether referred to as "fiber" or "vegetables," confer a protective effect, the epidemiologist has apparently fulfilled his role in disease prevention. To us, such an attitude does not seem justified in view of the past continuously preached emphasis on high-fat diet as a plausible risk factor in the etiology of coronary heart disease, which has kept research in preventive cardiology at a standstill for the past 20 years.[102]

Nevertheless, the most dangerous consequence in epidemiology is stagnation. It is much easier to repeat previous observations than to look for a new hypothesis.

It must be recalled that the consistency of observations in the vast majority of recent studies may still mask an entirely different variable. Although we seem to favor the fiber theory, albeit not necessarily bran,[103] we cannot discard the potential etiologic contribution of fats nor the possibility that these two components may act synergistically.

By the same token, it has yet to be determined whether the physicochemical properties of fiber are indeed operating to provide metabolic protection, or whether the main factor is an anticarcinogenic effect of certain vegetables which also happen to be high-fiber items, as indicated by Wattenberg's laboratory studies.[60,61] Descriptive data on low disease incidence in developing societies and among Seventh Day Adventists, who conform to vegetarian diets; the results of the majority of well-designed case-control studies, and experimental evidence are compatible with both interpretations. Only the accumulation of more data can yield a definite answer.

The strength of epidemiology lies in the fact that data obtained from independent studies, using a variety of methodological approaches and populations, build toward a hypothesis that is then fitted into a model; but, despite the apparent simplicity of the epidemiologic method, it does have limitations.

Although the hypothesis that the etiologic agent in colon cancer is either diet-acquired or metabolically produced is very tempting, it is by no means exclusive. Effort should still be directed toward a microdissection of specific fiber and fat compounds and toward scrutiny of a multitude of other parameters that are strongly correlated with both low-fiber- and high-fat-consumption patterns.

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8

Dietary Fiber and Lipid Metabolism: An Update

Jon A. Story

I. INTRODUCTION

The origins of the current interest in the role of dietary fiber in lipid metabolism came from a large body of epidemiological data that appeared in the early 1970s. These data compared the incidence of diseases common in the Western world with their incidence in native African populations.[1-3] The extremely high consumption of dietary fiber in the African populations studied was suggested as a possible explanation for their decreased susceptibility to "Western"-type diseases. A great deal of discussion has ensued concerning the validity of these arguments as well as possible mechanisms for the involvement of dietary fiber in individual disease processes.[4-7]

During this time, we have put forward a suggested mechanism for the action of dietary fiber on lipid metabolism.[8,9] This discussion will center on the evidence that is accumulating concerning the validity of our suggested mechanism and review possible alternatives and additions to the original theories.

II. WORKING HYPOTHESIS

The main involvement of dietary fiber in lipid metabolism centers around its interactions in bile-acid metabolism with resulting changes in lipid absorption and excretion and, further, in synthesis and degradation of lipids. The

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observation that commercial rations and some dietary fiber sources resulted in lower serum cholesterol levels in rabbits[10–12] and increased excretion and pool sizes of cholic acid in rats [13] prompted investigation of possible mechanisms by which dietary fiber may exert its effects. Other studies[14,15] also indicated reduced bile-acid synthesis and cholesterol absorption when alfalfa was compared with cellulose as a source of dietary fiber.

The interaction of bile acids with dietary fiber was first reported by Eastwood and Boyd.[16] They observed that appreciable quantities of bile acids in the small intestine were sequestered with the insoluble portion of the intestinal contents. Subsequent *in vitro* experiments[17,18] indicated that some sources and some fractions of dietary fiber adsorb bile acids. In general, these studies indicate that there is a great deal of variation in the ability of various sources of dietary fiber to adsorb bile acids. Likewise, some fractions of dietary fiber, such as lignin, seem to adsorb bile acids better than others. The mechanism involved seems to be hydrophobic in nature but cannot be totally attributed to hydrophobic interactions. More recent evidence concerning this adsorption phenomenon will be discussed later.

The demonstration of bile-acid adsorption by dietary fiber made possible the formulation of the current working hypothesis for the mechanism of the role of dietary fiber in lipid metabolism. The adsorption of bile acids by dietary fiber has two main effects on cholesterol metabolism (Fig. 1). First, adsorption increases excretion of bile acids in the feces, which reduces the amount returning to the liver via enterohepatic circulation. To compensate, the liver synthesizes more primary bile acids. If this increase in degradation of cholesterol is not met by increased cholesterol synthesis, cholesterol levels decrease. This phenomenon is similar to that observed with bile-acid sequestrants such as cholestyramine. Second, if bile salts are adsorbed by dietary fiber in the small intestine and are unavailable for micellar interactions, absorption of dietary and biliary cholesterol, as well as all lipids dependent on the micelle for absorption, would be reduced. Again, depending on the efficiency of the control of cholesterol synthesis, serum and tissue cholesterol levels would decrease. Potentially, other lipid levels would also decrease as a result of decreased absorption.

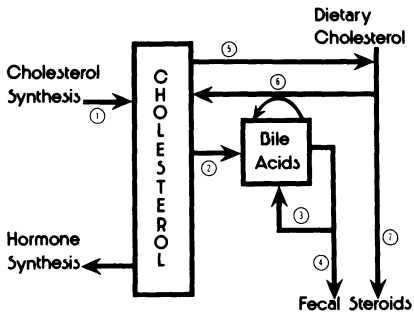

Figure 1. Cholesterol and bile-acid metabolism. 1: Cholesterol synthesis; 3-hydroxy-3-methylglutaryl coenzyme-A (HMG-CoA) reductase; rate-controlling step for cholesterol synthesis. 2: Bile acid synthesis; cholesterol 7α-hydroxylase, first and rate-controlling step in bile-acid synthesis. 3: Enterohepatic circulation of bile acids. 4: Fecal excretion of bile acids. 5: Biliary cholesterol. 6: Cholesterol absorption requiring bile salts. 7: Fecal excretion of neutral steroids.

The balance of this discussion will evaluate the validity of the working hypothesis in light of recent evidence concerning the nature and magnitude of changes in lipid metabolism.

III. EVALUATION OF HYPOTHESIS

A. Adsorption of Bile Acids and Salts

Subsequent to the observations that bile salts are adsorbed or bound to dietary fiber,[16–18] a great deal of evidence has accumulated concerning this phenomenon. It soon became obvious that generalization about the amount of various bile salts or acids bound by one type of dietary fiber was usually in error.[19,20] Each source of dietary fiber finds each of the bile acids or salts to a different degree. Similar information has been used to theorize about the mechanisms involved in adsorption. A primary mechanism of adsorption appears to be hydrophobic in nature, but other mechanisms are probably involved.[17,20]

Of major concern to those working with the adsorption process was the possibility that absorption of solvent with dissolved solute was responsible for a majority of the observed binding. Eastwood *et al.*[21] have designed a method for measuring adsorption in the absence of absorption. A standard *in vitro* incubation of dietary fiber with a bile-acid solution is followed by repeated washings with buffer. Data derived from this method (Table 1) indicate that

Table 1. Adsorption of Deoxycholic Acid by Dietary Fiber before and after Washing with Buffer

	Deoxycholate adsorbed (%)			
	2.5 mM[a]		5.0 mM[a]	
Dietary fiber	I[b]	II[c]	I	II
Carrot[d]	80	65	80	65
Pea[d]	74	51	67	53
Bran[d]	53	32	42	23
Celery[d]	63	32	61	34
Bran[e]	39	26	33	19
Alfalfa[e]	38	24	38	27

[a]Concentration of deoxycholic acid in phosphate buffer (pH 8.0).
[b]I: Initial adsorption.
[c]II: Adsorption after one washing with phosphate buffer (pH 8.0).
[d]From Eastwood *et al.*[21]
[e]From Story *et al.*[72]

adsorption is real and is independent of the water-holding capacity of dietary fiber. Gross binding is, however, definitely influenced by the amount of solute held by absorbed solvent.

Adsorption of bile salts from micellar suspensions was first attempted by Balmer and Zilversmit.[22] They observed that a stock diet and several dietary-fiber-containing components of a stock diet (alfalfa meal, ground wheat, corn, etc.) bound significant quantities of both cholesterol and taurocholate from micelles.

Eastwood and Mowbray[23] subsequently examined adsorption of micellar components from micelles typical of those found in various parts of the small intestine. They found that adsorption is minimal in the jejunum where micelles are rich in the products of triglyceride digestion. In the ileum, adsorption is more likely to affect bile-salt absorption. In the large intestine, the amount of adsorption is dependent on the relative amounts of primary and secondary bile acids which, in turn, are partly determined by the microflora activity of the cecum and large intestine. This activity is also affected by the source and amount of dietary fiber present.

Recently, Vahouny *et al.*[24] have also examined the binding of bile salts and cholesterol by several sources of dietary fiber in micellar solutions. Alfalfa meal bound 10% of micellar cholesterol and displayed a preference for unconjugated bile acids. Cellulose and bran did not bind bile salts, but bran did bind a significant portion of micellar cholesterol present (38%). These results indicate an *in vitro* interaction of alfalfa and bran with micellar lipids. The exact role this effect might play in lipid absorption is not clear, since previous studies with alfalfa and bran showed only alfalfa to be hypocholesteremic.

Since the adsorption phenomenon appears to be real and not just an artifact of water absorption, an examination of the effects of particle size on adsorption should be revealing. Burczak and Kellogg[25] have recently examined the role of the particle size of oats and wood particles and their bile-acid-adsorption properties. Wood-shaving particle size was very closely related to the amount of bile acid (cholate, deoxycholate, and chenodeoxycholate) adsorbed, with adsorption increasing as particle size decreased. They did not observe the same relationship with oats, in spite of a higher level of adsorption. Deoxycholate adsorption seemed to be related to particle size, but cholate and chenodeoxycholate adsorption were not. Use of the Eastwood *et al.*[21] washing method might have indicated a difference in the real adsorption of all materials. If we are to ascribe adsorption of bile acids by dietary fiber to any of the classical adsorption mechanisms, surface area should definitely alter the amount of adsorption. Particle size is a simplistic method of altering surface area. A more thorough examination of this relationship should help shed light on the nature of the adsorption mechanism. Until then, measurement and control of particle size are steps toward avoiding confusion and misinterpretation of results.

A question of the importance of saponins in the adsorption process has been raised by Oakenfull and Fenwick.[26] Their data indicated that only materials containing saponin adsorbed bile acids in the system used. Additionally, extraction of saponins with 80% ethanol resulted in a loss of adsorption by these materials. Several points of disagreement between the data presented and those presented previously[17,18] need to be clarified. The pH of bile-acid solutions used, much lower than those used by others, has been shown to decrease adsorption.[17] Lignin, isolated by several methods, has been shown by other workers to adsorb bile acids.[17,20,27] This lack of adsorption of lignin[26] cannot be easily explained. These data emphasize the importance of control of methodology and attention to detail in organization of investigations.

Currently, we have examined the bile-acid adsorption of alfalfa and bran using a modification of the Eastwood *et al.*method.[21] Using two extraction schemes, we have sequentially removed various fractions of the plant material and measured the adsorption of the remaining fraction (Table 2). Adsorption was enhanced by the removal of saponins, possibly as a result of concentrated adsorbing components. No appreciable reduction in adsorption was seen until delignification, regardless of the extraction scheme used. These findings agree with earlier experiments conducted by Eastwood and Hamilton[17] and seem to be in direct conflict with the work reported previously by Oakenfull and Fenwick.[26]

Adsorption of bile acids by dietary fiber appears to be a key characteristic in its effects on lipid metabolism. However, we still face many problems in understanding the exact nature and mechanisms of adsorption. Careful control of conditions and materials used in adsorption will help solve these problems.

Table 2. Adsorption of Deoxycholic Acid by Various Fractions of Alfalfa and Bran[a]

Fraction	Alfalfa		Bran	
	2.5 mM	5.0 mM	2.5 mM	5.0 mM
Scheme 1				
Whole plant material	1.00 (38.3)[b]	1.00 (38.4)[b]	1.00 (38.2)[b]	1.00 (32.0)[b]
Less fat solubles	0.91	0.97	0.97	1.09
Less saponins	1.09	1.13	1.25	1.52
Less pectins	0.98	1.01	1.04	1.20
Less lignin	0.32	0.34	0.36	0.36
Scheme 2				
Whole plant material	1.00 (38.2)[b]	1.00 (35.9)[b]	ND	ND
Less saponins	1.09	1.20		
Less pectins	1.00	1.12		
Less lignin	0.34	0.25		

[a]3 ml [^{3}H]deoxycholate (2.5 or 5.0 mM) in phosphate buffer (pH 8.0) incubated with 100 mg adsorbing material.
[b]Whole plant material taken as 1.00. Actual percentage adsorption given in parentheses.

More basic questions concerning physical and chemical composition of the dietary fiber or dietary fiber components used in adsorption studies must also be considered before a complete understanding of the nature and importance of bile-acid adsorption in lipid metabolism can be established.

B. Lipid Metabolism

If we are to be able to accept the hypothesis of the interaction of dietary fiber with bile acids stated earlier, many changes in lipid metabolism would result which should be measurable in experimental animals. Among these should be a general decrease in lipid absorption, increased excretion of neutral and acidic steroids in the feces, decrease in tissue lipid levels, and, depending on the species in question, changes in synthesis rates of cholesterol, bile acids, and other lipids. This section will attempt to update our knowledge of the changes in these variables occurring with various sources and components of dietary fiber.

One of the first and possibly most important findings concerning dietary fiber was the observed inaccuracy of generalization. No two sources of dietary fiber seem to have the same effect on lipid metabolism. For example, in spite of its effectiveness in treating diverticular disease,[28,29] wheat bran was repeatedly shown to have little effect on serum lipids.[30] Arvanitakis *et al.*[31] reported a similar inability of bran to alter the hypercholesteremic effects of an atherogenic diet fed to rats. Serum and liver triglycerides and liver cholesterol increased in spite of the inclusion of bran in the atherogenic diet. However, the more recent finding that one type of bran (hard, red spring wheat) resulted in reduced serum cholesterol in humans[32] indicates that each source of dietary fiber should be considered individually.

A possible explanation for the differences in the effects of various sources of dietary fiber results from variation in the effects of the components of dietary fiber. The components occur in different proportions in each plant source and have dissimilar effects on lipid metabolsim. Thus, the net effect of a dietary fiber source may be determined by the proportions of these components.

As has been described earlier, lignin seems to be a very active component in bile-acid adsorption. Judd *et al.*[33] have shown lignin to be hypocholesteremic in rats fed at 3% of the diet. This was accompanied by a 14% increase in fecal neutral-steroid excretion but with little change in fecal acid steroids. We have also shown that lignin prevents progression of lipid accumulation in rats fed a 0.5% cholesterol diet.[34] Lignin has been used in humans to lower serum cholesterol[35,36] with inconsistent results. Experimentally used lignin may have little in common with lignin as it occurs in plants. Isolation methodology results in serious modification of lignin's structure. This problem occurs with most of the components of dietary fiber and is of central importance in the clarification of the role of fiber, as present in the diet, in lipid metabolism.

Cellulose has, in general, been found to have little effect on lipid metab-

olism. Tsai *et al.*[37] fed 7% cellulose with 0.5 % cholesterol to rats and observed an increase in liver cholesterol level (32%) and no change in serum cholesterol. Others have observed little change in serum or liver cholesterol levels in response to cellulose feeding.[14,15,33] Looney and Lei[38] found no change in the serum cholesterol of rats fed cellulose (0.8% or 16%) except when accompanied by copper deficiency, which they considered possibly a problem in copper availability rather than a direct effect of cellulose on lipid metabolism. Hamilton and Carroll[39] have reported increased levels of serum cholesterol in rabbits fed 20–40% cellulose in a cholesterol-free, semipurified diet. A diet of this sort, containing cellulose, has been previously found hypercholesteremic and atherogenic when compared with a commercial diet fed to rabbits for many years.[40–42] In chickens, cellulose (15%) does decrease both serum and egg yolk cholesterol levels.[43] Much of this work was done with α-cellulose from wood, which would have properties different from cellulose from food sources and thus may alter the observed effects.

Little evidence has been generated concerning the effects of purified hemicellulose on lipid metabolism because of its lack of availability from any source. Some work has been done with materials containing large proportions of hemicellulose. Psyllium seed has been shown to prevent accumulation of cholesterol in rats[44] and man.[45,46] In both cases, an increase in bile-acid excretion rates has also been reported.[44,46,47] Little recent work has investigated this relationship further.

The components of dietary fiber which have received the most attention have been pectins and gums; these are mainly water-soluble materials. Pectin has been repeatedly shown to prevent accumulation of cholesterol in a variety of experimental animals and diets. Several studies on rats have reported decreased plasma and/or liver cholesterol in response to pectin feeding.[34,37,48-50] Pectin has also been shown to reduce serum cholesterol in rabbits[51] and chickens.[52,53] Ershoff and Wells[48] reported that a methoxyl content of 10% or more was essential for this hypocholesteremic effect in rats. More recently, Judd *et al.*[54] have not found any relationship to methoxyl content but indicate the effects are closely related to the viscosity of the pectin used. Early investigations with rats indicated that this reduction was accompanied by an increase in bile-acid excretion but not in neutral-steroid excretion.[55] Human experiments have reported an increase in both neutral- and acidic-steroid excretion,[56] but the magnitude of change in steroid excretion resulting from pectin feeding did not seem to be sufficient to cause the observed change in plasma cholesterol level.

A large number of other noncellulosic polysaccharides have also been reported to prevent or reverse cholesterol accumulation in experimental animals. Guar gum has been reported to lower cholesterol levels,[37] while other gums have yielded conflicting results.[37,50,57] Again, a lack of analytical data, uniformity of materials used, and agreement on animal models has prevented an understanding of the exact role of these materials in lipid metabolism.

Under steady-state conditions, increases in bile-acid excretion are accompanied by increases in bile-acid synthesis. A concomitant increase in cholesterol synthesis can be expected. Reiser *et al.*[58] reported that rats fed a semipurified diet using cellulose as a source of dietary fiber had a much lower rate of cholesterol synthesis, liver microsomal 3-hydroxy-3-methylglutaryl-coenzyme-A (HMG-CoA) reductase. As seen in Table 3, none of the changes attempted returned the synthesis rate to the level of a stock diet with the exception of pectin added to replace one-half of the cellulose. Accompanying the increased HMG-CoA reductase, fecal neutral and acidic steroids, reduced by the semipurified diet, were returned to normal upon addition of pectin. We have also observed an involvement of alfalfa and bran in both cholesterol synthesis and degradation.[59]

Cholesterol absorption may also be affected by dietary fiber as a result of interactions with bile acids in the small intestine. Balmer and Zilversmit[22] reported decreased absorption of cholesterol in response to several sources of dietary fiber. Mathé *et al.*[60] observed reduced serum cholesterol levels in rats fed pectin (5%), and reduced liver cholesterol levels when either pectin or bran (10%) was fed. Using an isotopic dilution method for examining cholesterol turnover, they found that neither bran nor pectin changed the absorption coefficient for cholesterol significantly. Fecal excretion of steroids was not significantly increased by pectin feeding but was dramatically higher when a stock diet was fed. Using cannulation of the thoracic duct and measurement of appearance of a dose of radioactive cholesterol in lymph as a measure of absorption, Vahouny *et al.*[24] reported lowest rates of appearance when bran, cholestyramine, or cellulose was fed. Alfalfa and commercial rations yielded the highest rate of appearance (Table 4). These data seem to dispute the

Table 3. Effect of Dietary Components on Liver Microsomal HMG-CoA Reductase in Rats[a,b]

Diet	HMG-CoA reductase
Commercial ration (C)	100[c]
Semipurified diet (SP)[d]	26
SP with fat from C	24
SP + 0.05% cholesterol	26
SP + 0.04% β-sitoserol	46
SP with starch for sucrose	38
SP with soya protein for casein	55
SP + cellulose (7.5%) and pectin (7.5%)	115

[a]From Reiser *et al.*[58]
[b]HMG-CoA: 3-hydroxy-3-methylglutaryl coenzyme-A.
[c]0.447 ± 0.059 nmol/min/mg microsomal protein.
[d]Sucrose, 54% casein, 19.5%; cellulose, 14.5%; salt and vitamin mix, 4.5%; and fat mixture, 7.5%.

Table 4. Appearance of [^{14}C]Cholesterol in Lymph of Rats Fed Various Types of Dietary Fiber[a]

Diet	Absorption of cholesterol (%)			
	4 hr	8 hr	12 hr	24 hr
Commercial ration	15	29	40	53
Alfalfa[b]	16	27	33	48
Cellulose	10	18	23	34
Cholestyramine[c]	7	17	20	26
Bran	7	15	19	25

[a]From Vahouny *et al.*[24]
[b]Semipurified diet: 40% dextrose, 25 g casein, 14 g corn oil, 6% salt and vitamin mixes, and 15 g test material.
[c]Added at 2%, dextrose, 53%.

hypothesis of decreased absorption of cholesterol in response to the feeding of alfalfa or commercial diets. More complete information on cholesterol and bile-acid turnover was not available in these studies. Since neither bran nor cellulose adsorb appreciable quantities of bile acids, an alternate explanation for the observed effects on cholesterol absorption is required.

Fecal excretion of bile acids and neutral steroids has been reported to increase in most experiments in which the source of dietary fiber has resulted in a decrease in serum and/or liver cholesterol level. Nigro *et al.*[61] have recently investigated the effects of alfalfa, bran, and cellulose on fecal steroid excretion and susceptibility to intestinal chemical carcinogenesis (Table 5). As can be seen, when a high-fat diet (35%) is used in conjunction with 10% fiber material, concentrations of bile acids and neutral steroids were not changed significantly when compared with a fiber-free diet. However, total daily excretion of bile acids was increased significantly by alfalfa and cellulose, and neutral steroids by cellulose and bran. When a lower fat diet (7%) and 20 or 30% alfalfa, bran, or cellulose was fed, both fecal neutral- and acidic-steroid concentrations decreased significantly in all animals, while total daily excretion was not changed significantly. It was noted that increased susceptibility to chemical carcinogenesis was best correlated with fecal bile-acid concentration, an important consideration when examining the usefulness of dietary fiber in lowering serum cholesterol.

C. Other Possible Mechanisms

Many other factors that vary with the amount and source of dietary fiber have been suggested as partial explanations for the observed effects on lipid metabolism. Among these are transit time, alterations in microflora, and actions of specific microfloral metabolites. Few or no data have been generated

Table 5. Fecal Neutral- and Acidic-Steroid Excretion in Rats Fed Alfalfa, Bran, or Cellulose[a]

Dietary fiber		Fecal steroids[b]			
		Neutral		Acidic	
		mg/g dry feces	mg/rat/day	mg/g dry feces	mg/rat/day
Experiment I[c]					
None		1.00 (4.78)	1.00 (5.73)	1.00 (2.24)	1.00 (5.13)
Alfalfa	(10%)	0.71	2.08	1.03	1.44
Bran	(10%)	1.26	2.10	1.39	1.22
Cellulose	(10%)	0.95	2.82	0.82	1.27
Experiment II[d]					
None		1.00 (7.98)	1.00 (5.67)	1.00 (5.46)	1.00 (3.87)
Alfalfa	(20%)	0.32	0.79	0.49	1.20
	(30%)	0.29	0.88	0.37	1.16
Bran	(20%)	0.38	0.77	0.42	0.84
	(30%)	0.35	0.82	0.35	0.81
Cellulose	(20%)	0.22	0.78	0.34	1.24
	(30%)	0.29	1.27	0.19	0.76

[a]From Nigro *et al.*[61]
[b]Control levels in parentheses.
[c]Basal diet: 5% dextrose, 33% casein, 7% beef fat, and 6% salt and vitamin mixes. Dietary fiber source added at expense of dextrose.
[d]Basal diet: 3% dextrose, 25% basein, 35% beef fat, and 6% salt and vitamin mixes. Dietary fiber source added at expense of dextrose.

to support or deny many of these theories. It has been suggested, at first perhaps frivolously, that the lipoprotein profile may change in response to dietary fiber. Chen and Anderson[62] reported that while serum total cholesterol was reduced, high-density lipoprotein (HDL) cholesterol levels increased significantly in rats fed 10% guar gum, oat bran, or pectin (compared with 10% cellulose). Earlier, Berenson *et al.*[51] had reported reduced HDL in rabbits (as a percentage of total cholesterol) when pectin was added to commercial rabbit ration with cholesterol, serum total cholesterol was also decreased. Again, any generalization about the type of fiber fed would seem ill-advised. In humans, Durrington *et al.*[63] have reported no change in HDL, but low-density lipoprotein (LDL) cholesterol was reduced when pectin (12 g per day) was fed. Preliminary results reported by Anderson and Chen[64] indicate that 60 g/day dietary fiber from mixed dietary sources reduced LDL and increased HDL cholesterol levels in humans. The final HDL levels were above those of a normal control population. They suggested that fiber modifies lipoproteins by an alteration in the nature of the chylomicrons secreted into the lymph from the intestine. This could be a result of a change in the site or rate of lipid absorption or may be due to some other direct metabolic effect. Little is actually known about the nature of these changes, and proposed mechanisms remain speculative.

D. Effects on Experimental Atherosclerosis

Few experiments have dealt directly with the effects of experimental atherosclerosis since the early studies of Moore.[65] We have examined the role of dietary fiber (alfalfa, wheat straw, or cellulose) in the modification of the cholesteremic and atherogenic effects of soy protein or casein in a semipurified, cholesterol-free diet in rabbits.[66] Soy protein is less cholesteremic and less atherogenic than casein in this diet, when cellulose is used as a source of dietary fiber. When wheat straw was substituted, serum cholesterol levels and aortic atheroma were lowered in both protein groups, but were lowest in the soya-fed animals. When alfalfa was substituted, both cholesterol levels and atheroma were greatly reduced, and no difference between the two protein sources was observed.

Malinow *et al.*[67] examined the regression of preestablished atherosclerotic lesions in response to alfalfa in cynomolgus monkeys. Using a semipurified diet containing 1.2 mg cholesterol/kcal for a 6-month induction period and a similar diet with a 0.34 ms cholesterol/kcal and about 50% alfalfa meal for the 10-month regression period, they found a significant reduction in serum cholesterol and atheroma compared with a group receiving a diet with cholesterol but without alfalfa (Table 6). Alfalfa apparently counteracted the atherogenic effects of dietary cholesterol at a level similar to that found in the typical American diet. They have previously found that an alfalfa saponin preparation[68] prevented hypercholesteremia in monkeys and theorized that the saponin fraction was primarily responsible in this study on regression. Saponins apparently decrease cholesterol absorption.[69] As mentioned earlier, the saponin fraction of alfalfa is not essential for bile-acid adsorption, suggesting a multifaceted mechanism involving both dietary fiber and nonfiber components. Alfalfa is a very promising material for use as a hypocholesteremic agent, and elucidation of the mechanisms responsible for these effects needs to be completed before the clinical usefulness of alfalfa preparations can be evaluated.

Table 6. Effect of Alfalfa on Regression of Cholesterol-Induced Atherosclerosis in Monkeys[a,b]

Diet		Plasma cholesterol	Atherosclerosis	
0–6 months	6–24 months	(mg/dl)	Coronary[c]	Aortic[d]
SP1	—	701	1.00	1.00
SP1	SP2	287	0.63	1.23
SP1	SP2 + alfalfa	163	0.23	0.60
SP1	CR	318	0.33	0.60

[a]From Malinow *et al.*[67]
[b]Abbreviations: SP1, semipurified diet with 1.2 mg cholesterol/kcal; SP2, similar diet with 0.34 mg cholesterol/kcal; CR, commercial monkey ration.
[c]Coronary stated as % of encroachment; control 23.0%.
[d]Aortic as + to 5+ grade; control 3.0.

V. CONCLUSIONS

Many beneficial effects of dietary fiber on lipid metabolism have been observed which tend to support the original epidemiological observations. Some fractions and sources of dietary fiber lower tissue cholesterol levels and prevent experimental atherosclerosis. Some reduce fecal bile-acid concentrations and reduce susceptibility to experimental intestinal carcinogenesis. As yet, few of the responsible mechanisms have been elucidated. We are aware of the interactions of some components of dietary fiber with bile acids, and evidence indicates that this interaction is a major contributor to the observed effects on serum cholesterol. Changes in other lipid levels do not seem to be influenced as dramatically by this mechanism. Remaining to be clarified are the nature and extent of bile-acid adsorption by the fiber components of foods and the potential of this adsorption in altering human atherosclerosis.

The role of dietary fiber in lipoprotein metabolism is possibly the most intriguing current area of investigation. With the application of recent techniques, the nature and mechanism of such alterations should be forthcoming.

A major obstacle to organized progress is the lack of well-defined and consistent sources of dietary fiber. Components isolated from various plant sources often have little in common with the same material as it occurs in a foodstuff. However, there are few options to using these materials if one wishes to study individual fiber components. Likewise, sources of dietary fiber vary greatly and are impossible to control. It would appear that a thorough characterization of the dietary fiber used in any study should be carried out and reported. This may eventually give information which will indicate important physicochemical characteristics and allow prediction of the effects of a given dietary fiber based on its chemical and morphological structure.

An aspect of the involvement of dietary fiber in bile-acid metabolism that warrants concern is the potential for increased susceptibility to chemical carcinogenesis associated wtih increased bile-acid concentrations in the colon.[61,70,71] Fibers such as pectin that increase fecal bile-acid excretion without similarly enhancing fecal weight may be expected to represent a risk different from bran and other fibers that have predominant stool-bulking effects.

In general, we have greatly increased our knowledge of the role of dietary fiber in lipid metabolism. A great deal of work remains before a thorough understanding of the mechanisms involved can lead to application of this knowledge to human populations.

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Dietary Fiber: Effects on Plasma and Biliary Lipids in Man

Ruth McPherson Kay and A. Stewart Truswell

I. INTRODUCTION

The plasma lipoprotein profile bears an established relationship to the clinical appearance of atherosclerotic heart disease (AHD).[1,2] Continuiing refinements can be expected in our understanding of the relationship of individual lipoprotein fractions to atherogenesis and of the qualitative effects of specific dietary variables on the lipoprotein spectrum. However, expert committees in most Western countries have made general recommendations for dietary changes intended to reduce the incidence of AHD. These dietary recommendations have emphasized alterations in fatty acid and cholesterol intake.[3] Clinical experience indicates that such changes can be expected to reduce mean plasma low-density lipoprotein (LDL) cholesterol concentrations by about 15% but are insufficient to achieve the low levels typical of low-risk populations.

It is suggested that dietary factors in addition to fat and cholesterol may play a possibly significant role in the etiology of AHD. In the following pages, we discuss recent epidemiological and clinical evidence concerning the role of dietary fiber in the reduction of plasma lipids in man and its effects on biliary lipid composition. Mechanisms by which fiber may influence lipid metabolism and the clinical significance of such effects are also discussed.

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II. EPIDEMIOLOGICAL STUDIES

A. Non-Westernized Populations

Early protagonists of the "fiber hypothesis," including Trowell, Walker, and Burkitt, drew attention to the rarity of AHD and gallstones in central and southern Africa.[4–7] Age-specific death rates indicated that differences in life expectancy were not solely accountable; nor were genetic differences, since the manifestations of AHD rose dramatically with the acquisition of an occidental diet and life-style.

The low incidence of AHD in Africa was linked with a scarcity of a number of risk factors including cigarette smoking, obesity, and hypertension. Most notably, mean plasma cholesterol concentrations were very low. The dietary pattern of these populations was characterized by a high intake of fiber and complex carbohydrates. Fiber intakes averaged 60–80 g/day, four times the Western norm. Malhotra[8] has drawn attention to a similar pattern of high-fiber intake and low AHD incidence in the north of India.

The apparent negative association between fiber intake and AHD incidence in non-Westernized populations is by no means indicative of a causal link. Other aspects of life-style differ. In addition, a diet high in fiber is almost inevitably rich in complex carbohydrate, contains protein of predominantly vegetable origin, and is low in saturated fat and cholesterol. Further epidemiological and clinical studies were required to determine whether fiber has a direct influence on lipid metabolism or acts indirectly through displacement of lipid-active nutrients such as saturated fat.

B. Western Populations

Studies in more Westernized populations have also suggested that dietary fiber may contribute to the maintenance of low levels of plasma cholesterol.

In an international survey of nutrient intake and serum lipids in 1955, Keys and colleagues[9] noted that mean plasma cholesterol for men in Naples was 170 mg/dl compared with 233 for an age-matched group in Minnesota. Part of this difference (ca. 20 mg/dl) could not be accounted for by a prediction equation base on intake of fatty acids and cholesterol.[10] It was suggested that the large amount of fiber from fruit, vegetables, and legumes in the Naples diet might be partly responsible for the low levels of plasma cholesterol observed.[11]

Low concentrations of serum lipids or delayed onset of AHD have also been reported for various vegetarian groups including Seventh Day Adventists,[12] Trappist monks,[13] strict vegetarians, lacto-ovo vegetarians,[14] and persons following a Zen macrobiotic diet.[15]

An attempt has been made to link fiber intake to the development of AHD

within a Western population. Morris and colleagues[16] recorded 7-day weighed food intakes for 337 middle-aged men in England from 1956 to 1966. The data were reexamined in 1976, at which time 13% of the population sample had developed clinical manifestations of AHD. The results indicated that men with the highest intake of cereal-derived fiber had a lower rate of disease than the rest. The apparent protective effect of cereal fiber could not, however, be related to differences in known risk factors such as plasma cholesterol. There were suggestions of less cigarette smoking among the high-fiber group. More recently, Foster *et al.*[17] have reported a significantly higher prevalence of diverticular disease (DD) among patients with myocardial infarction (MI) (57%) than among age-matched controls (25%). Although fiber intake has been suggested as an etiological factor in DD, the data in no way confirm a direct relationship between fiber intake and clinical AHD.

If dietary fiber is a significant factor influencing plasma lipids, some relationship between usual fiber intake and plasma levels of cholesterol and triglycerides might be expected within a normal population. Kay *et al.*[18] have addressed this question in a study of 200 healthy Canadian males aged 35–59 years. Data on nutrient intake were obtained by the 24-hr recall method. The results indicated that men in the lower tertile of the plasma cholesterol and triglyceride distributions were consuming significantly more dietary fiber and significantly fewer calories as fat. However, there were also negative relationships between fiber intake and each of fat intake and adiposity. Multiple regression analyses indicated that whereas the percentage of calories consumed as fat was independently, positively related to plasma and triglyceride levels, the relationship of dietary fiber intake to serum lipids was largely mediated by coexisting differences in other environmental variables. Hence, in a free-living Western population, dietary fiber may exert its greatest effects on plasma lipids through displacement of more lipid-active nutrients.

III. CLINICAL STUDIES

A. Plasma Lipids and Lipoproteins

Clinical studies in man on the effect of dietary fiber can be divided into three main areas. These include the use of (1) purified fiber isolates, (2) natural concentrated fiber sources such as bran, and (3) native fibers fed in the form of whole foods. Each of these approaches has inherent advantages and limitations.[19] In many cases, human experiments must be of long duration; fecal collections and gastrointestinal intubations are sometimes required. The problems of adherence to protocols and patients' cooperation are obvious. An alteration in intake of fiber-rich material may necessitate concomitant changes in other dietary components. The chemical and morphological complexity of fiber also

makes the design and comparison of experiments difficult. Results may vary with the composition of the fiber, and the latter is dependent upon the age and species of the plant and the part of the plant from which the fiber is derived. Purified fiber isolates may appear to be an attractive alternative in many experiments. However, chemical isolation from the plant cell wall produces artifacts and may eliminate or modify important physiological actions.

1. *Effects of Purified Fiber Isolates on Plasma Lipids*

Purified preparations of cellulose, hemicellulose, lignin, and pectin have been tested in man. None of these represents a single homogeneous entity, and results of experiments have varied depending on the physical and chemical characteristics of the fiber used. In animal experiments, the nature of the background diet has appeared to modify the effects of various fibers on lipid metabolism.

Certain types of hemicellulose are mucilaginous in nature, and these have been reported to lower plasma cholesterol in man. Guar, a galactomannan from the legume *Cyanopsis tetragonoloba,* is hypocholesterolemic in normal man[20,21] and has been used clinically to reduce plasma cholesterol in patients with type II hyperlipidemia.[22] Psyllium seed colloid, based on arabinose and galacturonic acid, is a component of the stool-bulking agent Metamucil®. When fed at 24 g/day, this hemicellulose was found by Kies and Fox[23] to lower plasma cholesterol by 16%, confirming earlier reports.[24] Other mucilaginous hemicelluloses are hypocholesterolemic in animals.[25]

Numerous investigators have reported that pectin lowers plasma cholesterol in man under a variety of conditions[20,26–33] (Table 1). Although two studies indicated a negative result, [21,34] one gave no details of the experiment[21] and in the other,[34] a small dose (6 g/day) of pectin was associated with a nonsig-

Table 1. Pectin and Plasma Cholesterol in Man

Series	Experimental	Plasma cholesterol (% change)
Keys *et al.*[27]	24 Subj.; 15 g/day in biscuits; 3 wk	−5
Palmer and Dixon[28]	16 Subj.; 10 g/day in capsules; 4 wk	−6
Fisher *et al.*[29]	Cholesterol-free diet	0
	With dietary cholesterol	−18
Fahrenbach *et al.*[21]	23 Subj.; 6–12 g/day; 7–9 wk	0
Lopez *et al.*[30]	3 Subj.; 20–23 g/day; 5 wk	−13
Jenkins *et al.*[20]	7 Subj.; 36 g/day; 2 wk	−12
Kay and Truswell[31]	9 Young students; 15 g/day; 3 wk	−13
Durrington *et al.*[32]	12 Subj.; 12 g/day; 3 wk	−8
Delbarre *et al.*[34]	10 Hyperlipidemic subj.; 6 g/day; 6 wk	0
Langley and Thye[33]	11 Subj.; 10 g/day	Significant decrease
Miettinen and Tarpila[36]	7 Normal and hypercholesterolemic; 40 g/day; 10–14 days	−15

nificant decrease in plasma cholesterol. Because the palatability of this fiber is limited, the method of dietary incorporation is likely to affect adherence and clinical effect. The reduction in plasma cholesterol appears greatest when pectin is given in a gel form rather than as powder or capsules. Kay and Truswell[31] administered citrus pectin as a fruit jelly; acceptability and hypocholesterolemic response were generally good. In animal studies, Judd and colleagues[35] reported that the cholesterol-lowering effect of pectin was greatest in a low-fat, cholesterol-containing diet. High-methoxyl pectins appeared most effective.[35,37]

Moderate amounts of cellulose did not lower plasma cholesterol in man.[27,38,39] Shurpalekar *et al.*[40] reported that very large doses (100 g/day) reduced plasma cholesterol in children. The effect of carboxymethyl cellulose has not been reported in human experiments, although a hypocholesterolemic response has been demonstrated in animals.[41]

Lignins have been shown *in vitro* to bind bile acids to a variable extent.[42] A Kraft softwood lignin, Westvaco®, lowered plasma cholesterol in rats.[43] A similar preparation (1–4 g/day) had a clinically significant effect in patients with type II hyperlipidemia.[44] However, in a study by Lindner and Moller,[45] another lignin preparation (2 g/day) did not alter blood lipids.

In summary, purified fibers vary in their effect on plasma total cholesterol levels. In general, the mucilaginous fibers such as pectin and guar appear most effective. Triglyceride levels are not altered; few reports are available on effects on high-density lipoprotein (HDL) cholesterol levels.

2. *Effects of Fiber Concentrates Including Bran on Plasma Lipids*

Truswell and Kay[46] in 1976 summarized the human studies on the effect of wheat bran on plasma lipids. Table 2[47–68] represents an updated review of experiments on wheat fiber and plasma lipids in man. Several of these studies, including those of Jenkins *et al.*[20] Kay and Truswell,[51] and Munoz *et al.*[67] were carried out under conditions of rigorous dietary control. The results have been generally but not universally negative. Munoz and colleagues[67] demonstrated that, whereas soft wheat bran (similar to that used in most of the studies cited) had no effect on serum lipids, hard red spring (HRS) wheat bran (26 g/day) significantly lowered plasma total cholesterol level (−12%). It is not known if this effect was due to differences in fiber composition or to the presence of a pharmacologically active component in the HRS bran.

Although data are limited, there is disagreement concerning the effect of bran on HDL cholesterol levels. Whereas McDougall *et al.*[60] reported that HDL cholesterol rose following one year of bran therapy in three gallstone patients, Dixon[62] reported no change, and van Berge-Henegouwen *et al.*[68] found a significant decrease in HDL cholesterol in seven subjects after 2–4 weeks of bran ingestion. In two studies, bran has been reported to reduce plasma triglycerides.[48,68]

In contrast to the generally negative effect of wheat bran, oat bran does appear to have significant hypocholesterolemic properties. Unlike wheat bran,

Table 2. The Effect of Wheat Fiber on Plasma Total Cholesterol in Man[a]

Series	Experimental protocol	Plasma cholesterol (% change)
Eastwood[47]	28 Monks; 14 g bran; 2 wk	0
Eastwood *et al.*[39]	8 Men; 16 g bran; 3 wk	0
Heaton and Pomare[48]	6 Normal, 8 cholelithiasis; 38 g bran; 5 wk	0
Connell *et al.*[49]	23 Students; 28–57 g bran; 11 wk	0
Truswell and Kay[50] and Kay and Truswell[51]	6 Students; 23 g bran and 167 g whole-wheat bread; 3 wk	0
Jenkins *et al.*[20]	6 Men; 30 g bran, 25 g bran cereal, 52 g bran biscuits and 120 g whole-meal bread; 3 wk	0
Durrington *et al.*[52]	12 Men; 30 g bran; 6 wk	0
Bremner *et al.*[53]	5 Men with type IV HL; 50 g bran; 12 wk	0
Persson *et al.*[54]	14 Subj. aged 56–89; 20 g bran; 6 wk	−7
Heaton *et al.*[55]	19 Students; 180 g whole-wheat bread 19 wk	0
Brodribb and Humphreys[56]	40 Patients with diverticular disease; 24 g bran; 12 mo	0
Weinreich *et al.*[57]	25 Nurses; 24 g bran; 5 wk	0
Mathur *et al.*[58]	20 Normal, 10 HL; 40 g bran; 4 wk	
Raymond *et al.*[59]	12 Subj.; 72 g bran; 4 wk	0
McDougall *et al.*[60]	9 Normal, 9 cholelithiasis; 50 g; 4 wk	0
O'Moore *et al.*[61]	12 Patients; bran; 4 wk	0
Dixon[62]	16 Normal; bran and whole-wheat bread; 13 wk	0
Tarpila *et al.*[63]	22 PD patients; 25 g bran; 6–12 mo	0
Watts *et al.*[64]	11 Normal; 30 g bran; 8 wk	0
Letchford *et al.*[65]	17 subj.; no dietary control	[b]
Farrell *et al.*[66]	14 males; short experiment	[b]
Munoz *et al.*[67]	6 normal; 26 g SWW bran; 4 wk	0
	9 normal; 26 g HRS bran; 4 wk	−12
van Berge-Henegouwen *et al.*[68]	7 males; 35 g bran; 4 wk	−10

[a]HL, Hyperlipidemia; SWW, soft white wheat; HRS, hard red spring.
[b]Significant decrease.

it contains a glycan and is somewhat mucilaginous. Anderson and Chen[69] have reported that oat bran significantly reduces LDL cholesterol. HDL cholesterol concentrations have tended to increase.

Other fiber concentrates, mainly particulate in nature, have also been tested. Bagasse, the fibrous residue of sugar beets, is apparently without hypocholesterolemic effect in man.[70] Corn bran did not alter plasma lipids in a study by Munoz *et al.*[67]; however, 26 g/day of soybean hulls reduced plasma cholesterol by 14% in normal males. Raymond *et al.*[59] added 60 g of mixed dietary fiber including wheat bran, soybean hulls, corn hulls, and cellulose to a liquid-formula diet and found no change in plasma cholesterol level. A liquid diet may not be an appropriate vehicle for the addition of fiber.

Although inconsistencies are present, the available data indicate that par-

ticulate fibers such as wheat bran are generally ineffective hypocholesterolemic agents compared to mucilaginous or partly mucilaginous fibers such as guar and oat bran.

3. Fiber-Rich Foods and Plasma Lipids in Man

In clinical studies in man, various fiber-rich foodstuffs have been reported to lower plasma cholesterol concentration. In certain of the experiments cited, such an effect may be partially ascribed to coexisting differences in fat, cholesterol, and protein intakes. However, other well-controlled studies suggest that native-food-derived fibers may exert an independent hypocholesterolemic action. As demonstrated in studies of purified fibers, various fiber-rich foods have dissimilar effects of lipid metabolism.

Vegetable sources of fiber have been reported to lower significantly plasma total cholesterol concentration. In controlled experiments by Keys *et al.*[11] plasma cholesterol levels were reduced by 16–19 mg/dl when 17% of calories as sucrose, lactose, and milk protein were replaced by sugars, starch, protein, and 45 g dietary fiber in the form of fresh fruits, vegetables, and legumes. In a later experiment by the same investigators, the isonutrient substitution of either bread or sucrose by a mixture of vegetables containing 40 g dietary fiber reduced plasma cholesterol levels by 20 mg/dl. In the same study, substitution of 20 g dietary fiber as fruit did not alter plasma lipids. However, other reports have indicated that a supplement of 2–8 apples per day may have a hypocholesterolemic effect.[25,71]

A number of studies suggest that fiber-rich legumes may lower plasma cholesterol in man. Luyken and co-workers[72] reported that plasma cholesterol was lowered by 12 mg/dl in men consuming 100 g brown beans *(Phaseolus vulgaris)* per day. Grande and colleagues[73] found that substitution of a mixture of legumes *(Phaseolus vulgaris, Phaseolus lunatus, Pisum sativum;* 500 kcal) for sucrose and soya lowered plasma cholesterol in middle-aged men, although the effect could not be confirmed in a group of much younger subjects.[74] Mathur *et al.*[75] reported that substitution of chickpeas (Bengal gram, *Cicer arietinum*) for wheat flour resulted in a slow fall in plasma cholesterol over 20 weeks in normal men; however, Grande *et al.*[74] did not demonstrate any change in plasma lipids in young men consuming chickpeas in a 2-week study. An impressive reduction in LDL cholesterol in patients with type II hyperlipidemia fed soya protein isolate has been reported by Sirtori *et al.*[76] This may have been due in part to the high fiber content of the preparation used. Soya is also rich in saponins. These compounds have been shown to reduce sterol absorption and lower plasma cholesterol in animals.[77,78]

Cereal sources of fiber have not generally been shown to alter blood lipids. The replacement of wheat flour by 140 g rolled oats lowered plasma cholesterol by 25 mg/dl in a study by de Groot *et al.*[79] In a more recent report by Judd and Truswell,[80] oats did not significantly reduce cholesterol levels when the diets were matched for fatty acid content.

B. Effects of Dietary Fiber on Bile Composition in Man

The use of fiber to improve bile composition followed the observation that rural Africans rarely form cholesterol gallstones.[81]

Most studies have used wheat bran. The effect on gallbladder bile composition has depended on the initial composition. When the bile was initially lithogenic, improvement followed; but in patients with normal bile composition, bran did not further reduce the lithogenic index. Pomare and co-workers[82] reported that a dose of 30 g/day significantly improved bile composition in patients with cholesterol gallstones and an initial lithogenic index of 1.5, and Watts and colleagues[64] noted improvement in bile composition in all five patients whose lithogenic index was initially greater than unity. The same dose had no consistent effect in patients with normal bile composition in the study by Watts *et al.*[64] and in another by Wicks *et al.*[83] A somewhat larger daily amount of bran (50 g) reduced the lithogenic index from 1.35 to 0.71 in patients with stones but did not affect a control population in a study by McDougall *et al.*[60]

Less information is available on the effect of other fibers on bile composition. Miettinen and Tarpila[36] reported that bile composition was not affected in normals, but one individual who initially had supersatured bile developed normal composition on therapy. Lignin, a noncarbohydrate indigestible form of fiber, reduces cholesterol gallstone formation in hamsters.[84] Kay *et al.*[42,85] have studied the effect of autohydrolyzed lignin. This type of fiber was tested in an attempt to find an agent which, as well as increasing fecal bile-acid losses, would specifically increase fecal excretion of the trihydroxy bile acid, cholic acid. The intention was to decrease the cholic acid content of the pool and simulate the effects of chenodeoxycholate feeding. Like cholestyramine, lignin bound dihydroxy bile acids more avidly than cholic acid *in vitro,* but binding of cholic acid relative to dihydroxy bile acids was equalized when the pH of the medium was lowered. A diet containing lignin and the colonic acidifying agent lactulose improved gallbladder bile composition in hamsters when compared with hamsters on a control diet.[85] There are no data on the effect of the mixed-fiber diet of Africans on biliary lipid composition, although the reported low incidence of gallstones in this group stimulated much of the investigation cited here.

The mechanism by which certain fibers improve bile composition is not firmly established. Strasberg and colleagues[86] demonstrated that controlled stimulation of bile-acid synthesis reduced the biliary cholesterol secretion rate in Rhesus monkeys. In accord with this observation, low doses of bile-acid-binding resin improved bile composition in subjects with cholelithiasis.[87] Pectin and lignin increase fecal bile-acid excretion and may behave in a similar manner. As will be discussed here, no agreement yet exists on the effect of wheat bran on fecal bile-acid output. Bran apparently causes other changes in colonic

bile-acid metabolism as indicated by a reduction in the deoxycholic acid fraction of bile.[60,82,83]

A reduction in bile-acid pool size is another abnormality reported in subjects with cholesterol gallstones.[88,89] Since the pool size is inversely related to the enterohepatic cycling frequency, fibers such as bran which decrease upper intestinal transit time might actually reduce pool size. More information is required on effects of various fibers on bile composition and bile-acid pool size in subjects with cholelithiasis.

IV. MECHANISMS

Whole-body cholesterol metabolism is schematically illustrated in Fig. 1. Although some types of dietary fiber appear to have little overall effect on cholesterol flux and pool sizes, others such as the mucilaginous fibers significantly decrease liver and plasma cholesterol ($CHOL_R$). A decrease in circulating cholesterol could result from net flux into tissue pools ($CHOL_S$) or enhanced fecal excretion of neutral and acidic sterols not compensated for by *de novo* cholesterol synthesis. The first possibility appears unlikely, since the decrease in plasma cholesterol in man appears to occur mainly in the LDL fraction.

Mechanisms by which dietary fiber may influence cholesterol synthesis and excretion are illustrated in Fig. 2.

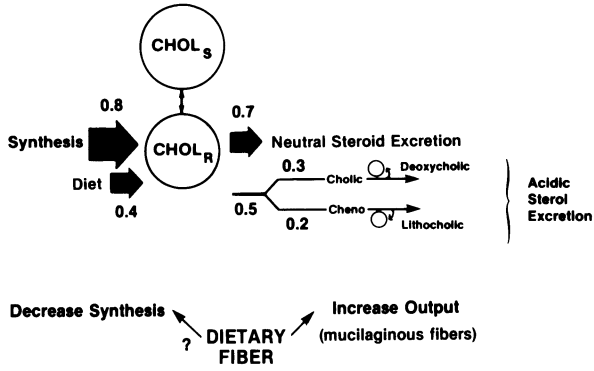

Figure 1. Cholesterol balance in man. Schematic representation of cholesterol and bile-acid metabolism in man. Interchange of cholesterol between slowly ($CHOL_S$) and rapidly ($CHOL_R$) exchanging pools is partly mediated by concentration of specific plasma lipoproteins. Reduction of plasma total cholesterol by dietary fiber is likely due to enhanced output of acidic and neutral steroids not fully compensated for by increased cholesterol synthesis.

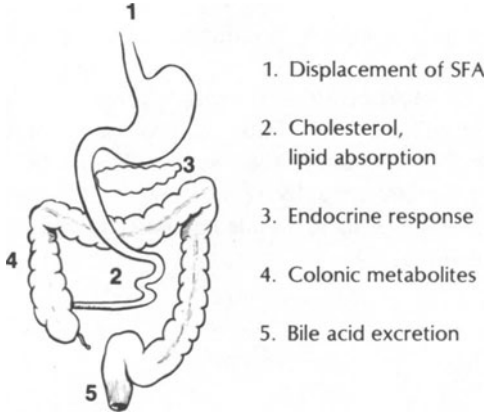

Figure 2. Possible mechanisms for the hypocholesterolemic effect of certain fibers. Changes in plasma cholesterol associated with increased fiber consumption may be mediated by a decrease in the intake of fat and cholesterol, reduced output of cholesterol and its metabolites in the stool, or alteration in cholesterol synthesis possibly due to fiber-associated changes in endocrine hormones or colonic metabolites or to enchanced fecal excretion of cholesterol and its metabolites. SFA: Saturated fatty acid.

A. *Displacement of Saturated Fat, Cholesterol*

A diet rich in fiber-containing foods is by nature high in complex carbohydrate and vegetable-derived protein. By displacement of food items that contribute saturated fat and cholesterol, fiber may indirectly result in lower plasma lipid levels. Kay *et al.*[18] reported that intake of dietary fiber and percentage of calories consumed as fat were inversely related in a normal population.

B. *Energy Balance, Nutrient Absorption*

1. *Energy Balance*

Obesity is associated with increased plasma cholesterol and triglyceride concentrations. It has been suggested that dietary fiber may prevent or mitigate obesity by reducing overall food intake. However, a causal link between fiber intake, energy intake, and excess body weight is by no means established.

In a study of 200 normal adult males by Kay and co-workers,[18] subjects with increased relative body weight were found to consume significantly less fiber and carbohydrate. However, energy intakes were similar for lean and overweight groups, suggesting that the altered dietary pattern in the latter group represented a conscious attempt to eliminate starchy foods popularly assumed to be fattening.

There is evidence that dietary fiber does reduce the availability of ingested nutrients.[31,90,91] Southgate and colleagues[91] demonstrated that dietary fiber supplementation increased daily fecal energy loss by 20–95 kcal; the cumulative effects of such a change in net energy balance may be significant.

2. Gastric Emptying, Glucose Absorption, and Endocrine Response

Many types of dietary fiber modulate glucose absorption resulting in reduced postprandial levels of glucose and insulin. Leeds, *et al.*[92] have demonstrated that this effect is due in part to delayed gastric emptying in the presence of viscous fibers. Fiber may also alter small-intestinal transit rate and movement of glucose to the absorptive mucosal surface. A full description of these effects is given by Anderson and Chen[93] and in Chapters 10 and 11 of this volume.

Insulin has been reported to increase cholesterol synthesis[94] and hepatic synthesis and secretion of very-low-density lipoprotein (VLDL).[95,96] It is significant that the mucilaginous fibers that appear to have the greatest effect on plasma total cholesterol concentrations are of similar importance in their effects on glucose metabolism.

Blood levels of other hormones affecting lipoprotein metabolism, such as glucagon, are also altered by dietary fiber.[97,98]

3. Lipid Absorption

Pectin, guar, and other fibers increase fecal fat excretion, but this effect is not of quantitative significance. More important changes may occur in the route and site of lipid absorption.

Jenkins[99] has reported that guar significantly enhances early postprandial chylomicronemia. Such an effect might represent decreased triglyceride clearance because of lower plasma insulin levels and lipoprotein lipase activity or because of a reduction in chylomicron size. Alternatively, Jenkins[99] suggests that guar and pectin might actually facilitate micelle formation and the absorption of fat via the lymphatic route. There is evidence that significant amounts of dietary long-chain fatty acids are transported in the portal vein. If mucilaginous fibers promote lymphatic absorption, alterations in HDL metabolism might be anticipated. Chen and Anderson[100] have reported that guar increases HDL cholesterol levels in rats. Clearly, more information is required on effects of different types of fibers on the lipid absorption pattern.

C. Cholesterol Absorption and Fecal Steroid Excretion

Many types of isolated and native fibers have been shown to bind bile acids and cholesterol *in vitro*. Acidic-sterol adsorption has been most extensively studied. Adsorption of bile acid is influenced by the physical and chemical form of the fiber, the polarity of the bile acid, the type of bile-acid micele, and the osmolality of the intestinal contents.[14,42,101,102]

1. Cholesterol Absorption

Pectin, cellulose, and alfalfa decreased lymphatic absorption of sterol in the rat, whereas wheat bran had no effect.[103,104] Vahouny and colleagues[105] also demonstrated that incorporation of fiber into the diet influenced subsequent cholesterol absorption. Fasting animals previously fed bran or cellulose absorbed less labeled sterol than did control animals. These results suggested that morphological changes may have occurred in the upper intestine because of fiber ingestion. Reduction in bile-acid availability for cholesterol absorption appeared unlikely, since, in other studies, neither of these fibers caused a great increase in fecal bile-acid output.

Human and animal experiments demonstrating that the hypocholesterolemic effect of pectin is greatest when the diet contains cholesterol[106] support the concept that malabsorption of exogenous cholesterol may be a factor in the cholesterol-lowering response. However, significant reduction of plasma cholesterol due to pectin was also noted in animals fed a cholesterol-free diet.[107]

Consistent with a reduction in lymphatic cholesterol absorption was the observation that certain fibers increased fecal neutral-steroid excretion in animals and man.[31,108] Human studies demonstrated that pectin enhances stool output of cholesterol and its bacterial degradation products[31]; however, other hypocholesterolemic fibers did not appear to alter fecal neutral-steroid loss.[24]

2. Fecal Bile-Acid Excretion

The effect of dietary fiber on plasma cholesterol concentration is generally believed to be largely mediated by enhanced fecal excretion of bile acids. A summary of reports on the effect of various fibers on fecal bile-acid excretion in man is given in Table 3.

There is considerable disagreement on the effect of wheat bran on fecal bile-acid excretion. In a total of eight human studies, two found an increase on therapy,[60,109] two a rebound increase after discontinuing therapy,[39,51] one a variable increase,[110] and two no change.[70,111] Tarpila and colleagues[63] actually observed a decrease in fecal bile-acid excretion during bran-feeding in patients with diverticular disease. This effect was associated with a decrease in cholesterol synthesis. Wheat bran has not been found to reduce plasma cholesterol in most of the studies cited above.

Pectin,[31,35,112] guar,[112] cellulose,[40,113] psyllium seed hydrocolloid,[24,113] bagasse,[70] and various food-derived fibers[114] significantly increased fecal bile-acid output under diverse conditions. Mucilaginous fibers form gels in the small intestine that could interfere with the absorption of both cholesterol and bile acids.[115] Other fibers may exert their effects on acidic-sterol output through adsorption of less-polar bile acids in the colon.

It is of interest that an increased fecal bile-acid output due to fiber was not always accompanied by a reduction in plasma cholesterol.[70] Similarly, low doses of cholestyramine (0.05 g/kg) more than doubled fecal acidic-sterol

Table 3. Effect of Dietary Fiber on Fecal Bile-Acid Excretion in Man

Reference	Fiber	Subjects	Amount[a]	Duration	Fecal bile-acid excretion (% change)
Miettinen and Tarpila[36]	Pectin	2 Normal 7 Hyperlipidemic	30	2 wk	+75
Kay and Truswell[31]		9 Normal	15	3 wk	+40
Jenkins *et al.*[112]		7 Normal	36	2 wk	+34
Jenkins *et al.*[112]	Guar	7 Normal	36	2 wk	+84
Antonis and Bersohn[114]	Mixed sources	14 Normal	15	15–39 wk	+26
Raymond *et al.*[59]		8 Normal and hyperlipidemic	60	4 wk	0
Kretsch *et al.*[115]		6 Normal	93	15 days	+111
Stanley *et al.*[113]	Cellulose	22 Normal	15	16 days	+25
Shurpalekar *et al.*[40]		10 Normal, aged 8–10 yr	100	10 days	+45
Stanley *et al.*[113]	Psyllium	22 Normal	15	16 days	+70
Forman *et al.*[24]		2 Normal	9.6	6 wk	+302
Walters *et al.*[70]	Bagasse	9 Normal	10.5	12 wk	+50
Mathur *et al.*[75]	Legumes	10 Normal	[a]	55 wk	+55
Eastwood *et al.*,[39]	Wheat bran	8 Normal	16	3 wk	0
Walters *et al.*[70]		8 Normal	39	3 wk	0
Cummings *et al.*[109]		6 Normal	64	3 wk	+90
Jenkins *et al.*[111]		6 Normal	36	3 wk	0
Kay and Truswell[51]		6 Normal	54	3 wk	0
McDougall *et al.*[60]		5 Normal	50	3 wk	+240
Tarpila *et al.*[63]		22 with diverticulitis	70	12 mo	−49

[a] "Large amount" of Cicer arietinum added to a high-fat diet.

excretion but did not consistently alter plasma lipid levels in man.[116] This suggests that reduction of plasma cholesterol levels by dietary fiber may be due to a number of interacting events resulting in increased fecal steroid excretion not fully compensated for by *de novo* cholesterol synthesis.

D. Other Mechanisms

There has been some speculation, but little concrete data, concerning other mechanisms by which fiber may influence cholesterol metabolism. Alterations in colonic flora, production of bile-acid metabolites, and absorption of short-chain fatty acids derived from the fermentation of fiber may be of some significance.

Information on the effects of dietary fiber on colonic flora is complex and inconsistent.[117,118] In rats, the cholesterol-lowering effect of pectin was not altered by the simultaneous administration of an antibiotic.[119] There is evidence

of fiber-associated alterations in bacterial activity as indicated by a reduction of bacterial metabolites in the fecal neutral-steroid fraction in individuals consuming high-fiber diets.[110,120] Wheat bran has been shown to reduce the proportion of deoxycholic acid in bile,[60,64,82,83] suggesting a decrease in the bacterial formation or absorption of secondary bile acids. Qualitative differences in the effect of bile acids on cholesterol metabolism[121] are recognized, but the effect of deoxycholic acid is apparently to decrease plasma cholesterol.[122–124]

Anderson and Chen[93] have suggested that the colonic production and absorption of short-chain fatty acid metabolites of fiber may alter hepatic fatty acid and triglyceride metabolism. More data are required before the possible relationship of biochemical events in the colon to cholesterol metabolism can be fully assessed.

V. CLINICAL SIGNIFICANCE OF DIETARY FIBERS

A. Pharmacological Applications

Guar has been shown to be of therapeutic usefulness in the treatment of type II hypercholesterolemia.[22] Mucilaginous fibers such as guar, pectin, and oat bran may have a particular therapeutic advantage over cholestyramine in disorders of lipid metabolism associated with impaired glucose tolerance. The limited palatability of these fiber isolates is likely to preclude widespread clinical applicability.

Treatment of cholelithiasis with dietary fiber supplements has received some attention. The effect on bile composition is slight in comparison with chenodeoxycholic acid. Clinical trials are required to determine the effect of dietary fibers on biliary cholesterol concentration following gallstone dissolution. Fiber may have a therapeutic role as an adjunct to chemotherapy.

B. Dietary Significance

As discussed here, an increased intake of foods rich in dietary fiber may indirectly reduce plasma lipid concentrations by displacement of saturated fat and cholesterol.

Some, but not all, types of dietary fiber produce direct effects on plasma total cholesterol concentration. In general, fibers present in fruits and vegetables have the greatest hypercholesterolemic action. It is generally accepted that possible changes in plasma lipids due to alterations in fiber intake are quantitatively minor in comparison to the effects of dietary fatty acids and cholesterol. As illustrated in Fig. 3, a 25% reduction in total fat intake coupled with an increase in the polyunsaturated fraction could be expected to reduce total plasma cholesterol by 21 mg/dl.[10] Concomitant decreases in dietary choles-

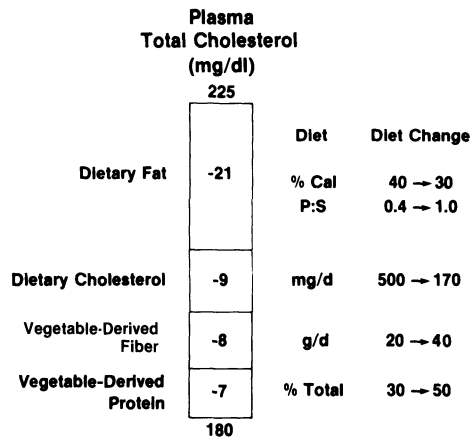

Figure 3. Expected changes in plasma total cholesterol due to alteration in dietary fat, cholesterol, protein, and fiber. Mean plasma cholesterol concentration for adult males in the United States is currently 225 mg/dl. A reduction of 45 mg/dl might be expected if these dietary changes, including a doubling of fiber intake, were made. The direct effect of fiber would account for approximately 18% of the observed effect.

terol[125] and in the proportion of animal-derived protein[126] might elicit further changes of −9 and −7 mg/dl, respectively. If, in addition, the intake of vegetable-derived fiber were doubled, the data of Keys *et al.*[11] and Grande *et al.*[74] suggest that a further drop in plasma cholesterol of 8 mg/dl could be achieved. More information is clearly required on the qualitative and quantitative effects of individual fiber-rich foods on the plasma lipoprotein spectrum.

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Dietary Fiber and Carbohydrate Metabolism

David J. A. Jenkins

I. INTRODUCTION

Much of the interest in the relationship of dietary fiber to carbohydrate metabolism has stemmed from the suggestion that diabetes should be included in the long list of Western diseases that are associated with a deficiency of dietary fiber.[1] Work in this area has been further stimulated by the results of trials of fiber in the treatment of diabetes. Kiehm *et al.*[2] and Anderson and Ward[3] found that when diabetic patients on low doses of insulin were treated with high-carbohydrate, high-fiber diets, insulin requirements were reduced. Jenkins *et al.*[4,5] showed that addition of guar gum to the diet lessened glycosuria in diabetics regardless of insulin dose. Results from Miranda and Horwitz[6] indicated that feeding a high-cellulose bread to diabetics flattened the glucose profile throughout the day. These studies opened up the possibility of developing treatments for diabetics aimed at modifying small-intestinal events. They also presented the opportunity to explore and develop the results of such changes in terms of overall carbohydrate metabolism. This, in turn, stimulated work to determine types of dietary fiber which may be most effective in modifying glucose tolerance and in defining the physicochemical properties responsible for these effects. Also, practical questions concerning mode of administration, timing with the meal, and the nature of the best background diet have been raised.

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II. DIETARY FIBER AND CARBOHYDRATE TOLERANCE TESTS

Campbell's work on the postprandial glucose response to carbohydrate loads in the form of whole apples or whole potatoes stressed the importance of the fiber component in reducing the glycemic response by comparing it with the feeding of the same amount of carbohydrate in refined form.[7] This work has been extended by studies on the effects of apple fed to subjects as whole apple, as pureed apple, or as apple juice. Results showed that, apart from the increased satiety produced by eating whole apples, the apple juice produced a significantly greater insulin response and a subsequent underswing in the blood glucose level from 60 min onward. Though the puree produced only a modest insulin rise, similar to the whole apple, it also caused a resulting undershoot similar to that seen when juice was consumed.[8] Such results emphasized the importance of dietary fiber in modifying the glucose and insulin response to carbohydrate loads and stressed the importance of the relationship of the dietary fiber to the carbohydrate with which it was associated. Thus, in the case of apple puree, even though there had been no removal of fiber during processing, the disruption of the fiber architecture of the apple resulted in a blood glucose response not very dissimilar to that seen with apple juice where all the fiber had been removed.

In historical terms, wheat bran had been considered a possibly important source of dietary fiber in modifying the glucose tolerance test. Evidence for this was educed from the fact that mortality figures for diabetes fell in Britain during the Second World War when the extraction rate for wheat was raised[1] so that more cereal fiber was consumed. However, the work of Jeffreys[9] showed that only a small reduction in glycemia was seen when wheat bran with glucose syrup was fed to normal volunteers. As a result, Jenkins and co-workers undertook a comparative study where a number of forms of dietary fiber or fiber analogues were tested for their ability to modify a 50-g glucose tolerance test. Of these, guar gum, a galactomannan obtained from the cluster bean, was found to be the most effective. Much work has been done with this fiber supplement by incorporating it into such foods as bread and soup and into meals fed to both normal volunteers and diabetics. These experiments have confirmed its effect in lowering the postprandial glycemia.[10–14]

III. FIBER FOODS AND FIBER PHARMACOLOGY

Before proceeding to the mechanisms of action of dietary fiber on glucose tolerance, it is important to distinguish between the consumption of natural high-fiber foods and the consumption of foods to which refined fiber has been added. Consumption of natural foods may produce little rise in blood glucose. However, when their fiber components are refined and added to some other form of food, they produce only a minor flattening of postprandial glycemia,

as is seen when wheat bran has been added to test meals. The object of the pharmacological approach is to define those forms of dietary fiber which can be used to supplement high-fiber foods and so accentuate the flattening in postprandial glucose rises so that the effect is therapeutically useful.

The major part of the following discussion will deal with the pharmacological aspects of fiber in modifying carbohydrate absorption for two reasons: first, to illustrate general principles; second, because little work has been done on whole foods. However, this should in no way be taken to suggest that an investigation of fiber in the context of whole foods would be any less rewarding or necessary in terms of its therapeutic implications.

IV. MECHANISMS OF ACTION OF FIBER IN RELATION TO CARBOHYDRATE METABOLISM

A. Importance of Viscosity

In an attempt to define the type of dietary fiber that should be most useful in flattening the glucose tolerance curve, Jenkins *et al.*[10] compared the effect of adding the equivalent of 12 g of fiber or fiber analogues to 50-g glucose tolerance tests taken by four to six healthy volunteers. The substances looked at included guar gum and gum tragacanth (Fig. 1), both galactomannans from the cluster bean used as thickeners in the food industry. Pectin, a partially methoxylated polygalacturonic acid, was also studied. It is an almost ubiquitous component of plant fiber and has been used for centuries as a thickener of jams and marmalades. Apples and citrus fruit are particularly good sources of pectin. Methyl cellulose (a synthetic fiber and a bulking agent), wheat bran (a compound particulate fiber), and cholestyramine (a nonabsorbable synthetic anion-exchange resin), were also tested. In all cases, there was a flattening of the blood glucose response, most marked in the case of guar and tragacanth. Not only were the peak rises reduced but also the 2-hr blood glucose levels were elevated. The postprandial elevation is similar to that seen by Haber *et al.*[8] when apple rather than apple juice was ingested. Fig. 2 shows that when the four viscous agents guar, tragacanth, pectin, and methyl cellulose were used, there was a correlation between both the peak rise of blood glucose and the 2-hr blood-glucose level with the viscosity of the test solutions of these four substances. The effect of viscosity is further illustrated by mild acid hydrolysis of guar gum, so rendering the material nonviscous (Fig. 3, upper panel) where the effects on postprandial glycemia were completely abolished.

B. Reduction of Insulin Response

The effect on the glucose tolerance is independent of increased insulin release as illustrated in Figure 1 and Figure 3. If anything, the insulin is dis-

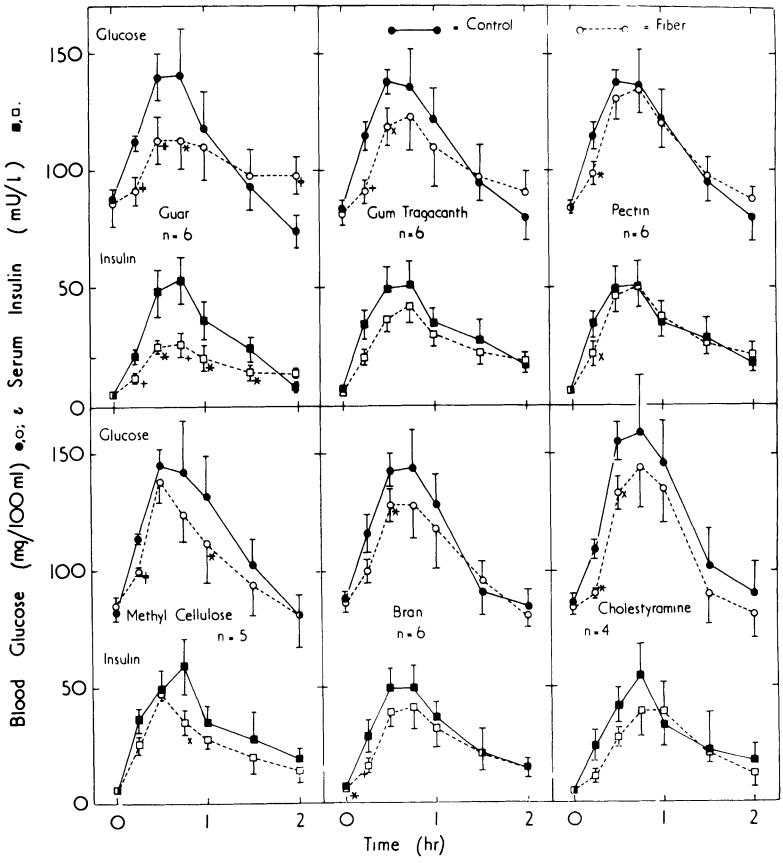

Figure 1. Effect of addition of 12 g fiber (dry wt) as guar, tragacanth, pectin, methyl cellulose, wheat bran, and cholestyramine on the postprandial glucose and insulin responses to test meals containing 50 g glucose, 25 g xylose, 30 g liquid lactulose (50% w/w), 40 g pure lemon juice, and 400 ml water.

proportionately flattened in relation to the blood glucose, and the effect on glucose tolerance cannot be attributed to an increase in insulin release. This independence from increased insulin release is even more clearly demonstrated in a study performed in eight maturity-onset diabetics who were fed breakfast test meals containing 106 g of carbohydrate in bread and marmalade. Sixteen grams of guar was baked in with the bread and 10 g of pectin was mixed into the marmalade. The fiber-enriched meal produced a marked flattening of the postprandial glycemia and an even more marked flattening of the postprandial insulin response (Fig. 4).[12] Similar effects have been observed with other fiber-rich test meals.[11,13–15]) In general, there is an overall flattening of the endocrine response induced by viscous forms of dietary fiber, as seen by the flattening of the gastric inhibitory peptide (GIP) response after guar-supplemented meals

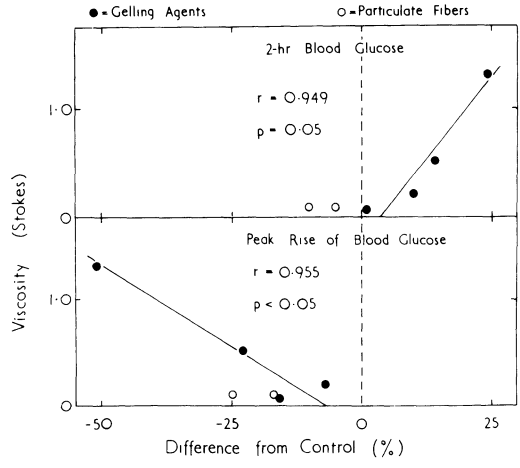

Figure 2. Viscosity of 1% solutions of six fiber preparations plotted against the percentage difference from control of the 2-hr blood glucose (upper panel) and the peak rise in blood glucose (lower panel). ●: Guar, tragacanth, pectin, methyl cellulose. ○: Bran, cholestyramine.

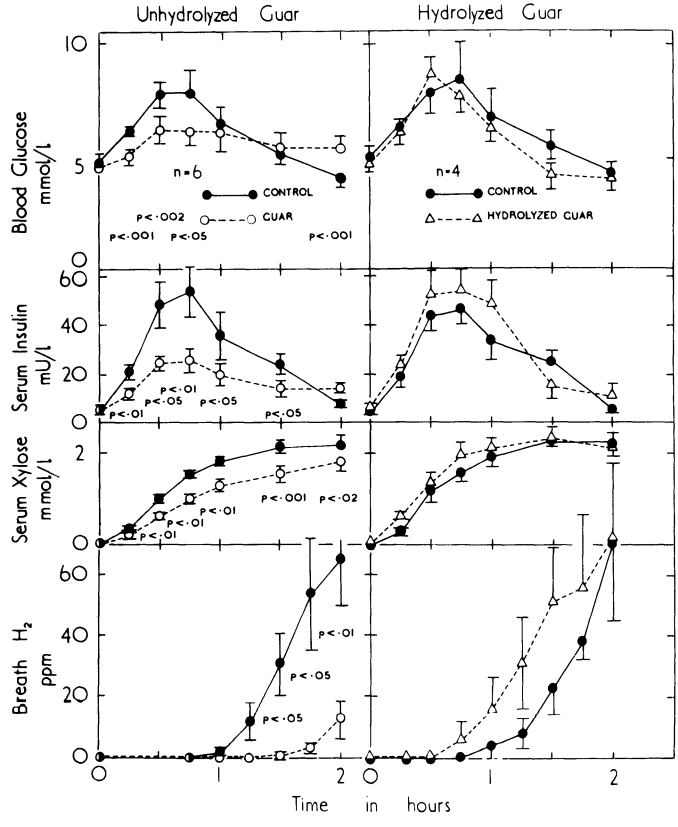

Figure 3. Effect of addition of 14.5 g unhydrolized guar (six subjects, left) or 14.5 g hydrolized guar (four subjects, right) on the postprandial glucose, insulin, xylose, and breath hydrogen responses to rest meals containing 50 g glucose, 25 g xylose, 30 g liquid lactulose (50 % lactulose w/w), 40 g pure lemon juice, and 400 ml water.

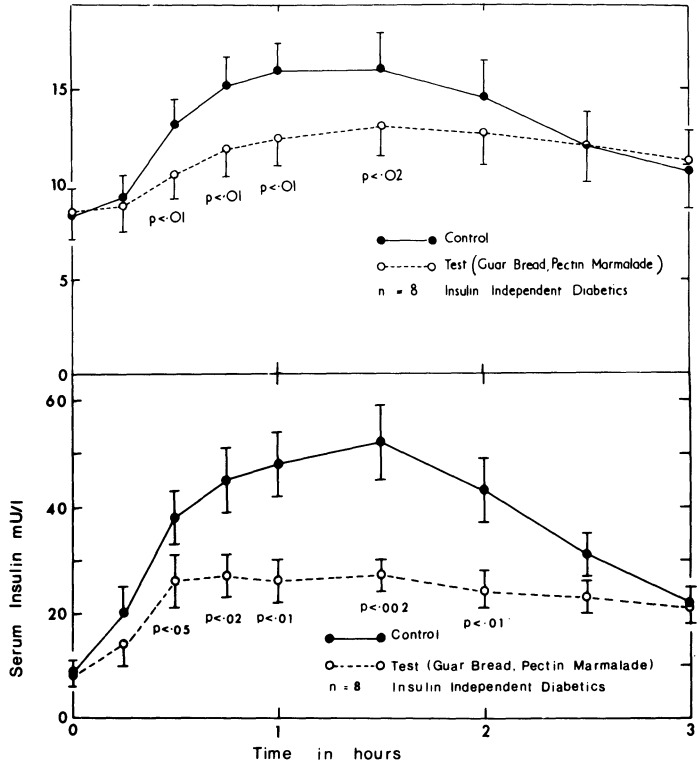

Figure 4. Effect on postprandial levels of glucose and insulin in eight noninsulin-requiring diabetics of adding 16 g guar to bread and 10 g guar to the marmalade in a test-meal breakfast containing 106 g carbohydrate.

in diabetics,[15] and of both GIP and enteroglucagon in patients after surgery who have received pectin with a glucose tolerance test.[16]

C. *Slow Absorption Rather Than Malabsorption*

That the depressed postprandial glycemic responses resulted from malabsorption of carbohydrate remained questionable. To test this, 25 g of xylose was also added to each of the test meals containing guar, tragacanth, pectin, methyl cellulose, bran, and cholestyramine. Urine was collected during the 2 hr of the tolerance test. The outputs in grams over 2 hr are shown with their respective controls in Fig. 5. Over this time period, significantly less xylose was excreted in the case of guar, tragacanth, and bran; only in the case of cholestyramine were the excretions similar.

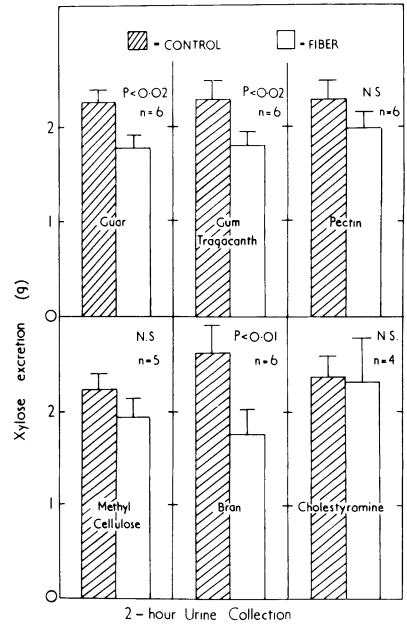

Figure 5. Effect of six fiber preparations on the 2-hr postprandial urinary xylose excretion (g in the 2-hr postprandial period) after a standard test meal (as in Fig. 1) containing 25 g xylose.

However, when in the case of guar, collections were continued as 2-hourly aliquots for 8 hr (Fig. 6), it was seen that although in the first 2 hr more xylose was excreted in the control, thereafter more xylose was excreted in the test situation. Thus, at the end of the 8-hr period, the xylose excretion was greater in the test than in the control. The time and course of excretion seemed to be merely shifted to the right, which indicated a slower absorption of xylose from the small intestine.[10]

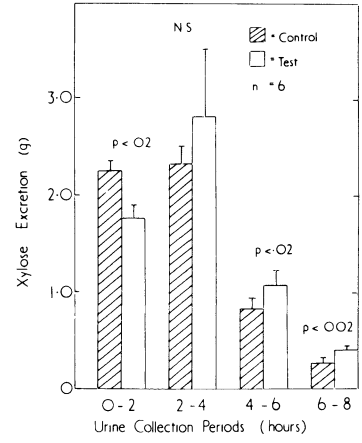

Figure 6. Effect of 14.5 g guar on urinary xylose excretion (g/2 hr) over the first 8 hr (postprandial) collected in 2-hr aliquots and compared with the control meal (as in Fig. 1).

Further work suggesting that guar does not induce carbohydrate malabsorption comes from studies of hydrogen evolution. Malabsorbed sugars are fermented in the colon with hydrogen evolution. A proportion of this hydrogen diffuses back into the blood stream and is exhaled in the lungs, where it can be detected, by gas chromatography, in the breath. This test has been used to assess carbohydrate malabsorption.[17] When guar was added to a glucose tolerance test, it was shown that no hydrogen was evolved over 6 hr; although when lactulose, a nonabsorbable sugar, replaced glucose in the test meal, hydrogen was evolved by 2 hr.[11] These results have been confirmed by Leeds *et al.*,[18] who also found no evidence that guar caused carbohydrate malabsorption.

D. *Gastric Emptying and Small-Intestinal Absorption*

The observation that delayed absorption of xylose accounts for the flattening of postprandial glycemia is consistent with the observation that delayed mouth-to-cecum transit times are associated with ingestion of the viscous forms of dietary fiber. Addition of the nonabsorbable sugar lactulose to fiber-test meals allowed the measurement of the first detectable hydrogen in the breath (Fig. 6). Thus, an indication of the time taken for the lactulose to reach the first bacterially colonized portion of the gut, namely the cecum, was given. This method, developed for malabsorption, has been shown to give a reliable measurement of mouth-to-cecum transit time.[19] Using this method, results for guar, tragacanth, pectin, methyl cellulose, bran, and cholestyramine (Fig. 7) demonstrated that only the viscous substances, guar and tragacanth, delayed mouth-to-cecum transit time to any extent. Figure 8 illustrates the significant relationship of mouth-to-cecum transit time with viscosity.[10] The importance of viscosity is also emphasized by the fact that when guar was hydrolized and rendered nonviscous, the blood and urinary xylose patterns reverted to normal, and the mouth-to-cecum transit time, as measured by hydrogen evolution from lactulose, was more rapid (Fig. 3, bottom panel).

One of the major remaining questions is whether the effects are due to delayed gastric emptying or to a decrease in the rate of small-intestinal absorption, secondary, for example, to an increase in the thickness of the unstirred layer which might result from the presence of fiber. Leeds and colleagues[20] studied the effect of pectin on gastric emptying in the dumping syndrome using ^{113}In and recording gastric emptying with a gamma camera. Their work indicated that, although pectin delayed gastric emptying and significantly reduced the maximum fall in plasma volume after oral glucose, the lack of a significant relationship in normal individuals between the rate of gastric emptying and the level of the postprandial rise in blood glucose suggested that other factors might also operate. The importance of meal viscosity on gastric emptying and glucose absorption has been confirmed in the rat when grades of guar of vary-

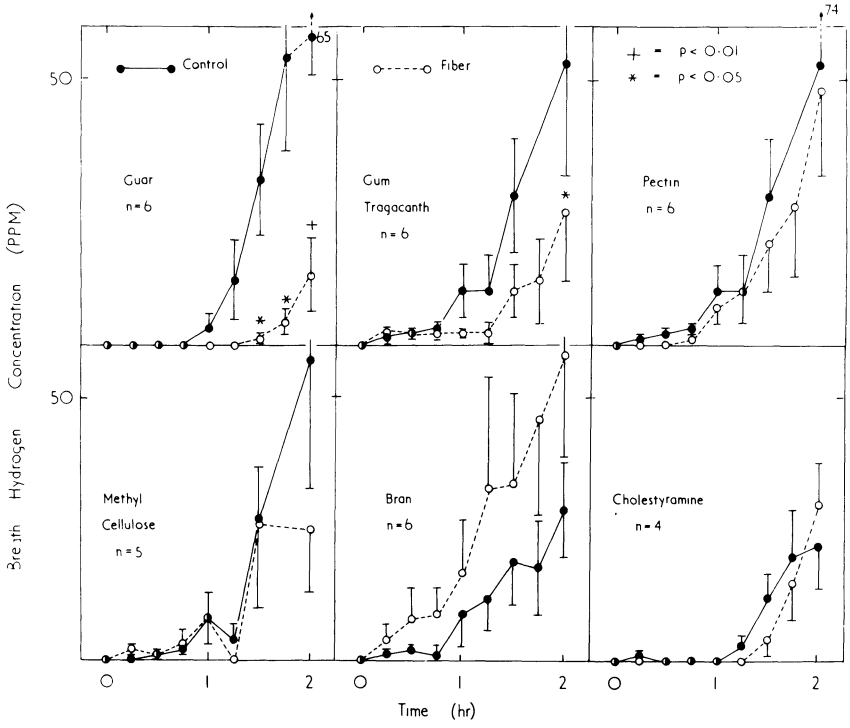

Figure 7. Effect of six fiber preparations on postprandial hydrogen evolution after a standard test meal (as in Fig. 1) containing 30 g lactulose solution (50% lactulose w/w).

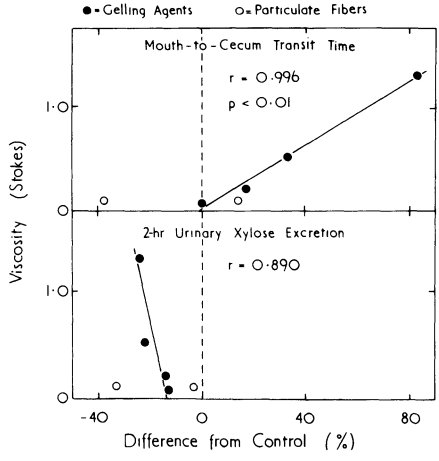

Figure 8. Viscosity of 1% solutions of six fiber preparations plotted against the percentage difference from control of mouth-to-cecum transit time (upper panel) and 2-hr urinary xylose excretion (lower panel). ●: Guar, tragacanth, pectin, methyl cellulose. ○: Bran, cholestyramine.

ing viscosity were used.[21] Further work with normal volunteers, using gamma camera scanning of radioactive indium for gastric emptying, suggests that delayed gastric emptying may be of great importance in flattening the postprandial glycemia.[22] Similar effects were achieved with propatheline. However, study of one individual with a complete gastrectomy demonstrated a reduction in the area under the glucose tolerance curve after addition of guar or pectin. Nevertheless, the authors concluded that the stomach was of major importance for the action of these forms of dietary fiber.[22]

On the other hand, pectin has been found useful in modifying the glucose tolerance curve and preventing postprandial hypoglycemia in patients who have undergone a variety of gastric surgical procedures ranging from vagotomy and pyloroplasty to Polya and Bilroth gastrectomies.[23] In addition, these patients produced less hydrogen in their breath after taking pectin with the glucose load (Fig. 9). It seems likely, therefore, that pectin also reduced glucose malabsorption,[23] since the hydrogen is evolved from malabsorbed carbohydrate reaching the cecum and being fermented there by bacteria.[19] This action may be explained by the ability of viscous forms of dietary fiber to slow mouth-to-cecum transit time.[10] Thus, by preventing the gastrointestinal hurry seen after gastric surgery, they may allow time for glucose to be absorbed more completely from the small intestine. This might be interpreted as allowing more glucose to be absorbed in the presence of guar. Evidence that the small intestinal events may still be of importance comes from *in vitro* work using dialysis tubing containing glucose solution to which guar and pectin had been added. It can be shown that these substances delay the diffusion of glucose out of the dialysis bags in proportion to their viscosity. This does not appear to be a chemical binding in that, with time, the concentration on both sides of the dialysis membrane is the same[24]

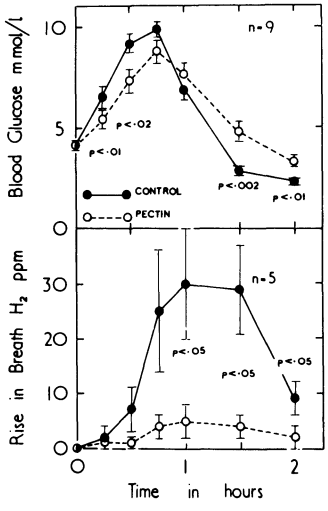

Figure 9. Blood glucose concentration in nine post-gastric surgery patients (upper panel) with end expiratory hydrogen concentrations in five of these patients (lower panel) during the 2-hr period after taking 50 g glucose (●—●) and after taking 50 g glucose with 14.5 g pectin (o---o).

E. Rate Phenomenon

The action of the gel-forming dietary fibers and, perhaps, dietary fiber in general, appears to be related to its ability to slow the rate of nutrient absorption, with resulting flatter postprandial levels of glucose, metabolites, and hormones. It is still not possible to assess the relative importance of gastric emptying and delayed small-intestinal absorption. Both functions are likely to operate but, at present, gastric emptying has received the major experimental attention. The concept of the virtues of slow and prolonged absorption may well be seen as the current extension of the debate "nibbling versus gorging."

V. PREREQUISITES FOR MAXIMUM EFFECTIVENESS

A. High-Starch Diets

The work of Kiehm *et al.*[2] and Anderson and Ward[3] has demonstrated clearly the value of using diets rich in both fiber and starch. In fact, the original fiber hypothesis emphasized this point.[25] In addition, it appears that not all starch produces the same response in terms of postprandial glucose and insulin levels.[26] Rice and corn produce flatter glucose and insulin responses than dextrose and potato. One is tempted to speculate here that in the same way that whole apple produced a different picture after ingestion from that produced by apple puree, so the intact nature of rice* and corn grains may be responsible for flattening and, therefore, delaying absorption. Obviously, against the background of these sorts of food, fiber supplementation is likely to be most effective. The lack of therapeutic gain resulting from giving guar against a background of high mono- and disaccharide intakes was shown in a study where total carbohydrate intake was kept constant, but where the proportion of mono- and disaccharide was increased.[27] Here 26 g of sugar was given instead of starch in the control period. The resulting urinary glucose output was twice the original control output, even after addition of 25 g of guar to the diet had produced a 45% reduction in glycosuria (Fig. 10).

B. Intimate Mixing with Carbohydrate Foods

Recent work has emphasized that in order to be effective, fiber supplements must be mixed intimately with the carbohydrate portion of the foods, as is the case with natural "whole" foods. All studies that have shown modification of postprandial glycemia and insulin responses with added dietary fiber

*This has now been confirmed by O'Dea, K., P. J. Nestel, and L. Antonoff, Physical factors influencing postprandial glucose and insulin responses to starch. *Am. J. Clin. Nutr.* 33:760–765, 1980.

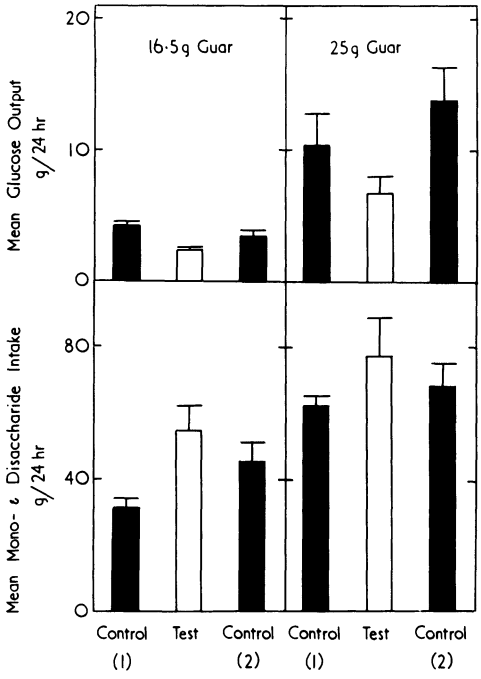

Figure 10. Effect of guar and sugar intake (g/24 hr, bottom panels) on urinary glucose output (g/24 hr, top panels) in one diabetic patient over two 3-week periods, during the middle week of which the patient took either 16.5 g guar (left panels) or 25 g guar (right panels).

have observed these principles.[11,13–15] Studies on the effect of guar added to bread and soup suggest that the greatest effect is achieved when the guar is incorporated into the soup as part of the meal.[13] Thus, the guar may not only cover the carbohydrate in the soup but also be absorbed by the bread. When incorporated into the bread, it will have little effect in preventing the rapid absorption of carbohydrates in the soup (Fig. 11). However, the 5 g of guar was so effective when used in soup form that, although greater significance was achieved, little further flattening occurred when guar was added to both bread and soup (Fig. 11). Failure to mix the guar adequately with the carbohydrate portion of the meal has been shown to render it without effect in terms of flattening postprandial glycemia.[28] It has also been demonstrated that when guar is taken before a glucose tolerance test rather than with the glucose tolerance test, its effectiveness is completely lost[29] Fig. 12). The importance of mixing the fiber supplement with the starchy carbohydrate portion of the food cannot be stressed too much.

VI. GENERAL CONSIDERATIONS

Apart from the use of sugar, it is likely that those factors which have been implicated in exacerbating the dumping syndrome will also tend to negate the

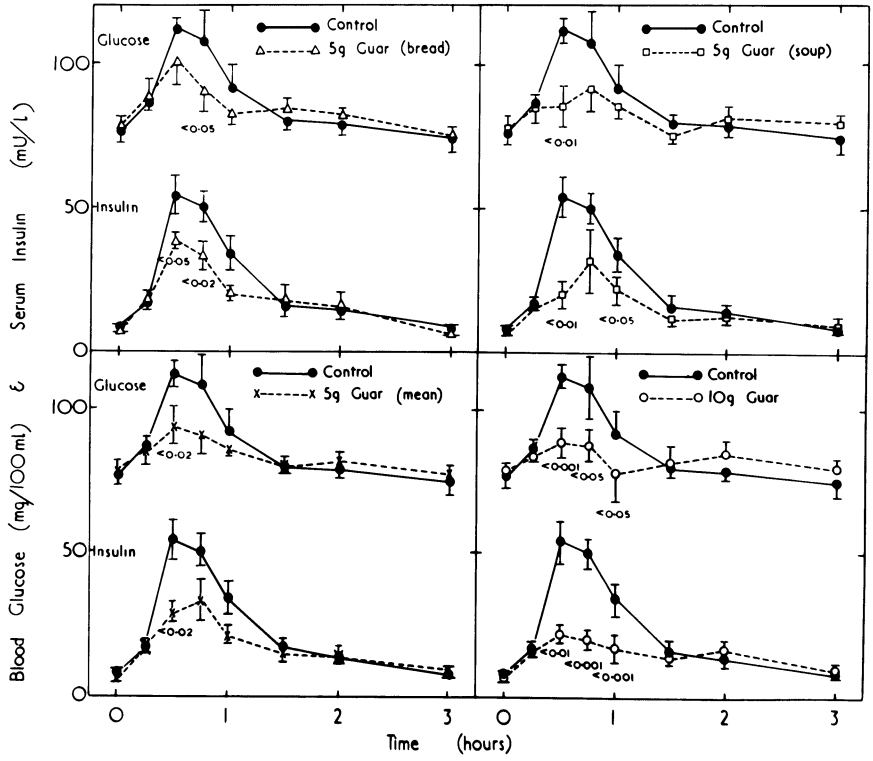

Figure 11. Mean blood glucose and serum insulin in five subjects after taking a control meal (●—●) or test meals of bread and soup containing 5 g guar in bread (Δ---Δ, upper left panel), 5 g guar in soup (□--□, upper right panel), mean of bread and soup 5-g guar results (×---×, lower left panel) or 10 g guar as 5 g in both bread and soup (o---o, bottom right panel).

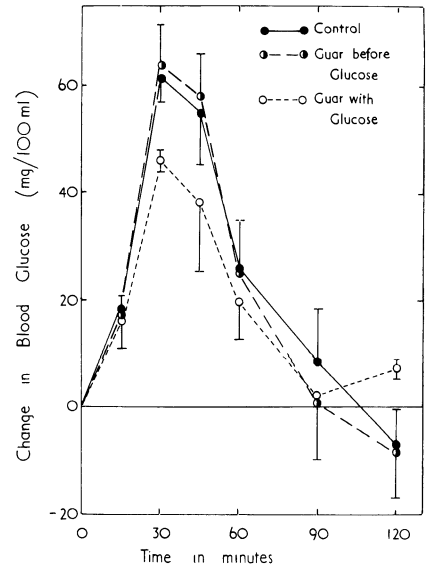

Figure 12. Effect on postprandial blood glucose of taking 14.5 g guar immeadiately before 50 g glucose (o---o) or together with 50 g glucose (o---o) as compared with 50 g glucose alone (●—●, control).

action of dietary fiber. The aim in both situations is to slow gastrointestinal transit. Thus, excess fluid with meals or the ingestion of gastrointestinal stimulants such as wines and spirits is likely to minimize the effectiveness of any fiber supplement.

With all fiber supplements, palatability is a major consideration. Some people find it difficult to adhere to natural high-fiber diets. Equally, diets containing large amounts of any dietary fiber supplement which has not been palatably processed will probably be discontinued. Inevitably, because of altered gastrointestinal events, confusing reports appear in the literature about the action of dietary fiber by those who have given it in a particularly unpalatable form.[30]

A. *Effect of One Fiber Meal on the Next*

Not all the actions of dietary fiber on carbohydrate metabolism can be ascribed to events within the gastrointestinal tract. The progressive reduction in insulin requirements seen on high-fiber diets suggests that other mechanisms are also operant.[3] When glucose loads, both with and without guar, were given in the morning and a further glucose load without guar was given 4 hr later (Fig. 13), the glucose tolerance curve that followed the early morning guar and glucose load was considerably flattened compared to the first glucose load with no guar. It is unlikely that much guar would have remained in the stomach to

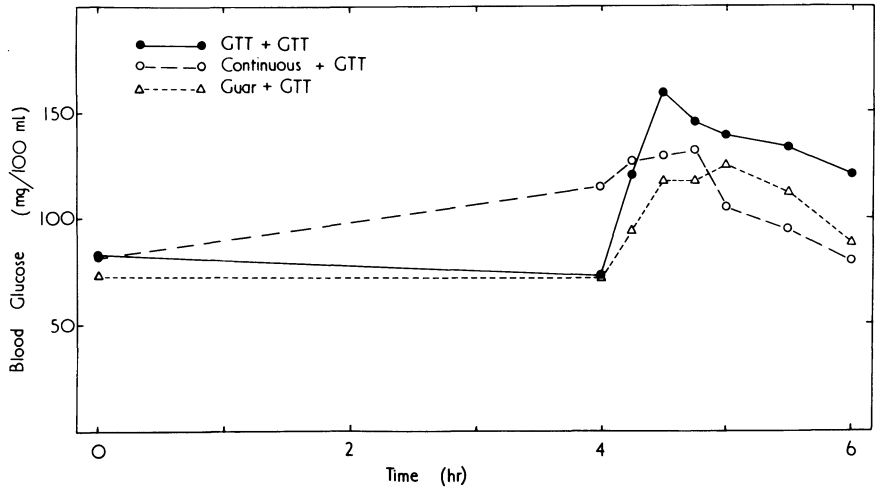

Figure 13. Effect on blood glucose of taking two 80-g glucose loads separated by 4 hr (●—●, control) when either 23 g guar was added to the first glucose load (Δ---Δ) or the first glucose was taken evenly over the first 4 hr load (o---o).

modify either of the two subsequent glucose tolerance tests, both of which were given without guar. To check whether slow release of carbohydrate had been responsible for this following the guar meal, the initial glucose load was spread over the entire 4 hr prior to the start of the formal glucose tolerance test at that point. A similar picture of flattening occurred with hardly any rise in the blood sugar after ingestion of the glucose load at 4 hr. This suggests that dietary fiber, by prolonging the time course over which carbohydrate is absorbed and at the same time minimizing the endocrine response, allows the subsequent meal, regardless of whether it contains fiber, to be taken up more readily by peripheral tissues.[31] Part of the explanation for this effect may lie in the fact that, as shown previously,[8] ingestion of refined carbohydrates tends to produce a rebound hypoglycemia. This itself will be counteracted by mobilization of free fatty acids with ketone body synthesis. It is interesting that in this study, ketone bodies rose after glucose alone between time 0 and 4 hr and fell over the same time course after glucose had been given with guar at time 0. Such effects may be progressive with each successive fiber meal and so account for the longer-term effects of dietary fiber.

B. *Long-Term Effect of Dietary Fiber*

Feeding bran supplements to middle-aged patients with diverticular disease has been shown to improve glucose tolerance over 6 months.[32] In young, healthy volunteers, however, 6 weeks' supplementation of the diet with 35 g pectin failed to produce any alteration in glucose or insulin response (Fig. 14).[33] In terms of correcting abnormal carbohydrate metabolism by dietary fiber, the

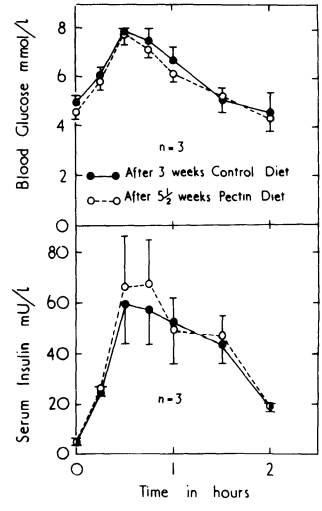

Figure 14. Effect on blood glucose and serum insulin of 6 weeks' pectin administration (35 g/day) in 3 volunteers on metabolic diets who took identical breakfasts immediately preceding and at the end of the period of pectin supplementation.

latter study is obviously not relevant, since the healthy volunteers had normal glucose tolerance.

Perhaps of greater importance, in the long term, is the sparing of urinary glucose loss, which may occur with successful high-fiber therapy in diabetics. With this therapy, the effective carbohydrate intake from the diet will be increased. Increased carbohydrate intakes have been shown to improve glucose tolerance and insulin sensitivity in both healthy men and diabetics.[34-36] Although, in many instances, the reduction in urinary glucose output may not have contributed to a large increase in metabolized carbohydrate, it might be seen as a step in the right direction. Conversely, work on carbohydrate deprivation and high-fat diets fed to normal volunteers has shown the effect on raising the basal free-fatty-acid level and impairing glucose tolerance.[37] All these findings support the use of high-carbohydrate, high-fiber diets in the treatment of diabetes.[3]

VII. CONCLUSION

The action of dietary fiber in flattening the postprandial glycemia and endocrine responses appears to result from its ability to release carbohydrate slowly from the intestine. It therefore corresponds to "Lente Carbohydrate." As it is with the whole-food approach to the modification of the postprandial glucose levels, so it must be with the pharmacological approach using refined dietary fibers. Thus, dietary fiber should be given intimately mixed with the carbohydrate portions of the food and should be provided largely as starch for maximum effectiveness. The actions of slow-release carbohydrate on metabolism are profound, as shown in studies of the treatment of diabetes. Further work remains to be done on the effect of natural foods and their fiber in modifying glucose absorption. This will also allow the definition of a background diet which is most suitable for the purified- or pharmacological-fiber approach to altering carbohydrate absorption.

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11

Dietary Fiber and Diabetes

James W. Anderson

I. INTRODUCTION

A. Therapeutic Potential of Dietary Fiber

Persons with diabetes mellitus may reap substantial benefits from increasing their intake of dietary fiber. The short-term use of selected fibers lowers blood glucose values and insulin requirements[1,2]; serum cholesterol and triglyceride values may also decline.[1,3] The long-term effects of fiber intake have not been evaluated, but two potential benefits can be proposed. First, improved diabetic control should lessen the likelihood of the specific complications of diabetes.[4] Second, improved diabetic control coupled with lower serum cholesterol and triglyceride values should lessen the risk of arteriosclerotic cardiovascular disease. Epidemiological evidence supports both these suggestions. In regions such as Japan, India, and the West Indies where the intake of carbohydrate and dietary fiber is high, the specific complications of diabetes are less frequent than in Western countries, where the fiber intake is low.[5–7] Heart attacks and diabetic gangrene among persons with diabetes are less common in India and Japan than in the United States.[6,7] Thus, an increase in dietary fiber intake by persons with diabetes may improve diabetic control; the risk for the small-blood-vessel complications specific for diabetes as well as for large-blood-vessel disease may be decreased.

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B. Dietary Fiber and the Prevalence of Diabetes

In general, the prevalence of diabetes is lower in populations with high fiber intakes than in Westernized populations with low fiber intakes.[8] Among primitively living people, where most of the energy requirements are provided by unrefined carbohydrates containing large amounts of dietary fiber, diabetes is uncommon. In many industrialized urban populations, where intake of unrefined carbohydrate and dietary fiber is low, the prevalence of diabetes is quite high. West and Kalbfleisch[8] reported that the prevalence of diabetes in 11 populations ranges from 2% in East Pakistan (now Bangladesh) to 17.2% in Pennsylvania. In East Pakistan, 83% of the energy came from carbohydrate and only 7% from fat; presumably the dietary fiber intake was high. In a Pennsylvania city, the diet differed from the Pakistani diet in several ways: (1) carbohydrate intake, at 47% of total energy, was much lower; (2) most of the carbohydrate was in a processed or refined form[9]; (3) the dietary fiber intake was very low; and (4) the fat intake, providing 40% of energy was much higher.[8]

The fiber-depletion hypothesis of the etiology of diabetes was formulated by Trowell.[10] It was based on the observations that, first, diabetes is rare among African villagers who have high-fiber diets but is common in Western urban people who have low-fiber diets and, second, the death rate from diabetes declined during wartime and coincided with an increase in dietary fiber intake from high-fiber breads (discussed in detail in reference 10). Many epidemiological observations[5–8] are consistent with this hypothesis. Within one or two decades after changing from a high-fiber to a low-fiber diet, Yemenite Jews and the Transvaal Bantus[10–12] showed an increase in the prevalence of diabetes. Thus, available data show an inverse correlation between the intake of unrefined carbohydrate plus dietary fiber and the prevalence of diabetes. However, there are many other dietary differences between primitively living people and highly industrialized urban populations, in addition to environmental, genetic, socioeconomic, and exercise-related dissimilarities.

II. SHORT-TERM EFFECTS OF FIBER

A. Fiber Supplements

The innovative studies of Jenkins and colleagues[13–18] demonstrated that fiber-rich meals were followed by less hyperglycemia than were fiber-poor meals. The effects of dietary fiber on postprandial glycemia were observed in normal individuals and in patients with chemical diabetes. Water-soluble fibers, especially guar, were much more effective in lowering postprandial glycemia than were water-insoluble fibers such as those contained in wheat bran.[16]

They also fed test meals with or without soluble-fiber supplements to insulin-dependent diabetes patients.[13] When the test meals without fiber were given, postprandial glucose values were consistently higher than values after meals containing fiber. For five to seven days, in an alternating sequence, patients with diabetes were fed control diets and diets with approximately 25 g guar per day; fasting blood glucose values and glucose excretion were significantly lower on the guar-supplemented diets than on control diets (Figure 1). These studies[15,17,18] indicated that fiber supplements decreased postprandial glycemia and urine glucose excretions in diabetes patients and suggested that dietary fiber might have a beneficial role in the long-term management of diabetes. Monnier and colleagues[19] have confirmed the observations of Jenkins *et al.*[13,14,16] by demonstrating, in patients with chemical diabetes, that fiber supplements decrease the glycemic response to oral glucose administration.

Miranda and Horwitz[20] also demonstrated that fiber-supplemented diets were associated with significantly lower postprandial glucose values in insulin-treated individuals with diabetes than the values associated with low-fiber diets. They fed low-fiber or high-fiber diets for 10 days in a random sequence. The low-fiber diets provided approximately 3 g crude fiber per day, and the high-fiber diets provided approximately 20 g crude fiber per day. They calculated the nutrient and energy contents of these diets using data from standard sources.[21–23] These standard sources provide information on total carbohydrate, which includes available carbohydrate and unavailable carbohydrate (fiber). They attempted to feed diets that were equivalent in nutrient and energy contents and differed only in their fiber content.

As we have noted,[24] however, these standard sources[21–23] overestimate the energy and avilable carbohydrate content of high-fiber foods. We have recom-

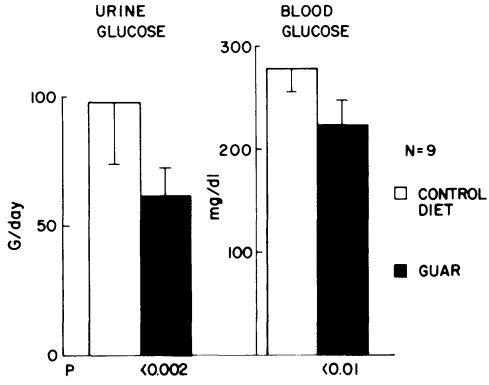

Figure 1. Response of diabetic patients to guar-supplemented diets. Patients were fed control diets for 5 days and guar-supplemented diets (23 g guar per day) for 5 days in alternating sequence. From Jenkins *et al.*[2]

Table 1. Composition of Low-Fiber and High-Fiber Diets[a,b]

	Low-fiber diet		High-fiber diet	
	g/day	% Energy	g/day	% Energy
Protein	96	20	101	23
Available carbohydrate (total)	218	44	146	32
Simple carbohydrate	156	—	118	—
Complex carbohydrates	62	—	28	—
Fat	78	36	90	45
Fiber (total)	16.4	—	47.5	—
Crude[c]	3.0	—	20.3	—
Kilocalories	1962	100	1829	100

[a]Diets used by Miranda and Horwitz.[20]
[b]Nutrient, fiber, and energy values were computed by Beverly Sieling, R.D., from the data of Anderson *et al.*[24]
[c]Values from diet examples of Miranda and Horwitz.[20]

puted the nutrient, fiber, and energy values of their diets (Table 1). The high-fiber diets provided less available carbohydrate, more fat, and less energy than the low-fiber diets. Nevertheless, the major differences were that the high-fiber diets provided three times the total fiber of the low-fiber diets. Fasting plasma glucose values were similar for the two diets, but postprandial glucose values were significantly lower (Fig. 2) for the high-fiber diets than for the low-fiber diets. Plasma glucagon levels also were significantly lower for the high-fiber diets. Since the same doses of insulin were maintained and plasma-free insulin concentrations were similar throughout this study, the lower postprandial plasma glucose values and the occurrence of more hypoglycemic reactions for the high-fiber diets suggest that fiber ingestion may increase sensitivity to insulin. Thus, these studies[13,15,17–20] from three different countries suggest that

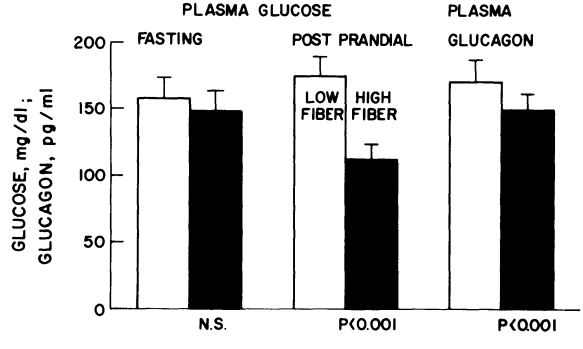

Figure 2. Response of diabetic patients to low-fiber and high-fiber diets. Patients were fed low-fiber diets (3 g crude fiber per day) for 10 days and high-fiber diets (20 g crude fiber per day) for 10 days in an alternating sequence. From Miranda and Horwitz.[20]

fiber-supplemented diets might have distinct therapeutic advantages for persons with diabetes.

B. High-Fiber Diets

Most people on this planet eat large amounts of unrefined carbohydrate-containing fiber. Some physicians in India, Japan, and other countries have encouraged their patients with diabetes to restrict their carbohydrate intake and attempt to follow a "Western-type" diabetic diet.[5–7] Several groups in India,[25–27] however, have documented that high-carbohydrate diets are well tolerated by their patients with diabetes and recommend a high-carbohydrate diet as the standard treatment for diabetes. Singh,[28] for example, demonstrated the therapeutic utility of high-carbohydrate, high-fiber diets for persons with diabetes. In the United States, the concept of increasing carbohydrate intake and restricting fat intake is gaining wider acceptance.[29,30] On our metabolic ward, we have compared the effects of conventional diets with high-carbohydrate, high-fiber (HCF) diets on the glucose and lipid metabolism of patients with diabetes or hyperlipidemia. Our results[3,31–34] will be briefly summarized.

Representative control and HCF diets that we have used are presented in Table 2. Control diets provide about 43% of energy as carbohydrate and are similar to traditional American Diabetes Association (ADA) diets. However, our control diets contain less cholesterol and more fiber than do most ADA diets. The HCF diets used in the hospital provide 70% of energy as carbohydrate and 30–40 g fiber per 1000 kcal. All diets are prepared from commonly available foods and no purified or semipurified fibers are used (see Table 3).

Table 2. Composition of Control, HCF, and Maintenance Diets[a]

	Control		HCF		Maintenance	
	g/day	% kcal	g/day	% kcal	g/day	% kcal
Protein	98	20	96	19	96	19
Available carbohydrate (total)	215	43	351	70	275	55
Simple	100	—	94	—	80	—
Complex	115	—	257	—	195	—
Fat (total)	83	37	23.6	11	57	26
Saturated	19	—	4.7	—	13	—
Monounsaturated	43	—	9.5	—	21	—
Polyunsaturated	15	—	6.9	—	15	—
Cholesterol	0.47	—	0.04	—	0.11	—
Fiber (total)	27	—	82	—	52	—
Insoluble	15	—	67	—	42	—
Soluble	12	—	15	—	10	—

[a]Values for representative 2000 kcal diets were computed from the data of Anderson *et al.*[24]

Table 3. Examples of 2000-kcal HCF Diets[a]

Breakfast	
Skim Milk, 246 g	Skim milk, 123 g
All Bran®, 60 g	Corn flakes, 40 g
Whole-wheat muffin, 40 g	Whole-wheat muffin, 40 g
Orange, fresh, 100 g	Grapes, fresh, 125 g
Morning snack	
Whole-wheat muffin, 40 g	Whole-wheat muffin, 40 g
Banana, 100 g	Apple, fresh, 125 g
Noon meal	
Whole-wheat muffin, 40 g	Whole-wheat muffin, 40 g
Saltines, 25 g	Soup: Tomato juice, 150 g
Chili: Tomato juice, 200 g	Brown rice, 60 g
Kidney beans, 125 g	Roast beef, 30 g
Steak, 15 g	Lima beans, 150 g
Onions, 10 g	Celery, 125 g
Bran, 25 g	Pears, canned, 100 g
Carrots, 125 g	
Corn, 100 g	
Afternoon snack	
Brown rice, 50 g	Whole-wheat bread, 46 g
Whole-wheat muffin, 40 g	Pork, lean, 15 g
	Celery, 125 g
Evening meal	
Brown rice, 60 g	Lettuce, 20 g
Pork, 15 g	Whole-wheat muffin, 40 g
Green beans, 150 g	Roast turkey, 15 g
Diabetic slaw, 165 g	Beets, 125 g
	Peas, 125 g
	Cabbage, 150 g
	Lima beans, 100 g
	Peaches, canned, 125 g
Evening snack	
Skim milk, 123 g	Whole-wheat muffin, 40 g
Whole-wheat bread, 46 g	Skim milk, 123 g
Pork, lean, 15 g	Corn flakes, 35 g
Other	
Instabutter®,[b] 10 g	Instabutter, 15 g
Coffee, tea, diet cola	Diabetic jelly, 10g
	Coffee, tea, diet cola

[a]The nutrient and fiber contents of these two diets are similar to the values given for the HCF diet in Table 2.
[b]A fat-free, liquid product, containing milk protein, which resembles melted butter.

The control and HCF diets are designed to be weight maintaining throughout the study; our balance studies indicate that the control and HCF diets provide virtually identical amounts of energy. The difficulty with providing isocaloric diets using standard values[21–23] for energy and carbohydrate was noted (Table I) in the description of the study of Miranda and Horwitz.[20] We observed that patients lost weight on HCF diets when we used the standard values for energy. Consequently, we have had to compute new values for energy and available carbohydrate for foods that we use.[24] We have analyzed over 30 different diets and found that our computed values for protein and fat are virtually identical to measured values. Values for the fiber content of our diets are provisional; neutral-detergent residue measurements underestimate the total fiber content of these diets,[24] and we currently are measuring the water-soluble and -insoluble fiber content to provide more accurate estimates.

1. *Glucose Metabolism*

Most patients received control diets for 5–11 days followed by HCF diets for 14–28 days. Insulin doses were adjusted to maintain fasting plasma glucose values of approximately 150 mg/dl and urine glucose excretion of less than 10 g/day. The response of a representative patient is presented in Fig. 3. On the control diet, insulin doses were increased to achieve better glucose homeostasis and then maintained at 32 U/day. On this insulin dose, fasting plasma glucose values averaged 165 mg/dl and urine glucose valued averaged 6 g/day for the last 6 days on the control diet. On the HCF diet, fasting plasma glucose values dropped promptly and the insulin dose could be rapidly decreased. After 16 days on the HCF diet, insulin therapy was discontinued. Without daily insulin injections, the fasting plasma glucose and urine glucose values on the HCF diet were similar to values while the patient was taking 32 U insulin daily on the control diets. This man has followed a 60%-carbohydrate, high-fiber maintenance diet for 2 years and has had satisfactory fasting plasma glucose values without insulin therapy.

On weight-maintaining control diets, insulin doses remained stable for 7–11 days. We have fed weight-maintaining conventional ADA diets (42–45% carbohydrate) to four lean patients hospitalized for 30–90 days without noting changes in insulin requirements. Other investigators[35,36] have documented that glucose homeostasis and insulin requirements are stable on weight-maintaining conventional diets. In sharp contrast, HCF diets are accompanied by significant reductions in insulin requirements in virtually all patients with diabetes that we have studied. The responses of seven patients receiving moderate doses of insulin are illustrated in Fig. 4. These lean individuals were receiving 25–40 U/day, and their requirements were stable on the control diets. On the HCF diets, insulin requirements fell to one-half of those on control diets, and fasting plasma glucose values were similar on the two diets.

The responses of 29 lean, insulin-treated individuals to weight-maintain-

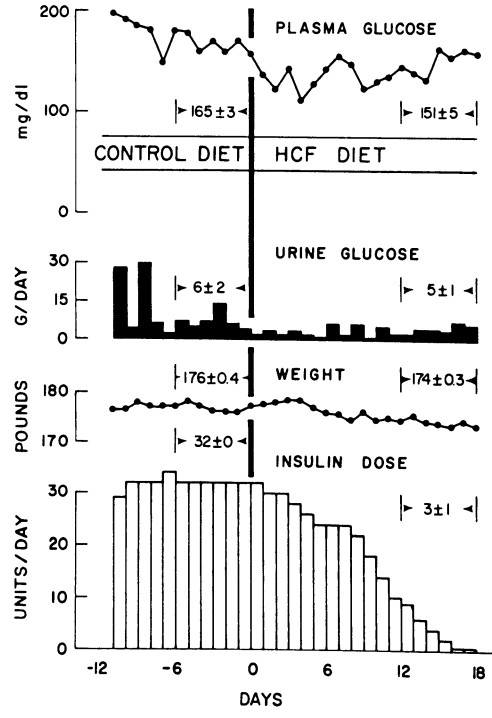

Figure 3. Influence of control and HCF diets (Table 2) on glucose metabolism of a diabetic patient. Reproduced with permission; from Anderson and Ward.[33]

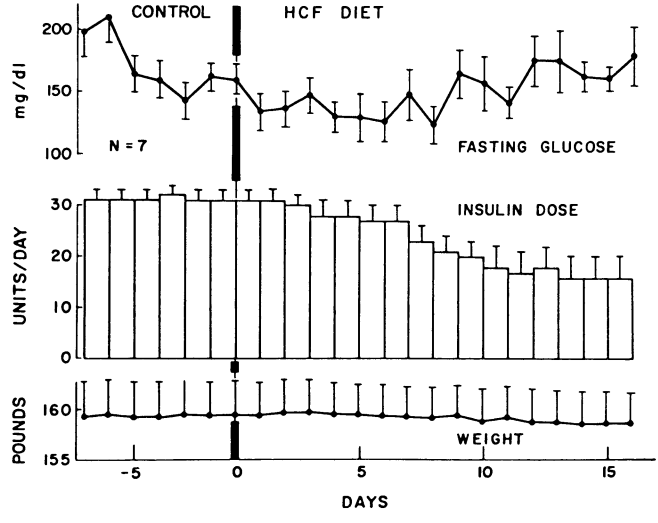

Figure 4. Responses of diabetic patients to control and HCF diets. Reproduced with permission; from Anderson and Ward.[33]

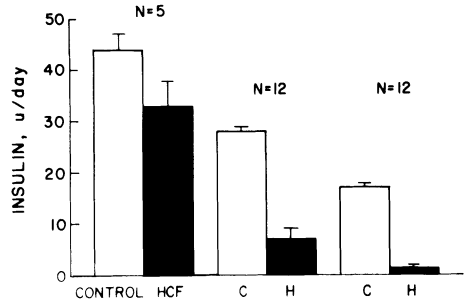

Figure 5. Insulin doses on control and HCF diets. Patients received control diets for 5–11 days and then HCF diets for 14–30 days.

ing HCF diets are summarized in Figure 5. Twelve individuals (Fig. 5, right panel) were receiving 15–20 U/day on control diets. On HCF diets, insulin was discontinued in 10 patients and the remaining 2 patients required only 2 or 6 U/day. Twelve additional patients (Figure 5, middle panel) required 22–32 U/day on the control diets; on HCF diets, their average dose dropped to 7 U/day. On the HCF diets, insulin was discontinued in five patients and the remaining patients required between 4 and 18 U/day. In these 24 patients, average fasting plasma glucose values and 24-hr urine glucose values were lower during the last week of the HCF diets than these values were for the control diets. Five insulin-dependent adults with the juvenile-onset type of diabetes have been treated with HCF diets (Fig. 5, left panel). On the control diets, insulin doses ranged from 40 to 55 U/day and averaged 44 U/day. On the HCF diets, insulin requirements dropped to 33 U/day (range 20–46 U/day). In three of these patients, diabetic management was distinctly improved on the HCF diets; plasma glucose excursions were smaller, there was less glycosuria, and insulin reactions were less frequent. These observations suggest that HCF diets that provide plentiful amounts of unrefined carbohydrate and fiber have distinct beneficial effects on the glucose metabolism and insulin requirements of selected patients with diabetes mellitus.

2. *Lipid Metabolism*

The effects of fiber ingestion on serum lipids in man are discussed in Chapter 10 of this volume and are reviewed elsewhere.[1] The serum lipid response to HCF diets will be summarized. HCF diets contain more carbohydrate and fiber as well as less fat and cholesterol than do control diets. Thus, changes in plasma lipids cannot be attributed solely to the fiber content of the HCF diet. Nevertheless, the favorable effects of HCF diets on serum cholesterol and triglyceride values will be reviewed.

Fasting serum cholesterol concentrations have fallen significantly in each of 50 patients treated with HCF diets, the values averaging 25% lower than with control diets. The response of 20 patients is presented in Fig. 6. On control

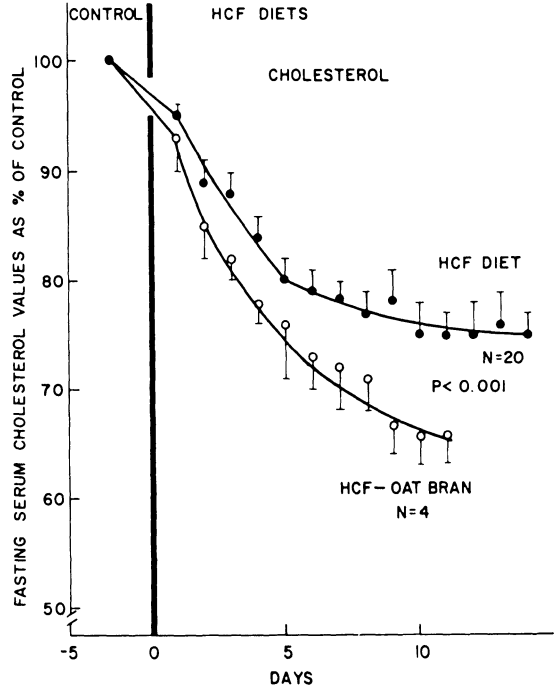

Figure 6. Serum cholesterol responses to HCF diets. Twenty diabetic patients received HCF diets (Table 2); four patients received oat-bran-modified HCF diets.

diets for 5–21 days, cholesterol values were stable. However, after instituting HCF diets, there was a rapid reduction in cholesterol values, which averaged 20% in the first 5 days. Values declined an additional 5% over the next 5 days and then remained fairly stable for the next 5–20 days. On our standard HCF diets, the major reduction occurs in the low-density lipoprotein (LDL) cholesterol concentrations, but the high-density lipoprotein (HDL) cholesterol values also decline.

Because ingestion of water-soluble fibers such as guar and pectins are accompanied by reductions in serum total cholesterol values,[1] we have done preliminary studies on the effects of oat bran, a good source of soluble fiber. Four men consumed modified HCF diets, which contained 100 g oat bran per day. These diets were similar in composition to our standard HCF diets, except that the HCF-oat-bran diets provided more soluble fiber. Serum total cholesterol values were observed to fall significantly more with HCF-oat-bran diets than with standard HCF diets (Figure 6). The HCF-oat-bran diets selectively lowered LDL cholesterol while elevating HDL cholesterol. Thus, LDL cholesterol values decreased by 36% on the HFC-oat-bran diets while HDL choles-

terol values increased by 82% ($p < 0.002$). These preliminary observations in humans that oat bran ingestion selectively lowers LDL cholesterol while raising HDL cholesterol values have been confirmed in rats fed oat bran in comparison to cellulose.[37] These observations have important implications in clinical medicine, because low-density lipoproteins are atherogenic whereas high-density lipoproteins are antiatherogenic.[38] Dietary maneuvers that selectively lower LDL cholesterol while raising HDL cholesterol values would have valuable therapeutic benefits for patients with hypercholesterolemia or ischemic heart disease.

The impact of dietary fiber on fasting serum triglyceride values has not been well delineated.[1] When diets are supplemented with purified fibers, semipurified fibers, or wheat bran, serum triglyceride values usually are not altered.[1] Our studies and the report of Albrink and colleagues[39] suggest that ingestion of a mixture of fibers from natural foods may lower fasting serum triglyceride values. We[40] have confirmed the observations of others[41] that high-carbohydrate diets often induce hypertriglyceridemia. However, after altering our diets to provide liberal quantities of dietary fiber, hypertriglyceridemia has not been a problem. Thus, our HCF diets providing 70% of energy as carbohydrate are accompanied by an average reduction in fasting serum triglyceride values of 18% ($p < 0.01$).

The responses of fasting serum triglyceride values of 44 patients with diabetes to control and HCF diets are presented in Fig. 7. When on control diets, 8 patients had triglyceride values below 100, 21 had values of 101–200 mg/dl, 8 had values of 201–300, and 7 had values of 301–400. There were no significant differences between values for control and HCF diets in patients with values below 200 mg/dl. When baseline values were between 201 and 300

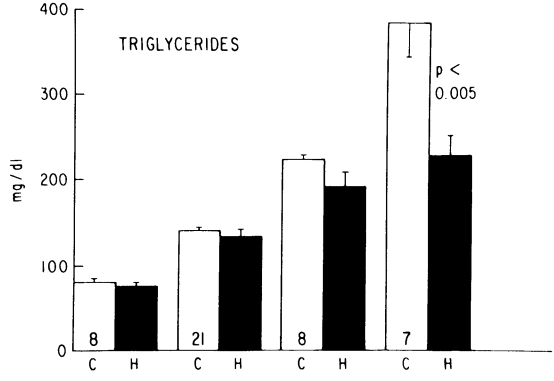

Figure 7. Fasting serum triglyceride values on control and HCF diets. These diabetic patients received control diets for 5–11 days and then HCF diets for 14–30 days. Patients were grouped on the basis of triglyceride values on control diets.

mg/dl, 7 of 8 patients had a reduction in triglycerides when on HCF diets. Those patients with more severe hypertriglyceridemia all had a reduction in triglyceride values when on the HCF diets.

The conventional dietary management of hypertriglyceridemia involves the restriction of simple and total carbohydrates.[42] Recent studies,[43–45] however, suggest that carbohydrate restriction is not essential in the management of most adults with hypertriglyceridemia. Encouraged by our observations in patients with diabetes (Fig. 7), we have evaluated the effects of HCF diets on 12 patients with distinct hypertriglyceridemia. These patients were admitted to our metabolic ward and fed weight-maintaining control diets for 4–7 days. Fasting serum triglyceride values ranged from 213 to 2970 mg/dl with mean values of 1148 mg/dl. These patients were then fed weight-maintaining HCF diets for 10–16 days. Whereas triglyceride values did not fluctuate significantly with the control diets, values fell dramatically with the HCF diets (Fig. 8). After an average of 12 days, fasting serum triglyceride values were 63% lower ($p < 0.01$), and cholesterol values were 32% lower ($p < 0.02$). No significant

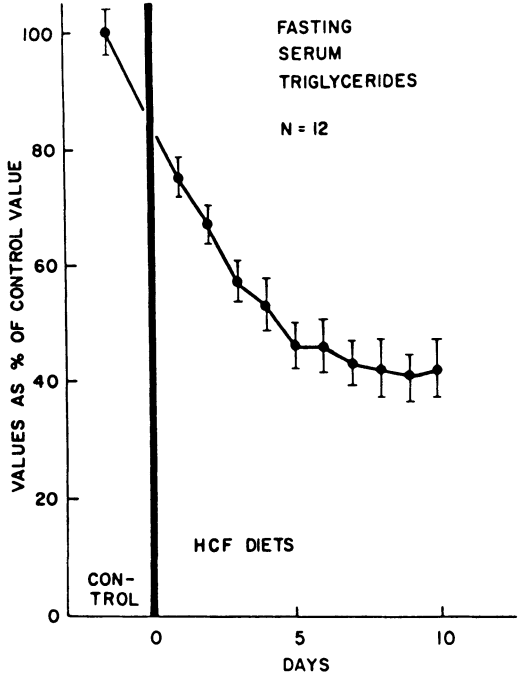

Figure 8. Response of hypertriglyceridemic patients to HCF diets. Triglyceride values averaged 1148 mg/dl on control diets. No significant alterations in body weight occurred on the HCF diets.

changes in body weight were observed. These studies suggest that the intake of generous quantities of fiber contained in a variety of natural foods prevents the expected "carbohydrate-induced lipemia."[46] HCF-type diets merit consideration in the initial management of patients with hypertriglyceridemia.

III. LONG-TERM EFFECTS OF FIBER

Throughout most of the world, people with diabetes are successfully managed with diets that include abundant to prodigious amounts of unrefined carbohydrate and fiber. The Western-type diet is atypical, because it is restricted in carbohydrate and fiber and has copious amounts of fat. Thus, in Western society we have the opportunity to evaluate the effects of introducing liberal quantities of fiber into the diet of people with diabetes. This can be done by supplementing the diet with fiber or by modifying the diet to provide high-fiber foods. Jenkins and colleagues[2,13,15,17,18] have assessed fiber-supplemented diets, whereas we[3,31–34] have evaluated high-fiber diets.

A. Fiber Supplements

Jenkins and associates[2,17] have studied the long-term effects of guar-supplemented diets on the glucose metabolism and insulin requirements of patients with diabetes. They have developed a guar crispbread that provides 20 g guar per loaf and is quite palatable. Six outpatients have maintained constant body weights over 5- to 11-week periods while ingesting approximately 20 g guar per day (Fig. 9). Urine glucose excretion fell in all six patients and insulin doses could be reduced in all five insulin-treated patients. Over an average of 8 weeks, insulin doses fell from 46 to 36 U/day.[2] The major reductions in insulin doses were achieved during the first 4 weeks of treatment with guar, and insulin doses remained fairly stable for up to 20 weeks of follow-up.[17] These observations suggest that guar crispbread may be a useful adjunct in the management of adults with either the juvenile-onset or the maturity-onset type of diabetes.

B. High-Fiber Diets

1. Glucose Metabolism

Since 1970,[3,31–34] we have investigated the therapeutic effectiveness of high-carbohydrate diets for persons with diabetes. We have evaluated high-carbohydrate diets that were low in fiber, high-carbohydrate diets with different types of carbohydrate, and high-carbohydrate diets with differing amounts and types of fiber. The HCF diets (Table 2) we developed have been used since 1976 because they have these characteristics: (1) they are accompanied by the

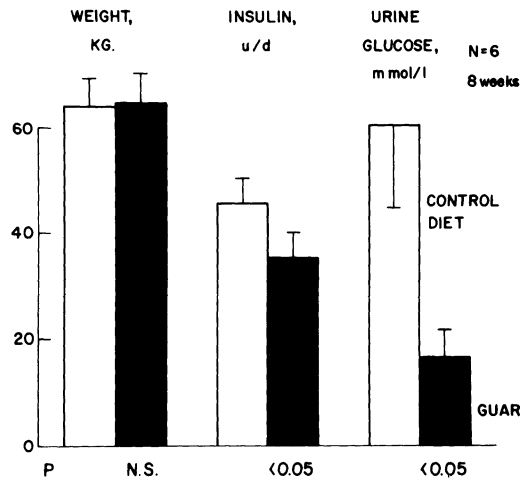

Figure 9. Long-term effects of guar-supplemented diets on diabetic patients. The diets of these patients were supplemented with guar crispbread providing 14–26 g/day of guar. From Jenkins *et al.*[2]

most rapid improvement in glucose metabolism and reductions in insulin doses, (2) they maintain normotriglyceridemia or reduce triglyceride values in hypertriglyceridemic patients, and (3) they are quite palatable and are not accompanied by noteworthy gastrointestinal or other side-effects. Our experience suggests that these HCF diets are the optimal diets for improving diabetic management in hospitalized patients. Because of their severely restricted fat content and very limited meat allowance, we have not recommended these diets for home use. The maintenance diets (Table 2), providing 55–60% of energy as carbohydrate and approximately 20–30 g fiber per 1000 kcal, have been developed for home use. These diets have a high degree of patient acceptance and can be followed well by motivated patients. The long-term effects of these maintenance diets will be summarized.

Most patients who have responded well to HCF diets in the hospital have expressed a desire to follow modifications of HCF diets, the maintenance diets, at home. Seventeen insulin-treated patients required an average of 27 U/day to maintain satisfactory glucose homeostasis on control diets (Fig. 10); on HCF diets their insulin requirements dropped to 7 U/day. These patients have followed the maintenance diets for 19 ± 3 months (mean ± SEM, range 4–51 months). On the maintenance diets, their insulin doses have remained stable. We have not had to reinstitute insulin therapy in any of the 13 patients whose insulin was discontinued on HCF diets. In sharp contrast, nine different patients responded equally well to HCF diets in the hospital but elected to resume their conventional diabetic diets after discharge. Their initial insulin doses averaged 23 U/day on control diets. When on the HCF diets, the average

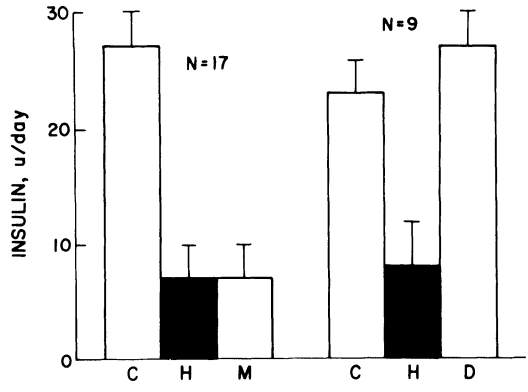

Figure 10. Long-term effects of HCF diets on insulin doses of diabetic patients. All patients received control (C) and HCF (H) diets in the hospital. Seventeen patients followed maintenance (M) diets (table 2) for an average of 19 months (left panel). Nine patients resumed conventional diabetic (D) diets as outpatients and insulin doses after a minimum of 3 months (right panel).

insulin dose was decreased to 8 U/day and insulin could be discontinued in 6 of these patients. Within 3 months after resuming conventional diabetic diets, all were taking insulin, and the average dose was 27 U/day.

After hospitalization for treatment with HCF diets, 11 lean patients were instructed in weight-maintaining maintenance diets for home use. They have followed these maintenance diets for 19 ± 4 months (range 5–44 months). They have maintained their lean body weight without significant alterations (Fig. 11). On control diets in the hospital, they received an average insulin dose

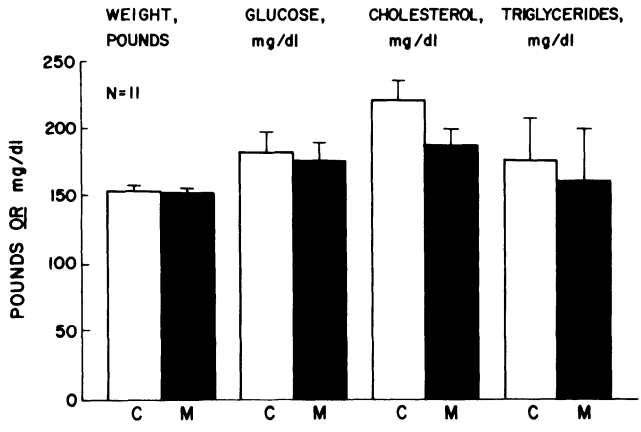

Figure 11. Long-term effects of maintenance diets on body weight, glucose, and lipid metabolism. Baseline values were obtained on control (C) diets in the hospital. Fasting plasma glucose, serum cholesterol, and triglyceride values were obtained after an average of 19 months on maintenance (M) diets as outpatients.

of 25 ± 5U/day; on maintenance diets their insulin doses have averages 11 ± 5 U/day. The average fasting plasma glucose values have been slightly lower with maintenance diets at home than the values with control diets in the hospital. These maintenance diets have been well tolerated, and we have not discerned any adverse effects.

2. *Lipid Metabolism*

When patients adhere closely to high-fiber maintenance diets, their fasting serum cholesterol and triglyceride values continue to decline. After 3 weeks on HCF diets in the hospital, serum total cholesterol values were 25% below control values (Fig. 6). This decrease in serum cholesterol is attributable to reductions in both LDL and HDL cholesterol concentrations. After discharge on maintenance diets, LDL cholesterol values remained stable or decreased, while HDL cholesterol values gradually rose to approximately twice the values at time of discharge. Thus, on control diets serum total cholesterol values averaged 222 mg/dl; after an average of 19 months on maintenance diets, values were 188 mg/dl (Fig. 11). Patients with hypercholesterolemia have a much greater reduction in serum total cholesterol values if they follow the maintenance diets closely.

Fasting serum triglyceride values also decrease after discharge from the hospital if patients closely adhere to maintenance diets. Thus on control diets in the hospital, 11 lean men with diabetes had fasting serum triglyceride values of 176 mg/dl; on maintenance diets after an average of 19 months, values averaged 161 mg/dl (Fig. 11). The serum triglyceride values appear to be the most sensitive indicator of compliance to the maintenance diets. We are treating several patients who have average triglyceride values above 1000 mg/dl on conventional diets despite treatment with clofibrate, 2 g/day. When they follow the maintenance diets closely, their triglyceride values are below 500 mg/dl; when they deviate from the diet, their serum triglyceride values frequently range from 1500 to 5000 mg/dl. The influence of maintenance diets on fasting triglyceride values cannot be related to changes in body weight or alcohol consumption. Our studies indicate that high-fiber maintenance diets are extremely effective in treating hypertriglyceridemia and moderately effective in managing hypercholesterolemia.

3. *Mineral and Vitamin Status*

One of the major concerns about the long-term use of high-fiber diets is that mineral or vitamin deficiency may develop.[47,48] Anderson *et al.*[49] have evaluated, in a limited fashion, the mineral and vitamin status of 15 patients with diabetes who have been on maintenance diets for an average of 21 months (range 5–44 months). The food intake of each patient was assessed by multiple food diaries and by multiple 24-hr recalls obtained by dietitians who have had extensive experience with HCF and maintenance diets. These data indicate that adherence to maintenance diets was remarkably good. These patients

Table 4. Mineral and Vitamin Studies of 15 Patients on High-Fiber Maintenance Diets

	Control diet values[a]	Maintenance diet values[a,e]
Serum calcium, mg/dl	9.5 ± 0.2[b]	9.6 ± 0.1
Serum phosphorus, mg/dl	3.5 ± 0.2[b]	3.4 ± 0.1
Serum alkaline phosphatase, IU/l	80 ± 7[b]	84 ± 4
Hemoglobin, g/dl	14.5 ± 0.4[b]	14.4 ± 0.5
Serum magnesium, mg/dl	1.8 – 2.6[c]	2.0 ± 0.1
Serum iron, μg/dl	50 – 150[c]	85 ± 7
Serum total iron-binding capacity, μg/dl	250 – 350[c]	320 ± 16
Serum carotene, ng/dl	50 – 200[c]	127 ± 22
Prothrombin time, seconds	11.9 ± 0.1[d]	11.9 ± 0.2
Partial thromboplastin time, seconds	23.2 ± 0.9[d]	23.3 ± 0.9

[a]Values are mean ± SEM.
[b]Values on control diet in hospital.
[c]Range of normal values for our laboratory.
[d]Control values measured at time patient samples were measured.
[e]Values after an average of 21 months on maintenance diet.

reported that carbohydrate provided 56 ± 1% (mean ± SEM) of energy, 21 ± 1% of protein, and 27 ± 2% of fat. Their fiber intake averaged 50 ± 3 g/day (range 36–65 g/day) or 30.8 ± 1.2 g/1000 kcal.

Serial measurements of the hemoglobin, serum calcium, phosphorus, and alkaline phosphatase were made. Prothrombin times, partial thromboplastin times, serum magnesium, iron, total iron-binding capacity, and carotene were measured after an average of 21 months on the maintenance diets. No significant alterations in hemoglobin, serum calcium, phosphorus, or alkaline phosphatase were noted (Table 4). Prothrombin and partial thromboplastin times, serum magnesium, iron, total iron-binding capacity, and carotene were also within normal limits after an average of 21 months on the maintenance diets. Thus, these high-fiber diets produce no evidence of deficiency of calcium, phosphorus, magnesium, or iron. Our indirect assessments suggest that these patients are receiving adequate quantities of the fat-soluble vitamins A (serum carotene), D (as indicated by serum calcium, phosphorus, and alkaline phosphatase measurements), and K (as indicated by prothrombin and partial thromboplastin times). Nutritional assessments using a variety of other parameters indicate that these patients are adequately nourished. Therefore, the maintenance diets seem to be well tolerated and to be nutritionally adequate.

IV. PROPOSED MECHANISMS

The physiologic effects of various fibers on glucose and lipid metabolism are not well characterized. Possible mechanisms of action of fibers on glucose,

cholesterol, and triglyceride metabolism have been reviewed elsewhere.[1,50] When conventional meals containing liberal quantities of fiber are eaten, the fibers may alter the transit time of the ingested material through the gastrointestinal tract, delay the digestion of nutrients, and alter the absorption of nutrients. As a result, certain nutrients usually absorbed in the small intestine may be delivered to the colon. In the colon, these nutrients may be absorbed, metabolized by bacteria, or incorporated into the fecal bolus and excreted (fiber-induced malabsorption). The response of various hormones to fiber-rich meals may be different from the response to fiber-poor meals[14,20]; this could alter the subsequent metabolism of nutrients in hepatic and extrahepatic tissues. Since most fibers, with the notable exception of lignin, are partially or totally digested in the colon,[51] the metabolic products of fiber digestion may alter nutrient metabolism. Short-chain fatty acids are major products of fiber digestion in the colon[52]; the short-chain fatty acids that are absorbed may alter hepatic and extrahepatic metabolism of nutrients. To examine the possible mechanisms by which high-fiber diets favorably influence the glucose and lipid metabolism of people with diabetes, the role that fibers may play in the digestion, absorption, and metabolism of carbohydrates and lipids will be reviewed briefly.

A. Glucose Metabolism

1. Glucose Absorption

When water-soluble fibers such as guar are ingested with glucose, the glycemic response is lower than when the same amount of glucose is ingested without fiber.[13,16] Presumably, these water-soluble fibers accumulate water and form gels in the intestinal tract,[1] apparently delaying the absorption of simple cabohydrates. Under these conditions, the reduced glycemic response seems to be largely related to a slowed absorption of sugars, and sugar malabsorption has not been documented.[16] When water-soluble fibers are incorporated into conventional meals, the glycemic response is also lower than after fiber-free meals.[13,14] Presumably, the absorption of simple carbohydrates is delayed, and the digestion and absorption of complex carbohydrates may be delayed. Under these conditions, some complex carbohydrates may escape into the colon.[53] Water-insoluble fibers such as cellulose or wheat-bran fiber also reduce the glycemic response to glucose.[19] Furthermore, when diets are supplemented with water-insoluble fibers such as that in cellulose-containing bread, postprandial glucose values are significantly lower than values on low-fiber diets.[20] It seems unlikely that these changes are due to gel formation; these water-insoluble fibers appear to reduce by other mechanisms the glycemic response to glucose after meals. Fiber-supplemented or high-fiber diets appear to induce improvements in glucose metabolism that cannot be related to the rate of glucose absorption, since, as we noted, HCF diets lower fasting plasma glucose values

obtained after a 12-hr fast. Long-term use of wheat-bran-supplemented diets improved glucose metabolism when no fiber was provided with the glucose load.[54] Thus, high-fiber or fiber-supplemented diets are accompanied both by lower postprandial glucose values that may be related to changes in the rate of glucose absorption and by long-term improvement in glucose metabolism possibly related to other mechanisms.

2. Hormone Responses

Serum insulin responses to fiber-supplemented meals or fiber-supplemented glucose loads are lower than to fiber-free meals or fiber-free glucose loads.[13,14,16] The slower absorption of glucose appears to evoke a smaller insulin response. Plasma glucagon values also are significantly lower on high-fiber diets than on low-fiber diets.[20] Since glucagon acts to oppose the action of insulin, the lower glucagon levels would enhance tissue sensitivity to insulin and improve glucose metabolism. The effects of fiber ingestion on gastrointestinal hormones such as gastric inhibitory peptide (GIP), vasoactive intestinal peptide (VIP), and gut-glucagon have only recently been investigated.[55] A diminished release of these hormones may contribute to the lower insulin responses observed after fiber ingestion.[56] Although the direct effects of these gastrointestinal hormones on glucose metabolism in hepatic and extrahepatic tissues have not been determined, their actions probably resemble the effect of glucagon more closely than that of insulin.[57] Thus, decreased secretion of pancreatic glucagon and various gastrointestinal hormones in response to fiber ingestion might lead to improved glucose metabolism and enhance tissue sensitivity to insulin.

3. Tissue Adaptation

Our observations (Figure 5) that insulin requirements of insulin-dependent diabetes patients were 25% lower when on HCF diets than when on control diets strongly suggest that HCF diets enhance sensitivity to exogenous insulin. Other reports[13,14,20] support this suggestion. Insulin reactions were more frequent on high-fiber diets than on low-fiber diets despite similar plasma-free insulin concentrations and indentical insulin doses on the two diets.[20] Diets supplemented with guar crispbread were accompanied by significant reductions in insulin requirements.[2,15,17] Several studies[40,58,59] demonstrating that in humans, high-carbohydrate diets improve glucose metabolism and lower insulin responses to oral glucose suggest that high-carbohydrate diets are accompanied by increased tissue sensitivity to insulin. Other studies have examined the mechanism in experimental animals for improved glucose metabolism on high-carbohydrate diets. We[60] have demonstrated that glycolytic enzyme activities in liver are higher when rats are fed high-carbohydrate diets than they are when the rats are fed low-carbohydrate diets. Others[61] have demonstrated that in rats, high-carbohydrate diets are accompanied by increased binding of insu-

lin to hepatic plasma membranes. Thus, improved glucose metabolism could result at the tissue level by enhanced binding of insulin to plasma membrane receptors or by intracellular changes in the activities of enzymes responsible for glucose metabolism.

The available data suggest that fiber-supplemented diets or high-fiber diets increase tissue sensitivity to insulin. Since our HCF diets are higher in both carbohydrate and fiber than control diets, we cannot at present specifically attribute an increased sensitivity to insulin to either the high-carbohydrate component or the high-fiber component of these HCF diets. However, we have documented that in humans, HCF diets are associated with significantly higher binding of insulin to circulating monocytes than are control diets.[34] We have used previously described techniques[62] for these measurements. In eight patients treated with HCF diets, there were twice as many insulin-binding sites per monocyte as there were in patients on control diets. The affinity of the specific insulin-binding receptors was also significantly higher in patients on HCF diets than in those on control diets. It seems likely that some of the apparent increase in insulin sensitivity observed with fiber-supplemented or high-fiber diets is related to an increase in insulin binding to tissue receptors.

B. *Lipid Metabolism*

1. *Cholesterol Metabolism*

Ingestion of certain fibers, especially the water-soluble fibers, is accompanied by significant reductions in serum cholesterol concentrations.[1] This hypocholesterolemic effect of water-soluble fibers may be related in part to increased fecal loss of bile acids and cholesterol.[1,50] Other factors undoubtedly contribute to the cholesterol-lowering properties of certain fibers. Fiber-induced alterations in glucose metabolism, in insulin secretion, or in glucagon secretion could influence hepatic metabolism of cholesterol. The influence of short-chain fatty acids absorbed from the colon on cholesterol metabolism has not been determined. Poorly defined alterations in gastrointestinal physiology could change the site and rate of absorption of cholesterol and fatty acids and thereby influence hepatic metabolism of cholesterol. The intestinal mucosa manufactures chylomicrons, very-low-density lipoproteins, and HDL components.[63] Fiber ingestion may alter the synthesis and secretion rates of these lipoproteins. At the present time, we are unable to explain how plant fiber ingestion would selectively lower LDL cholesterol while increasing HDL cholesterol concentrations (see Fig. 6 and Section II.B. 2). Further studies in both animals and humans are required to delineate specifically these effects of fiber ingestion on the synthesis and metabolism of cholesterol and cholesterol-rich lipoproteins.

2. Triglyceride Metabolism

The intake of generous amounts of fiber from a variety of natural foods is accompanied by a significant reduction in fasting and postprandial serum triglyceride values.[1,31–33] Very little attention has been directed to defining the mechanisms by which fiber ingestion could lower serum triglyceride concentrations. Fiber-supplemented diets are accompanied by a slight increase in fecal fat excretion; a large portion of this fat may be indigestible plant lipids such as cutins and waxes.[1] It seems extremely unlikely that fecal loss of lipids could account for the observed reductions in serum triglycerides.

Insulin has a pivotal role in the regulation of triglyceride synthesis in the liver.[64] Fiber-induced reductions in insulin secretion could decrease hepatic triglyceride synthesis; changes in serum concentrations of glucagon and gastrointestinal hormones also might alter hepatic metabolism of fatty acids. Alterations in the site and rate of fatty acid absorption could influence triglyceride metabolism. The triglyceride-rich lipoproteins (chylomicrons and very-low-density lipoproteins) are largely broken down by capillary-bound lipoprotein lipases in various tissues.[63,64] These enzymes are activated by insulin[64]; enhanced tissue sensitivity to insulin could increase activity of these enzymes. Furthermore, enhanced tissue sensitivity to insulin could attenuate the release of fatty acids from adipose tissue stores.[64]

The rates of catabolism of triglyceride-rich lipoproteins are influenced by the size of the lipoprotein particles.[63]; fiber-induced changes in triglyceride absorption may alter the size of chylomicrons or very-low-density lipoproteins. The catabolism of triglyceride-rich particles is dependent on the availability of activator lipoproteins[63]; fiber ingestion could also influence the availability of these activator lipoproteins. The influence of fiber on the intestinal secretion of various apoproteins could also alter triglyceride metabolism. Quite feasibly, alterations in the ratios of short-chain fatty acids originating from the colon to long-chain fatty acids absorbed from the small intestine could influence hepatic triglyceride synthesis and release of triglyceride-rich lipoproteins.[64] The interactions of many fiber-induced alterations in triglyceride and lipoprotein synthesis and metabolism could account for the observed changes in serum triglyceride values on high-fiber diets.

V. THERAPEUTIC USE OF HIGH-FIBER DIETS

Fiber-supplemented diets or high-fiber diets appear to be effective in the management of selected patients with diabetes mellitus,[2,3,15–17,31–34] reactive hypoglycemia,[65] hypercholesterolemia,[1] or hypertriglyceridemia.[1,31] Guar crispbread as a fiber supplement is palatable and well tolerated.[2,17] No evidence

currently available suggests that these supplements have adverse effects on mineral or vitamin metabolism. The use of 15–25 g of guar in the crispbread form has been outlined by Jenkins and colleagues.[2,17]

We have used HCF diets for inpatients and high-fiber maintenance diets for outpatients and find these diets well tolerated. We have observed no adverse effects of the diets for periods of up to four years. Our experience suggests that these diets warrant consideration for dietary management of many adults with diabetes. Modifications of the high-fiber maintenance diets have been useful in treating patients with reactive hypoglycemia, hypercholesterolemia, or hypertriglyceridemia. Our use of these diets will be outlined briefly.

A. *Diabetes Mellitus*

The fastest response of the plasma glucose levels and insulin requirements occur with HCF diets (Table 2) which provide 70% of energy as carbohydrate and approximately 40 g fiber/1000 kcal. With these diets, in the hospital, insulin doses can be rapidly reduced for many patients. The response to 60%-carbohydrate diets is much slower. When the therapeutic objective is to decrease or stop insulin or sulfonylurea (oral hypoglycemic) therapy, we usually hospitalize patients for a minimum of 7–10 days of treatment with HCF diets. During hospitalization, the patients are "withdrawn" from their customary diets and receive extensive instruction in maintenance diets. Adherence to the maintenance diet is much better if the patient has been hospitalized on the HCF diet and the patient and spouse have been given detailed instructions regarding this diet. Dietary compliance is greatly enhanced when adult members of the family understand the fundamental aspects of the diet and the rationale for its use.

Responses to high-fiber diets providing 55–60% of energy as carbohydrate are much slower in both hospitalized patients and outpatients. Our experience indicates that approximately 70% of energy must be provided as carbohydrate to achieve the dramatic responses that we observe in certain patients. However, when the therapeutic objective is to improve diabetic control and lower blood lipids, we frequently instruct patients in using the maintenance diets as outpatients. With these maintenance diets, we have been able to reduce insulin doses slowly and to discontinue insulin therapy in six lean patients over periods of 3–15 months.

To facilitate the use of maintenance diets, we have developed a food exchange system (Table 5) and an instruction booklet for patients.[66] The physician usually determines the energy requirement and the carbohydrate content of the diet (e.g., 55 or 60%). A typical dietary prescription would be 1800 kcal, 60% carbohydrate, high-fiber diabetic diet. The dietician elicits the food preferences of the patient and estimates the daily intake of the patient. The maintenance diet is then individually formulated for each patient. Usually the

Table 5. Food Exchanges for HCF and Maintenance Diets[a]

Exchange	Example[b]	Cho (g)	Prot (g)	Fat (g)	Fiber (g)	Energy (kcal)
Milk	Skim, 1 cup	12	8	0	0	80
A vegetable	Cabbage, 1 cup	2	1	0	2	13
B vegetable	Carrot, 1 medium	4	2	0	2	26
C vegetable	Corn, 2/3 cup[c]	16	2	0	3	75
Beans	Pinto, 1/2 cup	21	9	1	4	125
Cereal	Oats, 1/2 cup	30	6	2	10	160
Bread	Rye, 1 slice[c]	10	2	1	2	55
Fruit	Orange, 1 small	10	0	0	2	40
Meat	Lean beef, 1 oz	0	9	2	0	55
Fat	Margarine, 1 tsp	0	0	5	0	45

[a]Nutrient, total fiber, and energy values are average values for given exchange.
[b]The nutrient, fiber, or energy values for examples are not identical to average values for the exchange.
[c]These items are cooked; all other examples are uncooked.

patient and spouse participate in the initial instruction sessions. Patients are then seen at three- to six-week intervals, a diet history is taken, and the use of the diet is reviewed by the dietitian. An example of the maintenance diet is given in Table 6.

B. Reactive Hypoglycemia

In our experience, reactive hypoglycemia is usually of the "alimentary" or the "diabetic" type.[67] Jenkins and colleagues[68] have reported that fiber supplements are useful in the management of patients with reactive hypoglycemia resulting from gastric surgery. We have observed that our high-fiber maintenance diets, which are restricted in simple carbohydrates, are effective in the management of patients with both the alimentary type and the diabetic type of reactive hypoglycemia. Although some patients with disabling symptoms are hospitalized for 5–7 days of dietary management, most patients are instructed in the maintenance diets as outpatients. The diets used to treat patients with reactive hypoglycemia resemble the maintenance diets (Tables 2, 6), except that simple carbohydrates are restricted to less than 50 g/day. This is usually achieved by limiting the intake of milk and fruits.[65] These diets are well tolerated even by patients who have had 65–80% of their stomachs removed. Usually the maintenance diets reduce symptoms of hypoglycemia and prevent chemical hypoglycemia from developing after meals.

C. Hypercholesterolemia

Our maintenance diets for hypercholesterolemic patients resemble the alternative diets recommended by Connor and Connor[43] for the management

Table 6. Representative 2000-kcal Maintenance Diet

Meal	Exchanges	Food examples
Breakfast	1 cereal	Shredded wheat, 2 1-g biscuits
	½ milk	Skim milk, 4 oz
	1 bread	Whole-wheat toast, 1 slice
	1 fat	Margarine, 1 tsp
Morning snack	1 bread	Graham crackers, 2 squares
	1 fruit	Orange, medium
Noon meal	2 bread	Sandwich: Bread, 2 slices
	2 meat	Roast beef, 2 oz
	1 fat	Mayonnaise, 1 tsp
	1 B vegetable	Sliced tomato
	2 C vegetables	Corn, ⅔ cup
		Winter squash, 1 cup
	1 fat	Margarine, 1 tsp
Afternoon snack	1 bread	Rye crackers, 2 wafers
	1 fruit	Pears, canned, 2½ small halves
Evening meal	2 meat	Chicken, 2 oz
	3 C vegetables	Baked potato
		Corn, ⅔ cup
		Brown rice, 1 cup
	2 B vegetables	Peas, 1 cup
	2 A vegetables	Lettuce salad with tomatoes
	1 bread	Whole-wheat bread, 1 slice
	1 fruit	Fruit cocktail, ½ cup
	2 fat	Salad dressing; margarine, 1 tsp
Evening snack	1 cereal	Bran Buds®, ¾ cup
	½ milk	Skim milk, 4 oz
	2 fruit	Banana, 1 medium
	1 bread	Whole-wheat toast, 1 slice
	1 fat	Margarine, 1 tsp

of most patients with hyperlipidemia. The cholesterol-lowering properties of these diets can be related to the dietary cholesterol restriction (usually less than 100 mg/day), restriction of saturated fats, and the high fiber content. We modify the maintenance diets to provide increased quantities of water-soluble fiber from foods such as oats, corn, peas, and legumes.

D. Hypertriglyceridemia

Our experience with both HCF and maintenance diets in persons with diabetes or hypertriglyceridemia (Figures 8, 9, 11) indicate that the diets are useful in the management of hypertriglyceridemia. We have determined that high-carbohydrate, low-fiber diets induce hypertriglyceridemia while HCF diets reduce triglyceride values.[1,31,40] The mechanism of action of these diets, as

outlined above, is not known. We attribute reductions in fasting serum triglyceride values to the variety of fibers used from different natural foods. We do not know whether water-soluble fibers or water-insoluble fibers have a greater role in reducing triglyceride values. For treatment of severe hypertriglyceridemia (values over 2000 mg/dl), we hospitalize patients and feed them energy-restricted (800- to 1200-kcal) HCF diets until the serum triglyceride values fall below 1000 mg/dl. These patients are then instructed in maintenance diets for home use. For less severe hypertriglyceridemia, we instruct patients in maintenance diets similar to those used in the treatment of persons with diabetes. All patients are encouraged to reduce to and maintain a very lean body weight and to restrict greatly or eliminate the intake of alcohol.

VI. CONCLUSIONS

Diabetes mellitus is a common problem in Western society, with an estimated prevalence of 5% in the United States.[69] The prevalence of diabetes is much lower in primitively living people than in highly industrialized populations.[8] These observations have led to the hypothesis that fiber-depleted diets play a role in the etiology of diabetes.[10] Recent studies have demonstrated that fiber-supplemented diets or high-fiber diets lower blood glucose concentrations and insulin requirements in persons with diabetes. A liberal intake of fiber is accompanied by lower postprandial glucose values, less glycosuria, and lower insulin requirements than observed on control diets. Short-term studies in hospitalized patients have demonstrated that high-fiber diets lower insulin requirements and blood-glucose, cholesterol, and triglyceride values of persons with diabetes.

Two approaches are now being used to provide more fiber in the diet for the long-term management of diabetes patients. Jenkins and colleagues[20,17] are using guar crispbread as a dietary supplement; they report that these fiber supplements reduce glycosuria and insulin requirements of persons with diabetes and have been well tolerated for up to 20 weeks without adverse effects. My colleagues and I[3,31–34] have used high-fiber diets providing approximately 52 g of fiber per day from a variety of natural foods. These high-fiber diets are accompanied by decreased insulin requirements and lower serum cholesterol and triglyceride values. These high-fiber diets are well accepted by patients and have been used for up to 4 years without discernible side-effects.

Available evidence suggests that a generous intake of fiber may be beneficial for many adults with diabetes. Fiber intake improves diabetic control and may lower serum lipid concentration. Lower blood-glucose values may decrease the prevalence of the specific complications of diabetes. Improved diabetic control coupled with lower serum lipid concentrations may also retard the development of atherosclerotic vascular disease in persons with diabetes.

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12

Food Intake Regulation and Fiber

Kenneth W. Heaton

I. INTRODUCTION

The extraordinary commonness of obesity in urbanized communities is largely unexplained. Popular theories link it to physical inactivity or gluttony, but supporting data are scanty. Inability to limit food intake to the required physiological amount is generally blamed on a defect in the eater. However, in urbanized societies food itself is altered in many ways. One of the most drastic alterations is the fiber-depleting process in the manufacture of white flour and sugar.

In this chapter, fiber-depleted foods are considered synonymous with refined carbohydrates, although it is recognized that many contain nutrients other than carbohydrate. Refined carbohydrates include white rice, cornflour, cornflakes, pearled barley, sago, tapioca, glucose, glucose syrup, maple syrup, treacle, and molasses. Commonly forgotten are fruit juices such as apple, grape, and orange; also, sweet wines and even beer, with its maltose content, are overlooked. In unprocessed plant foods, carbohydrate is always embedded in fiber except for honey, which can be considered a natural fiber-free carbohydrate; but it has never been a major part of man's diet.

In recent years it has been suggested, notably by Cleave *et al.*,[1-3] that refined carbohydrates are responsible for most of the obesity in technological societies. This hypothesis was supported with emphasis on the protective role of fiber by Heaton[4] and modified to emphasize starchy foods by Trowell.[5]

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The fiber–obesity hypothesis is simple but often misunderstood. It does not state that increasing the intake of dietary fiber reduces the risk of obesity. After all, dietary fiber intake can be increased simply by eating more food. Nor does it claim that adding concentrated fiber supplements to the diet will prevent obesity, which is a pharmaceutical approach, not a nutritional one. The essence of Cleave's theory is that foods from which dietary fiber has been removed have common characteristics which render them intrinsically prone to cause obesity.

It is necessary to have a conception of dietary fiber that is not chemical but physical and three-dimensional to understand and judge this hypothesis correctly. In natural, or unprocessed, plant food, dietary fiber exists as a microscopic lattice-work or matrix, which entangles and traps the nutrients within cellular envelopes. It is impossible to separate fiber from nutrients and keep its physical properties intact. If this intimate association has a significant effect on the intake and availability of nutrients, studies in which separated fiber extracts are added to test meals can be expected to give misleading results. The effect of dietary fiber on nutrient intake and availability can be safely deduced only by comparing fiber-rich foods (natural or unrefined plant products) and equivalent fiber-depleted foods. In practice, this usually means comparing foods of different texture or physical form.

All natural plant foods are solid. This is true even of those composed mostly of water, namely fruit and vegetables. In these, dietary fiber is wholly responsible for the solidity of the food. For example, a 100-g apple can be regarded as 98 g of apple juice held together by 2 g of apple fiber, while a 100-g potato is 98 g of starchy mush rendered solid by 2 g of fiber. In plant foods with a low (4–12%) water content, such as grains and nuts, dietary fiber contributes to their solidity and provides a hard outer coat or shell. With nuts this must be removed before eating, but nuts are unimportant in man's diet. The outer coats of the all-important grains or cereals need not be removed, but in technological societies they generally are removed by milling before the cereal is boiled, leavened, and baked or otherwise prepared for eating. If whole grains are milled, resulting foods tend to have a coarser, heavier texture than if the seedcoat material is removed. For example, whole-meal bread is denser and requires more chewing than white bread. This may be partly due to the larger particle size of the whole-grain flour and to its different baking properties but, indirectly, this can be attributed to the extra fiber present.

Thus, an important property of dietary fiber in food is its effect on texture, rendering it coarse, hard, or even solid rather than liquid. A second property possibly important in the context of obesity is the entrapment or entanglement of nutrients within the fibrous matrix and inside individual cells. Both these effects, on texture and nutrient availability, can be reduced by processes other than removal of the fiber.

II. WORK AND RATE OF INGESTION

Common sense suggests that food made easier to eat is more likely to be eaten. Such experiments as have been done support this. Students were asked to drink through a straw as much as they liked of a thick milkshake. They drank more when the straw had a large bore than when it had a small bore, especially if they were moderately obese.[6] When obese people were given free access to shelled nuts most ate them, but most did not eat unshelled nuts.[7] Less motivation is required to start on an easy-to-eat food. Fiber-depleted foods require less effort to eat because they are softer in texture. When the fiber-depleting process results in soluble carbohydrate, the effort of eating is altogether removed. Sucrose dissolved in drinks accounts for about 50 g of the average Briton's daily carbohydrate intake. In this way, he obtains 200 kcal without any of the work of ingestion.

A deterrent effect of dietary fiber has not been demonstrated experimentally, but common experience suggests that a casual desire for a sweet-tasting snack is more likely to be indulged by drinking a can of Coca-Cola than by chewing up a sugar-equivalent amount of fruit, such as three or four medium-sized eating apples. Deterrence would probably be even greater if the refined sucrose present in Coca-Cola were presented as its parent material, a stick of sugar cane or a large lump of sugar beet. It can be argued that after weaning, it is abnormal for a mammal to obtain any calories at all in liquid form.

Plant foods are eaten faster when depleted of fiber. When normal subjects were asked to consume a meal of apples as quickly as they comfortably could, they required 17.2 min; when given an equicaloric amount of apple juice, only 1.5 min were required.[8] A large meal of whole-meal bread took 45 min to eat, while an equicaloric amount of white bread took 34 min.[9] The effect of fiber depletion on eating rate is obviously greater if it involves the conversion of a solid food into a liquid one.

Does more rapid consumption lead to greater overall intake? Data are limited but, in liquid-meal experiments, subjects ingested more if their rates of ingestion were artificially increased. This was true if the meal was drunk or pumped into the mouth.[10] Conversely, obese subjects were satisfied with less food if they slowed their eating by taking smaller mouthfuls, by chewing longer, and by drinking water between mouthfuls.[11] In the United States, many behavior therapists now teach their obese patients to eat more slowly.[12] Fiber-rich food itself (especially if it is raw) forces people to eat more slowly.

III. ENERGY DENSITY

Some published studies suggest that energy intake is influenced by the energy density of food (kcal or kJ/g).[12] It is often assumed that dietary fiber

dilutes the energy density of food and that fiber-depleted foods or refined carbohydrates have a high energy density. However, this is not necessarily the case. The dietary fiber content of most fruits is only 1–2%.[13] Hence, the energy density of apple juice is only 1–2% greater than that of whole apples. The sugar concentration and hence the energy density of artificial soft drinks or even sweetened tea and coffee is no greater than that of some fruits. Admittedly, the sugar in fruits is diluted to some extent by the saliva secreted during chewing. White flour is more energy dense than whole-meal, but the difference is relatively slight with 76% available carbohydrate in white flour versus 67% in wholemeal flour.

It is questionable whether the concept of energy density is biologically meaningful. It assumes that eating continues until a certain bulk of food has been consumed. This has never been demonstrated. On the contrary, the 19th century Irish peasant living mainly on potatoes ate up to 14 lb (6.5 kg) of food a day[14] while the traditional Eskimo, living on seal meat and fish (and having an exceptionally high caloric requirement) ate only 4½ lb (2.1 kg) of food daily.[15] It is more likely that eating stops when a certain degree of satiety has been achieved. The energy:satiety ratio of food is a more meaningful concept than energy density.

IV. SATIETY

Satiety is, of course, a subjective sensation, but it can be measured. One method is the use of a linear rating scale scored from, say, -10 to represent extreme hunger to $+10$ to represent extreme satiety. We used this method[8] to test the hypothesis that food is less satiating when it is depleted of fiber. Volunteers were presented with test meals of 482 g raw apples, eaten whole except for cores and stalks, and of 469 g juice made from the same batch of apples. The nutrient content of the two meals was the same. Immediately after the meal, the mean satiety score was significantly higher after apples than juice (6.9 ± 0.3 versus 1.4 ± 1.4) and the difference persisted for 2 hr. Subsequently, we have compared equicaloric meals of oranges and orange juice and also of grapes and grape juice. Again, the fruits evoked consistently higher satiety scores than the corresponding juices (Table 1).

In animals, chewing and swallowing movements stimulate the satiety center in the ventromedial nucleus of the hypothalamus.[17] Fruit could be more satiating than juice simply because it is solid and has to be chewed. When our volunteers consumed a liquid puree of whole apples, the mean satiety score (4.9 ± 0.6) was indeed lower than with intact apples, but it was still considerably higher than with juice.[8] This suggests that chewing is only a partial explanation for the satiating effect of fiber. The other mechanisms involved are unknown, but several are possible.[18] The water-holding properties of fiber make it likely

Table 1. Maximum Level of Satiety on a 0–10 Scale in 10 Healthy Nonobese Volunteers after Energy-Equivalent Meals of Fruit and Fruit Juices[a]

	Apples	Oranges	Grapes
Fruit	6.9 ± 0.3	6.4 ± 0.7	4.2 ± 1.1
Juice	1.4 ± 1.4	1.5 ± 1.3	0.8 ± 1.1
p	< 0.01	< 0.01	< 0.01

[a]The juice was made from the same batch of fruit in each case, and the fruit and juice meals were chemically the same except for the absence of fiber in the juices.[8,16]

that the gut contents are bulkier with fiber-rich foods, and distension of the stomach and small intestine induces satiety in animals.[17,19] The pattern of gut hormone release may be different and late hypoglycemia is prevented (see Section VI).

The satiating capacity of a food can also be assessed by asking volunteers to eat until they feel comfortably full and then measuring the amount eaten. Using this technique, Grimes and Gordon[20] compared whole-meal and white bread and found that 10 out of 12 subjects ate less whole-meal. Taking into account the butter on the bread, the energy taken in was 665 kcal with whole-meal and 825 kcal with white bread.[21]

It could be of great value to have tables showing the energy:satiety ratio of all the common foods to indicate their potential for causing overnutrition. Scientifically acceptable methods of measuring satiety must be developed.

V. LONG-TERM STUDIES

Single-meal experiments showing the satiating effect of fiber do not prove that a fiber-rich diet will restrict energy intake over days and weeks. Compensation could occur in the long term. The limited data available in man suggest that compensation does not occur.

We[22] have recorded the dietary intakes of 13 free-living middle-aged volunteers (all but one had asymptomatic gallstones) over two 7-week periods. The 3 males and 10 females, with relative body weights of 120 lb ± 5%, ate as much as they wished of animal foods and of permitted plant foods in both periods. In one period, the permitted plant foods were those containing white flour and other refined carbohydrates. In this period, whole-meal flour and other whole-grain foods were completely forbidden, while the intake of vegetables was restricted to three helpings per day, including potatoes. The intake

of fruit was limited to 10 items per week of which only 3 could be fresh. In the other period, the permitted plant foods were whole-meal flour and whole-grain foods together with unlimited fruit and vegetables, while the refined carbohydrates were excluded as completely as possible. Thus, in one diet the carbohydrate was all unrefined and fiber-rich, and in the other it was nearly all refined and fiber-depleted. This study was designed as an investigation into the nutritional consequences of eating refined carbohydrate. But, for a community like Britain where eating refined carbohydrate is the norm, it may be regarded as an examination of the effects of replacing fiber-depleted carbohydrates with unrefined fiber-rich ones. The order of diets was randomized. Each subject kept a detailed diary of his food intake every sixth day, and the data were analyzed by computer using the 1978 edition of the McCance and Widdowson food tables,[13] which are the first comprehensive tables to include data on dietary fiber. With four subjects, persuasion was needed to achieve a reasonably high intake of sucrose on the refined diet, but the results with them were no different from those with the nine who needed no persuasion.

The results are shown in Table 2. On the unrefined diet, the subjects' average weight loss was 1.6 kg in 7 weeks. They reduced their energy intake by 480 kcal (1.92 mJ) a day, that is, by 22%, compared with the refined-diet period. The subjects were not aware of their lower energy intake and none complained of feeling hungry. Seven subjects ate the refined diet first. With them, data were available on nutrient and fiber intakes before, as well as dur-

Table 2. Weight Change over 7 Weeks and Mean Dietary Intakes (g/day) of 13 Volunteers on ad libitum Refined and Unrefined Carbohydrate Diets[a]

	Refined (fiber-depleted)	Unrefined (fiber-rich)	Correlation of difference[b] with weight loss on unrefined diet (r)
Weight change (kg)	plus 1.6 ± 0.9	minus 1.6 ± 1.3[c]	—
Energy (kcal/day)	2192 ± 157	1712 ± 153[c]	0.69
Refined sugar	106 ± 7	6 ± 1[c]	0.88[d]
Total carbohydrate	266 ± 19	158 ± 15[c]	0.85[d]
Fat	93 ± 8	86 ± 8	0.54
Protein	75 ± 5	74 ± 6	0.41
Total dietary fiber	13 ± 1	27 ± 3[c]	−0.16
Cereal fiber	6 ± 1	15 ± 2[c]	0.35
Noncereal fiber	7 ± 1	12 ± 1[c]	−0.71[e]

[a]From Thornton *et al.* (1979).[22]
[b]Difference between intake on refined and unrefined diets in the seven subjects who ate the refined diet first.
[c]$p < 0.001$.
[d]$p < 0.01$.
[e]$p < 0.05$.

ing, the unrefined diet period, which made it possible to look for correlations between the change in weight and the nutrient and fiber changes. The only strong correlations were with the change in sugar intake and the change in total carbohydrate (which reflected the change in sugar) intake. There was no relationship between the change in weight and the change in intake of dietary fiber, except a weak correlation with noncereal fiber.

These data show that exclusion of refined carbohydrates from the diet leads to an involuntary fall in energy intake and weight and suggest that the loss in weight is due mainly to the removal of refined sugar. Fiber intake increases, but this is not directly responsible for the weight loss. Presumably, energy intake is adequate for physiological needs on a "natural," unrefined diet. This being so, energy intake must be excessive on a diet that includes refined carbohydrates.

The only comparable study is the 1942 study by Macrae *et al.*,[23] in which volunteers ate *ad libitum* a diet mainly of bread for a week. When the bread was whole-meal, they ingested 2468 kcal per day and when it was white, 2555. The difference of 87 kcal is small compared with that obtained in the study described above, but the design of the two investigations was different. Macrae *et al.'s* study was not truly an investigation of voluntary food intakes, since intake of sugar and, indeed, of all foods except bread was rigidly controlled on both diets. The short duration of the study and the artificial monotony of a diet providing three-quarters of its energy in bread must also limit the applicability of its findings.

Southgate and Durnin[24] compared the intake and output of nutrients and dietary fiber on low- and high-fiber diets. However, their data cannot be used in the present discussion because the investigation was in no way a study of voluntary food intakes; the subjects were obliged to eat their preordained rations, and the experimenters tried to maintain energy intake during the high-fiber periods. This sometimes caused complaints of discomfort in women subjects.[25] Similarly, in another study, volunteers who ate a controlled amount of carbohydrate in the form of refined sugars said they often felt hungry, whereas when they ate the same amount of carbohydrates as vegetable and cereal starches, with much or all of the fiber intact, they complained that they were being "stuffed."[26]

If eating fiber-free carbohydrate involuntarily inflates energy intake, then abstaining from it would be expected to cause involuntary weight loss. In Cape Town, 17 office workers were persuaded to reduce their sucrose intake from 85 to 12 g/day for 5 months and were instructed to maintain their weight by eating more of other foods. Despite this instruction, they lost an average 2.8 kg. In the same 5 months, 17 controls eating their normal diet gained 2.2 kg.[27] In a similar study, 11 men with known coronary heart disease agreed to avoid sugar-containing foods for 10 weeks. They were told that weight loss was not

desired, but on average they lost 1.2 kg (2.6 lb).[28] Sugar exclusion is part of virtually all slimming diets.

VI. INSULIN RELEASE AND THE RATE AND SITE OF NUTRIENT ABSORPTION

It is reasonable to suppose that rapid absorption of carbohydrate, and other nutrients, favors obesity. A diet of a given energy value is widely believed to be more fattening if it is consumed in one or two large meals than in several small ones. The infrequent meal pattern with its concomitant large surges of nutrient absorption is thought to lead to increased fat synthesis, "adaptive hyperlipogenesis." Carbohydrate is a particular cause, since every surge of absorbed glucose brings a corresponding surge of insulin release, and insulin stimulates lipogenesis. When glucose is absorbed beyond a certain rate, calculated as 10 g/hr by Sassoon,[29] the ability of the liver to store it as glycogen is exceeded and the surplus is converted to fat. Absorbed fructose is not insulinogenic but has a particular propensity to be converted to lipids if it reaches the liver above a threshold rate.

Hyperinsulinemia is well known as a complication of obesity, when it is blamed on peripheral insulin resistance, but it can also antedate it. Thus, animals that are made to overeat by destruction of the hypothalamic satiety center develop hyperinsulinemia before they are fat, and their obesity can be prevented by chemically ablating the pancreatic β-cells.[30] Animals injected with long-acting insulins overeat and become obese,[31] and it is common clinical experience that diabetic patients treated with insulin tend to become obese unless their diets are strictly controlled.

These considerations suggest that any dietary change that leads to more rapid absorption of carbohydrate and greater insulin release is likely to promote obesity.

Few studies have been published on the rate of absorption and insulinogenicity of different carbohydrate foods, but those that have suggest that (1) purified sugars are absorbed faster and are more insulinogenic than purified starches,[32,33] (2) starch is absorbed faster and is more insulinogenic when taken in fine particles than in larger ones,[34,35] and (3) removing fiber from a natural-sugar food (apples) increases its insulinogenicity[8] but makes no difference with a starchy food (bread).[20] The second and third points are germane to the present discussion and will be illustrated.

The plasma glucose and insulin responses of normal subjects to meals containing 50 g starch were found by Crapo *et al.*[35] to be significantly higher if the starch was fed as baked potato or bread than if it was given as white rice or corn (maize). These differences cannot be attributed to different amounts of

fiber, since the more insulinogenic potato has not less, but more, fiber than the less insulinogenic rice (i.e., 8.7 versus 2.7% dry matter). A reasonable explanation is that the potato has less solid texture and the flour, smaller particle size compared with rice and corn. When equicaloric amounts of whole-wheat bread and raw whole-wheat flakes were compared, there was a smaller plasma glucose response to the larger particle form of wheat.[34] This may be because the rate of hydrolysis of starch by amylase is influenced by particle size.[36] An additional but little studied factor affecting starch digestion and absorption is cooking. Raw potato starch is undigested by rats or humans[37,38] and swallowing soluble starch results in a flat plasma glucose response unless it is mixed with boiling water.[39]

The effect on glycemia and insulinemia of removing fiber from a sugary food was recorded in our apple study.[8] Equicaloric meals of apples and apple juice evoked similar rises in plasma glucose. But with juice, there was a rebound fall below the fasting level during the second and third hours after the meal that did not occur with the apples. The insulin response to juice was 50% greater than that to apples. We have found very similar differences between oranges and orange juice,[16] as has Kay[40] with blood glucose. With grapes and grape juice these differences were not apparent, possibly because the grapes were very rich in sugars (18%) and low in fiber.[16] The glucose and insulin responses to pureed apples were intermediate between whole fruit and juice, showing the importance of food texture as well as fiber content. Using mixed meals containing equal amounts of protein and fat as well as carbohydrates, Albrink[41] found that a liquid-formula meal evoked more than double the insulin response of a solid meal made up of beans, brown rice, and whole-meal bread. However, the carbohydrate was starch in the solid meal and glucose and dextrins in the liquid meal.

In all these experiments, the greater insulin response to the liquid fiber-free meals presumably represents the reaction of the pancreas to more rapid absorption of carbohydrate. Possible mechanisms include faster gastric emptying and greater release of the insulinogenic hormone, GIP, from the upper small bowel.[42]

A low blood glucose stimulates the appetite. The rebound fall in blood glucose that follows fruit juices, and presumably other sugary drinks, may promote obesity by encouraging an earlier resumption of eating.

Addition of purified guar and pectin to test meals flattened the glucose and insulin responses of normal subjects, diabetics and patients who had had gastric surgery.[43–45] In the surgical patients, it prevented rebound hypoglycemia.[45] These impressive findings may well have therapeutic importance, but they are drug-like not food-like effects. The doses and concentrations of pectin and guar used were far greater than can be found in natural foods. Furthermore, the effects are mediated by viscosity, which is not a major feature of food fiber.

Also, there is slowing of small-intestinal transit[43] and this transit is speeded by natural fiber, at least in wheat.[9] The published effects of pectin and guar are of doubtful relevance to a discussion of dietary fiber.

In summary, preliminary evidence suggests that the insulinogenicity and probably the rate of absorption of dietary nutrients are increased by four processes in constant use in civilized communities.

1. Separation of sugars from their natural fiber-rich matrix, or depletion of fiber.
2. Reduction of particle size by milling, which involves disruption of the fibrous matrix.
3. Conversion of solids to liquids or "mushes," which also involves disruption of the fibrous matrix.
4. Cooking of starch.

It must be emphasized that three of these processes disturb the fiber–nutrient relationship. The metabolic effects of a diet that has not been processed in these ways need to be examined systematically. Meanwhile, it is interesting to note that a raw high-fiber diet has been claimed to reduce or eliminate the need for insulin treatment in diabetes,[46] which suggests that raw food in general is less insulinogenic (see Chapter 11). It is also noteworthy that the foods most commonly avoided in slimming regimes are those resulting from the three processes that disturb the natural fiber–nutrient relationship.

VII. FECAL ENERGY LOSS

In energy balance terms, increased loss of energy in the stools is equivalent to decreased energy intake. There is ample evidence that as dietary fiber intake is raised, there is a rise in fecal energy. In the pioneering experiment of Southgate and Durnin,[24] young women on low-, medium-, and high-fiber intakes excreted 83, 127, and 210 kcal/day, respectively, in their stools. On the high-bread diets of Macrae *et al.*[23] the subjects excreted 99 kcal/day on white bread and 321 kcal/day on whole-meal bread. More recently, a combination of moderate amounts of whole-meal bread and bran raised fecal energy by 92 kcal/day,[47] and bran biscuits alone increased energy excretion by 58 kcal/day.[48] Kelsay *et al.*[49] showed that this effect is just as apparent with fruit and vegetable fiber as it is with cereal. In 12 middle-aged men, fecal energy was 117 kcal/day on a diet with fruit and vegetables present only in the form of juices and 255 kcal/day on a diet rich in whole fruit and vegetables but devoid of whole-grain foods.

Fecal analysis shows that this extra energy is present in fat and nitrogen as well as unchanged dietary fiber. Some of it may be in fat and nitrogen which are inseparable from cell wall material, but some is probably present in bac-

terial cell walls. It is not clear whether there is less efficient small-intestinal absorption on a high-fiber diet. When bran biscuits were added to the diet, there was a rise in fecal fat, but on gas liquid chromatography this had a fatty acid composition different from that of the dietary triglycerides.[48] On the other hand, large doses of pectin and guar gum increase fecal fat, though the additives are fat-free.[50,51]

VIII. EPIDEMIOLOGICAL EVIDENCE

The normal techniques of epidemiology are difficult to apply. To look for correlations between indices of obesity and intakes of dietary fiber does not necessarily test the hypothesis that fiber-depleted foods are intrinsically fattening. Fiber intake can be increased simply by eating more of everything. A diet can be low in fiber simply because it is based mainly on animal products, as are the traditional diets of the Eskimo and the cattle-herding African nomads. Nevertheless, in a community where everyone obtains most of his energy from plant foods, it may be appropriate to look for such correlations. In a study of 200 normal middle-aged men in Ontario, Kay[52] found a significant negative correlation between reported dietary fiber intake and an obesity index ($p < 0.01$).

IX. ANIMAL OBESITY

Spontaneous obesity has been described in several animals eating ordinary laboratory chow, which is based on whole-grain cereals. The energy:satiety ratio of chow and the availability of its energy are likely to be greater than those of natural foods such as leaves, shoots, seeds, and fruit. Systematic studies are needed of the effect of reducing the texture of food on food intake. Milling feed is said to increase the intake of a ruminant by 50%.[53] Work is also needed on the effect of removing fiber from an animal's diet. Rats fed "purified" corn starch had fat depots that weighed twice as much as those of rats fed whole corn.[54] The refined foods popular with humans are not necessarily attractive to animals. However, American rats have been described that ate a selection of supermarket snack foods including biscuits, chocolates, and marshmallows in preference to chow. In 60 days they gained 78 g more weight than chow-fed controls.[55]

X. PALATABILITY

The refined carbohydrates, white flour and sucrose, were developed partly because they were considered to be more palatable than their fiber-rich coun-

terparts. Both are included in a wide range of tempting baked goods, and sugar is also the major component of most confectionery and other "fun foods." Refined carbohydrates must be largely accountable for obesity caused by eating for pleasure rather than to satisfy hunger. Similarly, the addition of sugar to breakfast cereals and of jam to bread may encourage over-consumption of these otherwise bland and uninteresting foods. Finally, most baked goods and confectionery include fat as well as sugar. The mixture of sugar, with or without flour, and fat may encourage the consumption of fat which, eaten alone, would be rejected as unpalatable.

A. *Special Note on Sugar*

Sugar in the ordinary sense of cane and beet sugar must, as Cleave[3] has emphasized, be included in any discussion on dietary fiber. Its production is strictly analogous to that of fruit juice. A sweet-tasting but fibrous plant product is crushed (or in the case of beet, sliced and extracted with hot water) to obtain the sugar-rich juice or sap, and the fibrous part is discarded. The widely accepted if pejorative term, "empty calories," is no more appropriate of sugar than it is of apple juice. "Denuded" or "undefended" may be better adjectives for any carbohydrate that is separated from the fibrous matrix in which it was synthesized. Sugar and the other products of sugar refining, such as syrup and molasses, are such a familiar part of today's diet that it is difficult to remember how abnormal they are, in the sense that they are the only major foods in which carbohydrate is ingested with all its fiber removed. Certain drinks including beer and sweet-tasting alcoholic drinks are perhaps analogous, as are most fruit juices.

B. *Sugar and Obesity*

Far from being excluded, sugar should be given paramount importance in discussions of fiber and obesity. It has the following special features which put it under suspicion as the major dietary factor in obesity.

1. It is soluble and can be drunk. Even in solid foods it needs no chewing.
2. It is highly insulingenic, probably more so than its content of glucose would predict.[33]
3. Its fructose moiety is particularly liable to be converted into fat.
4. It is exceedingly palatable.
5. It is present in a huge range of processed and convenience foods.
6. It is, in fact, the cheapest source of energy in the British diet.
7. It is ubiquitous, and products containing it are on sale in every slot machine, every cafe, and almost every shop selling food, newspapers, or cigarettes.

All these features except the third are attributable wholly or in part to the fact that sugar has been separated from fiber before it is marketed.

XI. FIBER AND TREATMENT OF OBESITY

The fiber hypothesis states that avoiding fiber-depleted foods will help to avert obesity and to arrest its progress. It does not claim that avoiding such foods will cause the regression of obesity, though in practice, there is usually a modest loss in weight (see Section V). To obtain continued weight loss, energy intake must fall below requirements. For this to occur, further restrictions are necessary. Nevertheless, the greater satiety value of fiber-rich over fiber-depleted carbohydrates suggests that it would help a slimmer to stick to his diet if his carbohydrate allowance was provided in fiber-rich form.

Concentrated fiber preparations have long been used as "inert fillers" in slimming regimes. They seem to be effective provided a large enough dose is taken,[12] but palatability and compliance pose problems.

XII. SUMMARY

The fibrous architecture of plant foods is responsible for their solidity and firm texture. It also encloses the nutrients within cellular envelopes. Much traditional food processing aims to reduce the texture of food by disrupting its fibrous architecture. Actual removal of fiber is technologically difficult, and the process on a mass scale is a recent phenomenon. Its main examples are the sifting of bran from wheat flour and the separation of sucrose from sugar beet and cane. In the case of flour, this merely allows a further softening beyond that produced by milling. The change is more fundamental with sugar. An energy source is produced which is actually liquid, or at least soluble. Moreover, it is exceedingly palatable and versatile and is often combined with fat, which would otherwise be unpalatable. Fiber-depleted foods are quicker to eat than their intact counterparts and require less effort. Experimentally, more rapid ingestion of liquid food leads to a greater intake, and eating solid food more slowly leads to a lesser intake. Adding effort to the act of eating has been shown to deter and reduce intake.

A person stops eating when he feels sufficiently full or satiated. Satiety is a subjective sensation but can be measured. In single-meal experiments vegetable fiber, in fruit, and cereal fiber, in whole-meal bread, markedly increase the satiety value of food. The satiating effect of fiber is partly mediated by chewing, and the difference is most striking when solid is compared with fiber-free liquid. By removing fiber from his carbohydrate, civilized man deprives his food-intake-controlling mechanism of one of its major cues.

In the long term, excluding fiber-free sugar from the diet leads to involuntary if modest weight loss. Excluding all fiber-depleted carbohydrates led, in one study, to an 18% reduction in energy intake without the subjects being aware of eating less. Weight loss correlated strongly with sugar exclusion and not with fiber intake.

Insulin favors the synthesis and deposition of fat. Two studies have suggested that fiber-free carbohydrate evokes more insulin secretion than intact plant food, probably through more rapid absorption of glucose. The insulinogenicity of food may also be increased by softening it, reducing its particle size or even cooking. All these processes disrupt fiber.

Energy output in the feces is increased *pari passu* with the bulking action of dietary fiber. The precise source of this energy is unclear, but it represents a further way in which fiber may prevent energy intake from exceeding output.

The totality of evidence suggests that the consumption of fiber-depleted foods is an important factor in obesity. Fiber-free sugar is likely to be much more important than fiber-depleted starch. Prevention is likely to be most effective if fiber is retained in its natural spatial relationship to nutrients and the texture of the food is preserved.

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13

Dietary Fiber and Mineral Absorption

W. P. T. James

I. INTRODUCTION

The observation that diets rich in cereals produced rickets in puppies if they were also fed inadequate amounts of a fat-soluble vitamin was made by Mellanby[1] during the First World War. The historical development of the concept that phytate might be involved in this rachitic effect has been set out by Widdowson,[2] one of the pioneers in this field. The observations were extended to man more than 40 years ago by McCance and co-workers during studies on the nutritional effects of whole-grain bread and oatmeal.[3–5] At that time, the deleterious effect of many unrefined foods, particularly cereals, on calcium and iron balances was ascribed to their phytate content. Only recently has fiber itself been implicated, and the concern for the malabsorption of other minerals been extended to include zinc. Much of this older work is still relevant today, and, since these classic studies are often neglected when considering the problem of mineral malabsorption on high-fiber diets, they will be evaluated in this chapter.

Diets rich in fiber have a very different mineral content from diets containing small amounts of fiber. Minerals in plant foods are often closely associated with the plant cell wall and are involved in the structural framework and binding of the cellular polysaccharides.[6] Thus, calcium pectate seems to act as a cementing agent in the cell, and the complexing of zinc by pectin may explain the capacity of some plants to tolerate high levels of zinc in the environment, with zinc concentrations in such plants found to be above those nor-

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mally considered toxic to cytoplasmic enzymes. Magnesium is also bound within cell walls to the carboxyl and hydroxyl groups in the phenolic compounds of lignin.[7] Unrefined cereals also contain high concentrations of other elements. The potassium content of whole-grain flour is much greater than that of white flour,[8] and fiber-rich foods contain more silicon, chromium,[9] lithium, boron, manganese, and cobalt.[10,11] Since the refining of cereals leads to a marked fall in their mineral content, experiments undertaken to assess the effect of different forms of dietary fiber on mineral absorption often involve changes in mineral intake that may affect the body's ability to attain elemental balance.[12]

In mixed diets, an element, e.g., calcium, is derived both from the mineral intimately associated with the fiber of the plant cell wall and from calcium present in free form, as in, for example, milk. If fiber remains undigested as it passes through the small intestine, the calcium associated with the wall itself will remain unavailable for absorption within the small intestine. If the binding capacity of the fiber and phytate exceeds that of the plant's own minerals, minerals from other food sources will be complexed and thus rendered less available for absorption.

Animal and human studies have recently demonstrated that it is unwise to extrapolate from the binding properties of plants assessed by *in vitro* experiments to the ability of the body to absorb the element when ingested with the binding agent. Absorption may be very much better *in vivo* than that predicted from *in vitro* experiments; this disparity reflects the complex nature of the absorptive processes within the small intestine. Other food factors may promote elemental absorption, as shown in studies of iron uptake from food.

The traditional view that elemental absorption can take place only in the small intestine is also becoming increasingly untenable. An element may still be absorbed by the colon once the plant cell wall and associated structures are digested by microbial fermentation within the colonic lumen; the complex is thereby destroyed and the element is more readily transported into the body.[13]

II. CALCIUM ABSORPTION AND CALCIUM BALANCE

A. The Role of Phytate

The classic studies on mineral metabolism and the relative roles of phytate and fiber undertaken by McCance and Widdowson[3] in the early 1940s involved metabolic balance studies on five men and five women, who were investigated continuously for 9 months. The diets included wheat flour products providing 40–50% of the dietary energy. The effects of white flour with an extraction value of 69% were compared with those from brown flour of 92% extraction eaten as bread, cakes, pastry, and puddings.

Table 1. Calcium Intakes and Balances on White and Brown Bread[a,b]

Subjects (*N*)	White bread		Brown bread	
	Intake	Balance	Intake	Balance
Men (5)	580.2 ± 40.0	−26.6 ± 25.2	589.2 ± 24.6	−111.6 ± 26.9
Women (4)	425.8 ± 15.3	− 8.0 ± 4.9	520.3 ± 9.8	− 56.8 ± 9.7

[a]McCance and Widdowson,[3] Table 17.
[b]Bread provided 40–50% of the dietary energy, the white bread being made from 69%-extracted flour and the brown bread from 92%-extracted flour. Values are given as mg/day; mean ± SEM.

Table 1 summarizes the results on nine of the subjects fed both the white- and brown-bread diets for periods of from 2 to 3 weeks each. On white bread, the subjects were approximately in calcium balance despite an intake that would be considered very low by current United Kingdom recommendations. On transferring to brown bread, all subjects went into negative calcium balance, but this varied from a net loss of 10 mg/day of calcium in one individual to a maximum of 190 mg/day in another subject.

Since at this time phytate was considered primarily responsible for negative calcium balance induced by diets based on flour with a high extraction rate, McCance and Widdowson[14] also studied the effects of adding sodium phytate to white bread to see if it reproduced the effects of brown bread. The subjects received an intake of phytate that corresponded to the phosphorus content of brown bread (Table 2). Phytate produced a marked net loss of calcium from the gut. The change in absorption was greater than that observed on transferring from white bread to brown bread, but the brown bread may have had less phytate than the phytate-supplemented white bread. When phytate was added to white bread to simulate that in brown bread, yeast was omitted in the baking process, reducing the chance that phytate was hydrolyzed by the yeast. Also, a paucity of natural phytase in the low-extraction white flour to which phytate was added increased chances of the added phytate remaining

Table 2. The Absorption of Calcium and Phosphorus on Adding Sodium Phytate to White Bread[a]

	White bread	White bread + phytate
Calcium intake	492.0 ± 36.9	521.4 ± 25.5
Calcium absorption	133 ± 35.0	24.1 ± 26.0
Phosphate intake	1191 ± 52	2114 ± 127
Phosphate absorption	822 ± 41	1284 ± 71
% Phytate phosphate absorbed		49.6 ± 2.3

[a]Recalculated from McCance and Widdowson, 1942,[3] and including only the seven subjects studies for calcium and phosphate absorption on both diets. Absorption is calculated by subtracting fecal excretion from intake. Values are given as mg/day; mean ± SEM.

intact. From this study, one can conclude that the phytate in brown bread could account for the inhibitory effects of the bread without having to invoke the additional binding properties of fiber.

When phytate is fed to subjects accustomed to a high-phytate diet, the effect on calcium malabsorption is less marked,[15] a difference possibly reflecting the adaptive changes that occur in the intestine when several different types of calcium-binding agents are fed. When assessing different studies on cereal consumption, it is also relevant that different cereals may have very different effects on calcium absorption although their phytate content is similar. In Mellanby's studies[1] with puppies, different cereals had different rachitogenic properties; oatmeal was much more rachitogenic than wheat, rye, or barley. This is probably explained by the low phytase activity of oatmeal, while rye, for example, has a particularly high phytase content.[16]

McCance and Glaser's studies[5] showed that oatmeal can lead to severe hypocalcemia in man; but these observations cannot be extrapolated to the likely effects of a moderate intake of oatmeal, since McCance and Glaser's subjects were fed on an almost exclusively oatmeal diet.

A further experiment with dephytinized bread also served to emphasize the importance of phytate.[14] The 92%-extraction flour was dephytinized by incubating the bran in 10 volumes of dilute hydrochloric acid at a pH of 4.5 for 10 hr at 50°C. With hindsight, we know that this procedure would not only allow the phytase in the bran to hydrolyze the phytate, but would also solubilize water-soluble components of dietary fiber, including a high proportion of those fractions of fiber we now recognize as having cation-binding properties. The dilute-acid conditions would also have hydrolyzed an appreciable proportion of the noncellulosic polysaccharides. The incubation procedure led to a loss of 30% in the bran's weight, and 32% of the calcium was liberated into the solution together with all the phytic acid phosphorus and 74% of the total phosphorus. Also lost were 77% of the bran's potassium, 72% of its magnesium, and 41% of its nitrogen, but practically none of its small iron content. In order to discount the effect of dietary phosphate as such in their experiments, McCance and Widdowson ingeniously included an experimental period in which the extracted water was drunk and incorporated into the bread so that no net loss of elements occurred. This process of "selective" dephytinization led to a marked improvement in calcium absorption (Table 3). The substantial increase in absorption after dephytinization was therefore taken as confirmation that phytate was responsible for reducing calcium absorption. If phosphate alone were responsible for calcium malabsorption, the selective dephytinization procedure should have been without effect. Mellanby's[1] earlier experiments on puppies had also shown that the phosphate as such could not be considered responsible for the calcium malabsorption. The possibility that the improved absorption on "dephytinization" is in fact related to the destruction of dietary fiber will be considered next.

Table 3. The Intake and Absorption of Calcium from Diets Based on Different Types of Bread[a,b]

Type of bread	Intake (mg/day)	Absorption (mg/day)	Absorption (% intake)
Brown	561.8 ± 10.9	35.5 ± 17.5	6.5 ± 3.1
Dephytinized brown[c]	609.8 ± 12.5	164.8 ± 29.2	27.3 ± 5.0
Dephytinized and demineralized brown	517.7 ± 18.0	196.2 ± 28.1	37.7 ± 5.3
White	498.0 ± 14.0	189.5 ± 20.3	38.2 ± 4.2

[a]Recalculated from McCance and Widowson,[14] Table 4.
[b]The same six subjects were studied on each diet; periods were randomized and each lasted 2–3 weeks. Values are given as mean ± SEM.
[c]Mineral solution added after incubating bran to liberate phosphate and other ions from phytate.

B. Calcium Binding by Dietary Fiber

It is now recognized that calcium may be bound not only to phytate but also to dietary fiber. The uronic-acid components of fiber have been particularly implicated in the binding process because the pH characteristics of binding are in keeping with binding to ionized carboxyl groups; and a significant relationship exists between the uronic-acid content of phytate-free plant fiber and its ability to complex calcium.[13] On this basis, sufficient binding can occur to the "free" uronic-acid sites to complex 3.8 mmol (152 mg) calcium in a Western diet containing 17.2 g fiber and 12.3 mmol uronic acids; very much greater amounts of calcium would be bound on a high-fiber diet. Other cations, including magnesium, zinc, and iron, within fiber-rich foods could reduce the availability of free binding sites. The relationship of the other cations to the carboxyl groups of uronic acids in fiber-rich food is unclear. Tests on crude preparations of food reveal that additional binding still takes place despite the range of cations within the food. Fiber thus does seem capable of cation binding.

The question therefore arises as to whether the procedure used by McCance and Widdowson for phytase inactivation, also hydrolyzed pectins and other noncellulosic polysaccharides. Some of the dietary fiber, particularly the pectins, would have been extracted by the process. If the pectins and other noncellulosic fiber fractions had remained unhydrolyzed, they could still have exerted physiological effects in the "selectively dephytinized" bread. If present, their effects on calcium absorption were negligible (Table 3), since the dephytinization process could account for 84% of the improvement in calcium absorption observed when the subjects transferred from the brown bread to the white bread. If, however, the pectins and other calcium-binding fiber fractions were hydrolyzed, they might have accounted for the marked improvement in calcium absorption found when either the demineralized or dephytinized bread was fed and when the bread, which had supposedly been specifically dephytin-

ized, was used. Thus hydrolysis of the binding components of fiber in the dilute acid conditions could explain the improvement in calcium absorption associated with the dephytinization process.

Given the difficulties encountered in disentangling the actions of fiber and phytate, we must look at studies that involve the selective feeding of fiber or phytate. The phytate studies have been detailed and clearly show that phytate has a potent inhibitory effect on calcium absorption. Only recently have investigations with fiber been undertaken. Table 4 shows the results of a study, conducted on five medical students, in which 36 g pectin was added to a controlled diet and then calcium balance measured. Despite marked binding of calcium *in vitro,* the pectin failed to induce calcium malabsorption when fed *in vivo.* A study of similar design, but using 31 g wheat fiber, however, showed a marked change to negative balance. A further study[19] involving an increased uronic-acid intake, which has been briefly reported, found that feeding 12 men a mixed diet high in fruit and vegetable fiber led to calcium malabsorption. This would imply that potent cationic binding from the uronic-acid-rich fibers of fruit and vegetables can induce malabsorption, but no data were given on the phytate content of the diet. Some vegetables are known to be sources of phytate as well as fiber, so this study may not have involved a selective feeding of fiber without phytate. From the pectin study, we may conclude that fiber binding of calcium probably did not play an appreciable part in altering the absorption of calcium when brown bread was consumed by McCance and Widdowson's subjects.

Fiber components not containing uronic-acid moieties may also lead to calcium malabsorption even if they are poor calcium binders *in vitro.* Thus Ismail-Beigi *et al.*[20] fed 10 g cellulose to three subjects accustomed to eating a diet rich in both fiber and phytate. Fecal calcium increased with the cellulose supplement by 14, 17, and 39% in the three men, and all three went into negative calcium balance. Since calcium binding to cellulose *in vitro* is negligible

Table 4. A Comparison of the Effects of Different Forms of Fiber Supplementation on Calcium Balance[a]

	Pectin study[b]		Wheat fiber study[c]	
	Control	+ 36 g pectin	Control	+ 31 g wheat fiber
Number of subjects	5	5	4	4
Dietary intake (mg/d)	1280	1357	960	1302
Fecal excretion (mg/d)	1120 ± 35	1197 ± 43	672 ± 57	1121 ± 61
Urine excretion (mg/d)	195 ± 34	164 ± 38	255 ± 39	257 ± 26
Net balance (mg/d)	− 35 ± 21	− 5 ± 48	+ 32 ± 37	− 77 ± 37

[a]Values are taken from the third week of each dietary period (values ± 1 SEM).
[b]Cummings *et al.*[17]
[c]Cummings *et al.*[18]

(Branch, unpublished observations), clearly a marked discordance exists between the *in vitro* binding of calcium by fiber and the response to fiber feeding. In McCance and Widdowson's original experiments with dephytinization of bran, we can be confident that the dilute acid conditions did not hydrolyze the cellulose in the bran; therefore, the improvement in calcium absorption in McCance's studies must have been independent of cellulose intake.

Reinhold[21] has claimed that fiber rather than the phytate is responsible for calcium malabsorption induced by feeding fiber-rich diets. Originally Reinhold and his colleagues had concluded that phytate was primarily responsible for mineral malabsorption,[15,22] but their studies on the *in vitro* binding of cations to fiber[23] and the poor relationship between the destruction of phytate in cereals and the availability of soluble zinc for absorption to rat intestinal strips[24] led them to emphasize the role of fiber in limiting cation absorption. Since feeding cellulose to volunteers also led to mineral malabsorption,[20] it seemed clear that fiber could exert marked effects on mineral balance. The studies with cellulose are the only direct evidence of a fiber-related increase in fecal excretion of cations, and the choice of material, i.e., Solka Floc®, may have affected fecal output. Certainly men accustomed to much higher intakes of cellulose derived from natural food sources maintain calcium balance. The adaptation to new forms of food containing components that bind minerals may also explain the rather small effect seen by Reinhold in his studies with phytate. Most of Reinhold's subjects were Iranians already accustomed to a high-phytate diet. This dietary experience seems to minimize the effects of supplementary phytate on calcium metabolism, perhaps as a result of induction of human mucosal phytase.[25] Studies by Reinhold *et al.*[15] in Iran on tanok (unleavened wheat bread), which seemed to have a greater effect in inducing calcium malabsorption than that predicted from its phytate content, were on three men, only two of whom showed greater calcium malabsorption on tanok feeding. The detailed evidence (see Fig. 1 in reference 15) shows that calcium balance was becoming progressively less negative on tanok feeding until the last 10 days of the period. At this time, the tanok's phytate content was found to have increased, and this was coincident with increased calcium malabsorption and calcium imbalance. However, by the end of this second phase, adaptation seemed once more to be occurring.

More prolonged studies by Campbell *et al.*[26] on the effect of tanok on the metabolism of minerals were conducted on two Americans on their arrival in Iran. The marked change in food patterns was accompanied by gastroenteritis and the use of antibiotics. Despite these problems, mineral absorption was steadily increasing towards the end of the 11-week study, suggesting that adaptation to high-fiber and phytate-rich diets does occur. Thus, there is good evidence that normal food sources rich in fiber increase fecal calcium excretion, but much of the increase may relate to the associated phytate content of the foods. The effects of fiber seem to depend in some way on the type of fiber fed.

The effects of fiber on fecal calcium output may not depend on the cationic binding properties of fiber. It becomes increasingly apparent that the propensity to develop calcium malabsorption on feeding fiber may depend primarily on events in the colon rather than on the binding properties of fiber and the availability of calcium in the small intestine.

C. Calcium Absorption from the Colon

Traditionally, the colon has been considered predominantly an organ for extracting sodium and water from the residual digestive juices that the small gut has failed to absorb. Early studies on amino acid, glucose, and mineral transport seemed to show that the colon had little absorptive function of nutritional significance, and no function in calcium absorption. This view was reemphasized when it was demonstrated that calcium-binding proteins were present particularly in the duodenum and jejunum, with very little activity being found by immunofluorescent studies on this binding protein within the colonic mucosa.[27] The very low activity conformed with the Harrisons' *in vitro* demonstration[28] that the rate of calcium transport across the colon amounted to about one-tenth of that from the small intestine.

We were drawn to reexamine the colonic absorption of calcium when it became apparent that the calcium-binding properties of fiber alone were sufficient to complex all the calcium ingested by large numbers of people living in tropical environments. Adults in these communities may be ingesting only 400–500 mg (10–12.5 mmol) calcium each day.[29] We observed from *in vitro* studies that this quantity of calcium could be bound by 5–6 mmol uronic acid. With daily fiber intakes in Africa varying from 50 to 150 g, uronic-acid intake would be 30–110 mmol. This suggests that no calcium would become available for absorption in the small intestine, which is particularly true if it is recognized that these diets often contain a substantial amount of phytate, and that much of the calcium in these diets is derived from the indigestible cell wall structures themselves. Since adults in these environments are recognized as having a bone structure with at least the density of that found in adults in Western environments, there seemed a *prima facie* case for reconsidering colonic transport of calcium.

The importance of the colonic absorption of minerals has been elegantly demonstrated in pigs by Partridge.[30] The pig, as a large monogastric animal, is often used as a model for studies of gastrointestinal absorption. Partridge inserted reentrant cannulae in the terminal ileum so that he could distinguish between absorption from the small intestine and from the colon. Table 5 shows that on a low-cellulose diet, about 43% of the very high calcium intake was absorbed in the small intestine, but that an additional 31%, amounting to about 4 g/day of calcium, was absorbed from the colon. Thus the colon is making a substantial contribution to calcium balance in a growing pig fed a low-cellulose diet. Of greater interest is the response to the high-cellulose diet. Despite a

Table 5. The Fraction of Dietary Minerals and Phosphate Absorbed in the Small and Large Intestine of Pigs Fed Low- and High-Cellulose Diets[a,b]

	Low-cellulose diet				High-cellulose diet			
Mineral	Intake[c] (g)	Small intestine (%)	Colon (%)	Total (%)	Intake[c] (g)	Small intestine (%)	Colon (%)	Total (%)
Sodium	5.1	46	53	99	5.6	15	83	98
Potassium	4.6	90	6.5	96.5	4.3	88	−2	86
Calcium	13.5	43	31	74	13.2	44	19	63
Phosphate	9.9	64	17	81	10.2	69	5	74
Magnesium	1.09	−1	74	73	1.14	3	56	59
Zinc	0.12	10	50	60	0.13	24	52	76

[a]Calculated from Partridge (1978).[30]
[b]Pig size taken as 48 kg as suggested by Partridge.
[c]Intake estimated from data given by Barber *et al.*[31] on feed gain efficiency ratio, taken as 2.9 kg/kg and related to Partridge data on growth rate of 649 g/d. Intake includes the estimate of mineral intake from tap water.

twofold increase in ileal flow rates, calcium absorption from the small intestine was similar. There was, however, a substantial fall in colonic calcium transport so that the fecal calcium output increased. The combined absorption of calcium by the small and large intestine fell from 74% to 63% of the intake. A reduction in colonic phosphate absorption was also apparent on the high-cellulose diet.

Partridge's studies also revealed that colonic absorption of magnesium and zinc was particularly important for maintaining mineral balance, so that colonic events may well determine overall mineral absorption. Magnesium excretion increased when cellulose was fed; zinc absorption, however, seemed to be more efficient. These studies are of much greater nutritional significance than many of the isotopic studies with *in vitro* models of gut transport. Partridge's studies demonstrate that large amounts of mineral can be absorbed by the colon of the growing animal; colonic absorption may sometimes be responsible for up to 100% of the absorption of essential elements. On this basis, the mechanism whereby fiber leads to elemental malabsorption needs to be reevaluated. If pectin does bind calcium by complexing the calcium with its carboxylic acid groups, the observation that mineral balance can be preserved probably depends upon the pectin's being hydrolyzed by colonic bacteria with subsequent absorption of calcium from the cecum and colon. From Partridge's studies, we may infer that cellulose feeding of volunteers by Reinhold did not affect the small-intestinal component of calcium absorption because the cellulose binding of calcium is negligible. The colonic inflow of a relatively indigestible fiber, cellulose, in some way limited calcium absorption and led to an increased fecal output of minerals. Adaptation to changes in fiber and phytate intake may therefore depend primarily on colonic adjustments in either microbial metabolism or mucosal transport.

Further insight into the role of fiber and phytate in calcium and phosphate

metabolism comes from studies on the usefulness of cellulose phosphate in reducing the abnormally high rates of calcium absorption in patients with hypercalciuria.[32] Parfitt *et al.*'s work[32] (Table 6) shows that additional phosphate, given as sodium phosphate, tends to reduce calcium excretion by the kidney so that calcium balance improves. An equivalent dose of phosphate as phytate, although leading to an increase in fecal calcium output in all seven cases studied, led to an overall improvement in calcium balance in five of the seven patients. Of the additional phosphate, given as phytate, 46% was absorbed and served, as in the sodium phosphate trial, to reduce substantially the output of urinary calcium. At least half the phytate was hydrolyzed in the intestine, either by mucosal phytase or by bacterial phytases in the colon, for the phosphate to be subsequently absorbed. Even when Parfitt fed cellulose phosphate, 21% of the additional phosphate was absorbed and renal calcium excretion fell. We can be sure that no cellulose digestion occurred until the fiber entered the colon where, on an average fiber intake, 20–40% of the cellulose in foods, is digested.[33] Thus, the capacity for fiber to cause malabsorption may depend on the degree to which the calcium-binding components of fiber resist digestion in the colon. If they remain undigested, they may be capable of enhancing calcium output in the feces.

D. Fiber-Rich Diets and Bone Disease in At-Risk Groups

Whatever the origin of the malabsorption, the change in elemental absorption on feeding fiber-rich diets is of nutritional significance. If these diets are to be advocated, this aspect of their physiological effects must be considered. The importance of the effect of high-fiber diets on calcium metabolism has been reemphasized in recent years by the finding that vitamin-D deficiency and bone disease in Indian and Pakistani immigrants to the United Kingdom is extremely common.[34] These immigrants often maintain their original custom of eating large quantities of unleavened cereal as chupatties, and they become

Table 6. The Effect of Extra Dietary Phosphorus, Presented in Three Forms, on Phosphate Absorption and Calcium Balance[a,b]

Number of subjects	Extra dietary phosphorus	Phosphorus (mg/d)				Calcium (mg/d)		
		Intake	Urine	Feces	Balance	Urine	Feces	Balance
5	Sodium phosphate (6.26 g/d)	+ 1377 ± 37	+ 840 ± 61	+ 266 ± 27	+ 274 ± 39	− 125 ± 20	+ 7 ± 32	+ 117 ± 35
7	Sodium phytate (6–8 g/d)	+ 1369 ± 29	+ 484 ± 41	+ 743 ± 56	+ 147 ± 39	− 182 ± 17	+ 97 ± 30	+ 85 ± 35
3	Cellulose phosphate (15 g/d)	+ 1282 ± 43	+ 130 ± 29	+ 1029 ± 53	+ 136 ± 63	− 116 ± 4	+ 104 ± 28	+ 12 ± 27

[a]Data recalculated from Parfitt *et al.*[32]
[b]A positive sign in urine or fecal excretion indicates that excretion has increased above that observed on the control diet when no additional phosphate was given. Values indicate change in output or balance and are given as mean ± SEM.

more susceptible to vitamin D deficiency when living in Britain because they are less exposed to sunlight than in India and Pakistan.[35] The plasma concentrations of 25-hydroxyvitamin D fall progressively during the first year after their arrival; most Asians living in Glasgow are found to have low 25-hydroxyvitamin-D levels. In an Asian group living in a rural environment (Storkaway), where there is less atmospheric interference with the small spectrum of ultraviolet light responsible for vitamin-D synthesis in the skin, many more individuals had normal plasma 25-hydroxyvitamin-D concentrations. Nevertheless, the Storkaway Asians had, on average, a 25-hydroxyvitamin-D concentration of only 5.9 ng/ml compared with 12.1 ng/ml in a group of Glaswegian and London Caucasians at the same time of year. In a survey in Rochdale, Lancashire,[36] 50% of Asian adolescents were found to have a raised plasma alkaline phosphatase between March and July, when plasma vitamin D levels are at their lowest, and Asian schoolchildren in Birmingham have similar problems.[37,38]

Bone disease in Asian children and adults is associated with a marked fall in plasma 25-hydroxyvitamin D; this fall can be prevented by the provision of vitamin D, or by ultraviolet irradiation even if the chupatti diet is continued.[39] Dent and his co-workers[40] considered that a chupatti diet was irrelevant to the problem, but their study, on a child where surprisingly they failed to show an effect of chupattis on calcium balance, was conducted at a time when he was recovering from rickets and had a positive calcium balance of 400 mg/day even before ultraviolet light was started. Of more relevance is the observation of Ford and his colleagues[41] on Pakistani children with late rickets and women with osteomalacia. They remained at home but were told to eat a chupatti-free diet for 7 weeks, substituting leavened bread made from flour of low extraction. This dietary change led to a dramatic increase in serum calcium in all subjects at a time when no other dietary or environmental change was made. Similarly, Wills and his colleagues[42] observed a progressive increase in serum calcium to normal levels when a child with rickets was fed a diet low in phytate while in hospital.

Thus, evidence indicates that both a deficiency of vitamin D and the consumption of a high-fiber, high-phytate diet contribute to abnormalities of calcium metabolism in Asian immigrants. Despite the early emphasis on the importance of dietary sources of vitamin D, increasing evidence shows that these sources are of little nutritional significance in most people. Foods, such as margarine, which are specifically supplemented with ergocalciferol, can increase 25-hydroxyergocalciferol (25-hydroxy-D_2) concentration in the blood, but 25-hydroxycholecalciferol concentrations, reflecting skin synthesis of vitamin D, are usually very much higher. In healthy Caucasians who are ingesting margarine as a major source of ergocalciferol (vitamin-D_2), plasma concentrations of 25-hydroxyergocalciferol are usually 25–50% of 25-hydroxycholecalciferol (vitamin-D_3) levels when measured in February. This is the time of year

in Britain when D_3 levels are low, but the normal summer's exposure to sunlight usually doubles vitamin-D_3 concentrations by August.[43] A relationship exists between summer and winter plasma concentrations of plasma 25-hydroxyvitamin D so that, even in winter, total 25-hydroxyvitamin-D levels seem to be determined mainly by cholecalciferol stored in the liver, skin, and adipose tissue during the summer months.

Given the normal dominance of vitamin D_3 from skin synthesis in the supply of vitamin D for the body, differences in the amounts of dietary vitamin D from unfortified foods would not seem very relevant to the development of rickets and osteomalacia in the Asian community in Britain. Exposure to sunlight seems a far more important factor. Dietary factors are not unimportant in the development of bone disease, but the mechanisms responsible for the development of bone disease are unclear. Rickets has been generally regarded as a manifestation of vitamin D deficiency and not related to calcium deficiency per se. However, Mellanby,[1] in his original experiments on puppies, clearly showed that the addition of calcium to a phytate-rich diet prevented the puppies from becoming rachitic. The use of phytate-rich cereals did not produce rickets if dietary supplies of vitamin D were adequate, but, once the animals were in a state of marginal vitamin deficiencies, the development of rickets was determined by the calcium and phytate content of the diet. With increasing evidence that bone formation may be responsive to 24,25-hydroxyvitamin D[44] rather than to the 1,25-hydroxyvitamin D that is particularly active in determining calcium absorption from the gut, we may expect to see much of the confusion surrounding the interplay of calcium, vitamin D, and bone disease resolved in the near future. For the present, it seems reasonable to conclude that factors which reduce the availability of dietary calcium are potentially rachitogenic in animals or humans with marginal vitamin D deficiency.

McCance and Widdowson[3] in their early studies showed that the use of oral vitamin D for a 3-week period did not rectify the negative calcium balances induced by brown bread. Cummings[18] has also observed negative calcium balances on feeding whole-wheat products to medical students whose 25-hydroxyvitamin-D levels were normal. Since McCance and Widdowson's subjects were also unlikely to have been deficient in vitamin D, the implication is that the initial malabsorption of calcium on feeding brown bread occurs independently of the vitamin D status of the subjects.

The demonstration that the addition of calcium to bread could overcome the inhibitory effects of phytate led to calcium fortification of National flour in Britain during World War II. Criticism then arose because humans were thought to have considerable powers of adaptation, and if longer periods of study had been used, this adaptation would become apparent. Walker *et al.*[45] undertook studies on four individuals fed for a period of up to 9 weeks on a high-extraction bread diet which, in practice, contained less phytate than that in the studies of McCance and Widdowson. A careful analysis of their figures

shows that only one subject was studied for long periods without any additional dietary changes, and this subject showed an unaccountably abrupt change in calcium absorption after the fourth week on the brown bread. Nevertheless, as Walker *et al.* pointed out, evidence already exists that when an individual habituated to one level of calcium intake is suddenly placed on a lower intake, the time taken to readjust will depend on the magnitude of the difference between the two levels.

Adaptation to low calcium intake is certainly possible, as shown by Malm's[46] prolonged investigations on male Norwegian prisoners. Of 26 subjects who were changed from a calcium intake of 900–1000 mg/day to one of approximately 450 mg, 22 adapted satisfactorily, 10 doing so rapidly and 12 more slowly. Some men took many weeks before they came into positive calcium balance. Thus, in assessing the effects of phytate or fiber consumption on calcium balance, it is important to recognize that calcium losses may persist for many weeks before returning to normal. In the studies of Reinhold *et al.*[15] with phytate and tanok, negative calcium balance persisted for over 60 days in one of their three subjects. Cummings *et al.*[18] also found calcium malabsorption persisting for 9 weeks when a young man's calcium intake was reduced from 1.7 to 1 g/day in association with a high-fiber diet.

Despite these relatively short-term responses, however, there is good evidence that adaptation to both low-calcium and high-fiber diets occurs provided the subjects have adequate vitamin-D levels. In studies by Hegsted *et al.*[47] on Peruvian prisoners, the men maintained calcium balance on 100–200 mg of calcium with a diet based on rice. In the study by Cullumbine *et al.*[48] on Ceylonese medical students fed unpolished rice diets with an increased phytate intake of 117 mg/day for 18 weeks, after the initial negative calcium balance, fecal calcium excretion fell progressively throughout the experimental period. Calcium balance was achieved on a calcium intake of 600–850 mg after 6–12 weeks. Perhaps of greater importance was the classic study of Widdowson and McCance[49] on German schoolchildren who were undernourished and whose growth was then monitored for a year while they consumed diets in which one group received 75% of their energy needs from whole wheat, another group the same energy from 85%-extracted wheat, and a third group received wheat products made from white flour of 70% extraction. Despite the marked difference in fiber and phytate intake, the children in all groups grew well and there was no detectable difference between the growth response of the different groups. This is a very important study because it involved human feeding studies under conditions of rapid growth, when any deficiency in the diet would be most easily detected. No changes in hemoglobin or abnormalities of red-cell morphology indicative of iron defiency were found. This aspect of fiber and iron metabolism will be considered in section IV.

Since, in Widdowson's study, the high-extraction cereals were supplemented with calcium and provided such a large proportion of the dietary

energy, obviously any advice to increase fiber consumption by increasing the consumption of whole-grain bread is unlikely to lead to slower growth rates in children provided their calcium intake and vitamin D status are maintained. Adults who are not housebound can also probably adapt adequately to an increase in fiber intake without risking severe, prolonged calcium malabsorption. These conclusions are based on the assumption that the Norwegian and Peruvian prisoner studies can be applied to adults elsewhere; the assumptions relating to adaptation have not been tested by direct studies on either children or adults in the United Kingdom or the United States. The Asian community in the United Kingdom are already on a high-phytate, high-fiber diet; their high prevalence of hypocalcemia and bone disease constitutes a public health problem which requires that either their diet be modified to reduce its phytate content, or that the vitamin D status of this community be improved.

The other nutritionally susceptible group are the elderly, who have a high prevalence of osteomalacia and osteoporosis with vitamin D deficiency. They are also often constipated, in part because their total food intake has declined with a concomitant reduction in fiber intakes. If the elderly are to be encouraged to increase their fiber intake, the effect of such an increase on their calcium homeostasis should be evaluated. If bran is used to increase substantially their cereal fiber consumption to alleviate constipation, phytate intake will increase substantially. Bran administration to elderly subjects in doses of only 10 or 20 g/day[50] has been shown to lower, marginally, the concentration of ionized calcium in the serum. More detailed studies are clearly indicated.

III. DIETARY FIBER AND ZINC STATUS

The importance of high intakes of fiber in reducing the absorption of zinc has been emphasized by Reinhold *et al.*[15,51] in a series of studies conducted in Iran. In rural Iran, it is common to find malnourished children exhibiting slow growth and evidence of vitamin deficiencies. In addition to these nutritional problems, however, Prasad *et al.*[52] observed Iranian adolescent males with poor appetite, marked growth retardation, testicular atrophy, and hyperkeratosis, all signs previously induced in experimental animals by feeding a zinc-deficient diet. Prasad *et al.* observed a similar picture in Egypt[53] and established that the human syndrome was cured by zinc supplementation of the diet. Since then, the syndrome has been found in other parts of the Middle East[54] and is often associated with geophagia (a pica for eating earth, particularly clay) and iron-deficiency anemia.[55] In communities subsisting on tanok as their staple food, 80% of schoolchildren have low plasma-zinc concentrations. Even in more prosperous areas, 70% of village boys and 16% of the male adults have low plasma-zinc concentrations. Similar findings were observed in women and young girls. Intakes of zinc are not low, however, since a tanok-rich diet pro-

vides 20–30 mg zinc per day in an adult. The problem, therefore, is one of zinc availability.

Following these observations, Reinhold and his Iranian colleagues[15] conducted a series of studies on the effects on mineral balance of eating phytate and the unleavened, whole-grain bread tanok. Adding phytate to the diet of three volunteers led to a fall in the absorption of zinc, but the subjects still maintained zince balance. Feeding tanok reduced zinc absorption further in two of the three subjects but, as noted in section II.B, the phytate content on tanok feeding increased during the study. If Caucasians unaccustomed to eating tanok are placed on a typical Iranian diet, zinc balance may be impaired for some weeks and plasma zinc levels decline.[26] Reinhold *et al.* then assessed the effect of leavening bread on zinc availability, the zinc in the whole-grain flour having been labeled during the growth of the wheat grain by injecting the plant stems with radioactive zinc-65. Unfortunately, during the leavening of the bread with yeast, only 20% of the phytate was destroyed, so these studies cannot be used to assess the relative effects of fiber and phytate on zinc binding and availability. *In vitro* studies by Ismail-Beigi *et al.*[56] show that zinc binds to several types of fiber including cellulose, suggesting that binding may occur in association with the hydroxyl groups of fiber. Feeding purified cellulose increased zinc excretion by 17–26%, again suggesting that fiber may have a small effect *in vivo*.[20]

If these results of Ismail-Beigi *et al.* are related to Partridge's experiments[30] on the effect of cellulose feeding on zinc absorption in the pig, it becomes clear that zinc absorption may be mainly dependent on colonic absorption. In Partridge's studies, zinc balance was less sensitive to the effects of cellulose feeding than calcium balance, and this accords with Reinhold's studies on humans (Table 5).

The association between high-fiber diets and zinc deficiency in the Middle East constitutes an important public health problem. The question, then, is whether an increase in fiber intake in the West is likely to lead to similar problems. Hambidge and Walravens' careful studies[57] on the zinc status of a variety of different groups of children in the United States suggest that zinc deficiency may be much more common than thought based on our knowledge of the average food and zinc intakes of children in the United States. Thus, in a group of apparently normal chidren from middle- and upper-income families, 10 of 132 children aged 4–16 years had hair-zinc concentrations more than 3 SD below the normal adult mean. Eight of these 10 children had heights below the 10th percentile for their age, and 8 of the 10 children had weights at or below the 10th percentile. Detailed investigation showed that 7 had a poor appetite and 5 a diminished sense of taste. The children avoided eating meat, a rich source of zinc, even when it was readily available to them. After zinc supplementation with small doses of 0.2–0.4 mg/kg/day, taste acuity improved and hair-zinc levels increased, suggesting that the children were suffering not from

impaired zinc absorption as in the Iranian children, but from a deficient zinc intake. Subsequently, Hambidge and Walravens showed that children from lower-income families had an even lower hair-zinc concentration than that found in the middle and upper income group, and plasma and parotid salivary zinc concentrations were also significantly lower than normal.

Hambidge and Walravens' findings suggest, therefore, that marginal zinc deficiency may be far commoner in the West than has been realized hitherto. This may particularly apply to children below the age of five, since children from comparatively wealthy families in Denver, Colorado, have hair-zinc concentrations appreciably below those found in children from upper income homes in Bangkok, Thailand. Given the possible prevalence of zinc deficiency, it becomes important to establish whether an increase in fiber intakes in the West would affect zinc status.

The recent careful studies of Sanstead *et al.*[12,58] on five adult males suggest that diets similar to those normally consumed in the West can sustain zinc balance even when 26 g of dry milled corn bran is added to the daily bread. Similarly, the addition of an equivalent amount of wheat bran did not put the adults into negative zinc balance. Similar studies on eight adolescent boys[59] showed that a 14.2-g supplement of either cellulose, hemicellulose, or pectin changed fecal excretion rates of zinc from 9.64 mg on the basal diet to only 13.32 mg, 10.26 mg, and 9.63 mg, respectively, on the three experimental diets. Cellulose also had the greatest effect on fecal copper and magnesium outputs. Recent studies on young women[60] confirm that adding wheat bran as a 14-g/day supplement does not have marked effects on zinc availability despite the ingestion in this amount of bran of approximately 0.5 g of phytate and 6–7 g dietary fiber, including perhaps 2 g cellulose. In Sandstead *et al.*'s studies, nearly twice these amounts were fed without effect on zinc balance, the fiber being provided from a number of sources: soft white wheat bran, hard red spring wheat bran, corn bran, soybean hulls, and textured vegetable protein. On this basis, increasing the intake of fiber by 15–25 g is unlikely to affect zinc balances appreciably. Zinc balance seems less susceptible to interference by phytate and fiber than calcium balance.

IV. DIETARY FIBER AND IRON ABSORPTION

Elemental iron absorption is known to involve a complex interaction between dietary inorganic iron, derived from various food iron sources, and several components in the diet that affect the solubility and chemical form of the iron in the intestinal lumen. Organic iron absorption in the form of heme, the major form of iron in meat, is not affected by other dietary factors, is far more readily absorbed than inorganic iron, and has a separate mucosal uptake system.[61] It is customary, therefore, to think of a "two-pool" system for dietary

iron,[62] all the dietary forms of inorganic iron behaving as a single pool whose absorption can be promoted by the concomitant ingestion of some nutrients, e.g., amino acids and vitamin C, or inhibited by others, e.g., egg albumin or phytate.

Widdowson and McCance,[63] and McCance *et al.*[64] in their early studies on the effects of white- and brown-bread diets on mineral metabolism, studied iron balances by chemical methods. Feeding brown bread led to a decrease in iron absorption that resulted in two of the eight subjects (both women) having a net loss of iron on the brown-bread diet. Nevertheless, Widdowson and McCance's feeding studies after World War II showed that undernourished preadolescent girls grew well on a predominantly whole-wheat diet and after a year did not have lower hemoglobin concentrations.[49]

Phytates are known to form insoluble complexes with iron, which become unavailable even if fed in large amounts. Adding sodium phytate to white bread interferes with the absorption of ferrous and ferric iron.[65] Although phytate tends to reduce the absorption of nonheme iron, it does not affect heme iron uptake in man. Bjorn-Rasmussen[66] has shown that the addition of approximately 7% of bran to wheat, used to make a porridge, decreased iron absorption by 50%.

This effect may be minimized, however, if the bran is incorporated into bread and then eaten as part of a normal Western diet; Sandstead and his colleagues[12] found 26 g bran without an appreciable effect on iron absorption. Adding wheat products to the diet to increase fiber intakes by 36 g (equivalent in fiber terms to an addition of approximately 80 g bran) does lead to a fall in serum iron,[67] and this presumably reflects the binding of iron by the phytate and some of the fiber's components such as the hemicelluloses.[51] Some forms of iron-phytate do allow iron to be absorbed,[68] but the reason for these differences remains unclear.

V. CONCLUSIONS

The evidence presented in this chapter suggests that fiber-rich diets can induce marked malabsorption of nutritionally important minerals, but it is still not clear that the malabsorption relates to the fiber content of the food. Transferring to a high-fiber diet involves the greater consumption of a range of nutrients including phytate, which is known to have a profound effect on mineral absorption. The extent to which fiber-rich foods can reduce mineral absorption seems to depend on the type of food eaten. Some fibers, for example, those rich in pectin, may be expected to have relatively little effect on mineral absorption despite their ability to bind elements in tests conducted *in vitro*. The mechanisms underlying the gastrointestinal interactions of minerals and fiber-containing foods are far from clear. However, it is increasingly apparent that

colonic absorption may play an important role in preserving mineral balance and that the effects of fiber may depend on the way in which the fiber modifies colonic metabolism, bacterial growth, and mucosal transport.

Colonic absorption of calcium seems to be more readily affected than that of zinc or magnesium, so that calcium balance may be most susceptible to change when fiber-rich foods or bran are added to the diet. Slow adaptation can, however, occur in response to both fiber and phytate feeding. Adaptation to calcium imbalance depends on an adequate vitamin D status. Evidence suggests that in the presence of marginal vitamin D deficiency, the dietary availability of calcium determines the development of bone disease.

Individuals in Western communities, particularly children, may be eating a diet deficient in zinc. Selective increases in fiber or phytate could then lead to zinc malabsorption, but evidence on this is limited. Studies from the Middle East are interpreted as showing that phytate predominates in reducing the availability of dietary zinc. The absorption of other elements, such as iron, can be affected too, but other dietary factors, for example, vitamin C and amino acids, help to minimize the deleterious effects of fiber-rich and phytate-rich diets on iron absorption.

With the growing emphasis on the need to increase the fiber intakes of Western communities, it is important to ensure that this dietary change does not lead to a deterioration in the health of some sections of the community, such as the elderly, who are particularly prone to mineral deficiencies.

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14

Sources and Intakes of Dietary Fiber in Man

Sheila Bingham and John H. Cummings

I. INTRODUCTION

Dietary fiber has forced its way to our attention in recent years for two main reasons: its noticeable effect on bowel habit in an age when fecal output is probably lower than it has ever been, and the suggestion that lack of dietary fiber is the cause of many of our current health problems.

The epidemiological evidence that relates fiber intake to the etiology of diseases such as bowel cancer, appendicitis, diverticular disease, diabetes, obesity, and ischemic heart disease in intriguing; concerning such major causes of ill-health, it cannot be ignored. This hypothesis has been discussed for more than 10 years; yet rarely are such discussions about actual numbers, and when they are, their accuracy is seldom questioned. As this chapter will show, few data on dietary fiber intakes exist, and those may have to be modified as methods for measuring food intake overall and dietary fiber in particular evolve.

A. Problems of Food Intake Assessment

No method of measuring dietary intake is perfect, and no dietary data should be accepted without first ascertaining the method by which food intake was measured. In this chapter, food intake values have been taken from government food statistics, from household surveys, from studies of groups of sub-

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jects by interview, and from individuals by detailed weighing and recording techniques. Some of the African data were obtained as long ago as the 1920s, but the wealth of detail in these studies makes retrospective analysis of them possible.

The relative merits of the various methods of measuring food intakes have been well summarized elsewhere.[1,2] National statistics of food supplies and household surveys are probably valid for use in examining trends in fiber consumption. However, it is assumed that each member of the population consumes equal amounts of food regardless of age, sex, and so on, and inedible or other waste is not measured. The best method for measuring food intake in individuals relies on careful weighing and recording of all food and drink taken. It has been suggested that such scrutiny itself may disturb the person's normal eating pattern. Interview methods give reasonably accurate information for groups of individuals,[3] but the 24-hr-recall method has not stood up to independent checks.[4] Results in individuals obtained by interview are rarely the same as those obtained by weighing methods.[5,6] Food-frequency questionnaires do not yield quantitative information.

Few papers, of course, record fiber intakes; but it has been possible, using dietary fiber data from foods analyzed in the United Kingdom and other European countries and unpublished information, to add fiber calculations to many studies. Bearing in mind, however, the methodological problems still inherent in measuring dietary fiber intake, it may be some time before the final values are known.

B. *Problems in Dietary Fiber Analysis*

The development of suitable methods for the measurement of dietary fiber has suffered because of a conflict of interests. Historically, animal nutritionists have led human nutritionists in concern about fiber. The measurement of fiber in animal foodstuffs was directed towards predicting forage digestibility: hence the crude-fiber method. This method is not relevant to human nutrition; its many deficiencies have been identified by van Soest and McQueen.[7] The detergent system of fiber analysis[8] was also developed for use in animal nutrition. It is a quick and well-researched system but runs into problems when applied to human food; also, since it is gravimetric, exactly what it is measuring is unclear. It fails to recover the water-soluble polysaccharides, and some insoluble polymers are hydrolyzed by the hot acid detergent.[9] Several modifications have now been described.

Another approach is to treat a food sample with starch- and protein-removing enzymes and subsequently isolate, by filtration and extraction and again gravimetrically, a "fiber" fraction.[10,11] The digestion stage is designed to simulate what is happening to food in the human gut and particularly what is happening to fiber. Since the fate of fiber in the gut, especially in the small

intestine, is largely unknown, this objective is somewhat optimistic. The method also fails to remove all the starch and protein and loses some water-soluble polysaccharides.

The method for measuring dietary fiber described by Southgate first in 1969,[12] with its subsequent modifications,[13,14] has been the most suitable available for human nutrition in recent years. Most of the data in this paper are based on food analyses using his method[15,16] supplemented with data from McCance *et al.*[17] and, for a few foods, the method of Englyst.[18] The Southgate method itself has been criticized[9] again because of incomplete removal of starch, coprecipitation of intracellular compounds with cell wall material, and loss of some of the polysaccharides. The data in the papers reviewed in this chapter will therefore require modification, probably downward, to an extent dependent on the precise composition of the diets themselves.

Several other methods for measuring dietary fiber have been described.[19] Some, however, fall into the trap of trying to isolate a fraction of food that is not digested in the human small intestine. Such an objective is an unsuitable basis for an analytical method. Dietary fiber, chemically speaking, is polysaccharide and in terms of food composition is best seen as such. The problems of isolating dietary polysaccharides and then separating them into starch and nonstarch polysaccharides (which is equivalent to dietary fiber)[20] have been the objective of more recent methods for measuring fiber in food.[9,18,21] These methods will probably be the yardstick against which to judge others in the future.

II. FIBER INTAKES AND SOURCES

A. United Kingdom

While dietary fiber intakes in the United Kingdom are better documented than in most other countries, only a few publications so far deal with this subject.[22–26] In an attempt to measure dietary fiber intakes in the United Kingdom, we determined the food intakes of 63 adults aged 20–80 years, randomly selected from the population in part of Cambridgeshire.[23] Dietary fiber intakes were also calculated from the National Food Survey.[27] In the National Food Survey, housewives are asked to keep a record of their purchases of food for 1 week, together with details of food grown by the family. The weight of food coming into the house is calculated from these records and divided equally by the number of people living there. About 6500 households randomly selected from the electoral registers of England, Wales, and Scotland take part throughout the year, and the survey has been conducted annually since 1950. We have adjusted these data to account for inedible wastage in the calculation of dietary fiber intakes.

The survey of individuals was done by asking each person (randomly

selected from the electoral register) to weigh and record all food and drink taken over 7 days. The food records were then processed, using a computer program, to quantify individual fiber and nutrient intakes. Overall cooperation rates in the study were around 70%. Table 1 shows total dietary fiber intakes and its composition from both the survey of individuals and the National Food Survey. Total dietary fiber intake (nonstarch polysaccharide plus lignin) was about 20 g/day, most of which (13.8 ± 3.7 g/day) was noncellulosic, nonstarch polysaccharide hemicellulose. Vegetables contributed 41.3% (8.2 g) to total fiber intake; cereals, 30.5% (5.8 g); and fruit, 11.7% (2.3 g); and the remainder, 16.5% (3.3 g), was from mixed sources such as pies. No significant differences in fiber intakes were observed between the sexes (men, 20.1 ± 5.4 g/day; women, 19.8 ± 5.3 g/day). The close agreement between the average data from the National Food Survey and the individual survey was notable, as the two methods of assessing dietary fiber intake were quite different.

Southgate *et al.*,[22] also using the National Food Survey, arrived at a figure of 20.4 g/day for total dietary fiber intake in the British population in 1974. From a completely different data base, that of total food supplies for the population, they calculated that dietary fiber intakes in 1970 were 22.7 g/day. These independently derived data taken together reinforce the view that fiber intakes are around 20 g/day in the United Kingdom at present.

Using food tables for calculating fiber intake similar to those used by Bingham *et al.*[23] and similar dietary methodology, Morris *et al.*[24] measured food intake in 337 healthy middle-aged men. These were a representative sample of London bus drivers and conductors and staff of the principal banks. The survey was part of a prospective study, started in 1956, to try and relate the incidence of heart disease to dietary intakes. The main findings to come out of the study so far are that men who had the highest calorie intakes, the highest ratio of polyunsaturated to saturated fatty acids in their diet, and the highest dietary fiber intakes were least subject to ischemic heart disease. The subjects

Table 1. Mean Daily Intake of Dietary Fiber and Its Components[a,b]

Total and components of dietary fiber	Cambridgeshire, 1977	U.K. National Food Survey, 1976
Total dietary fiber	19.9 ± 5.3	19.7
Total noncellulosic polysaccharides	13.8 ± 3.7	13.9
Hexoses	7.4 ± 2.1	8.2
Pentoses	3.3 ± 1.3	2.5
Uronic acids	3.0 ± 1.0	3.1
Cellulose	4.7 ± 1.2	4.8
Lignin	1.4 ± 0.9	1.0
Energy (MJ)	9.1 ± 2.4	9.3[c]

[a]From Bingham *et al.*[23]
[b]Values are given as g/person/day.
[c]Provisional result from April to September 1977.

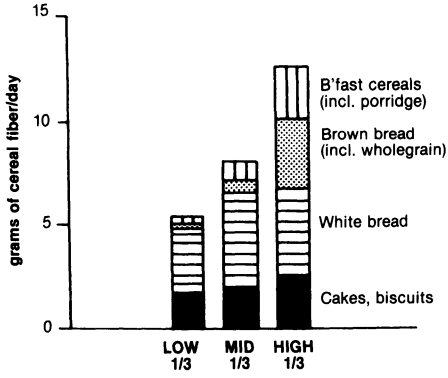

Figure 1. Sources of cereal fiber in thirds of distribution of 337 men in dietary survey of London (U.K.) busmen and bank employees, 1956–1966. (g/person/day) From Morris *et al.*,[28] with permission.

were divided into three equal groups (or "thirds") based on their dietary fiber intakes. No mean values are given in the paper, but intakes of fiber in the thirds were 5.6–15.4 g/day (lower third); 13.8–19.0 g/day (middle third); and 16.9–56.1 g/day (upper third). Cases of heart disease in the ensuing 20-year follow-up period were 22, 16, and 7, respectively.

The protection from heart disease afforded by dietary fiber observed in this study was, in fact, related to differences in intake of cereal fiber among the three groups rather than differences in fruit and vegetable intakes. Figure 1 shows, for the three groups, the intake of fiber from cereals and the sources. Interestingly, most of the cereal fiber came from white bread, cakes, and biscuits, with brown bread and breakfast cereals a major contributor only in the group with the highest intake. In this group, fiber intake from white bread, cakes, and biscuits was 6.8 g/day; from brown and whole-meal bread, 3.1 g/day; and from breakfast cereals, 2.6 g/day.

A further study, which used the United Kingdom food tables[29] as a source of dietary fiber data, was reported by Gear *et al.* in 1979.[25] In this study, dietary intakes were measured, by use of a questionnaire, in 189 subjects selected from the patient lists of family doctors in Oxford, England, and in 55 symptomless members of the United Kingdom Vegetarian Society. All the subjects were 45 years of age or older. Total dietary fiber intake for the general-practice population was 21.4 ± 8.2 (SD) g/day and 41.5 ± 12.6 g/day for the vegetarians. Sources of dietary fiber for the general-practice population were cereal fiber, 37%; vegetable fiber, 45%; and fruit fiber, 12%. The vegetarians obtained more fiber from cereals (40%), less from vegetables (35%), and much more from fruit (23%).

B. Europe

1. Holland, Belgium, Luxembourg, Italy, and France

Between 1963 and 1965, a dietary survey[30] was carried out for Euratom in 11 rural areas of the European Economic Community (EEC) to determine

levels of radioactive contamination of foodstuffs. The areas were chosen on the basis of their dietary patterns and likely cooperation rates. About 30 families per month were studied in each area, giving a total of 3725 families in 3 years. Each family weighed all their food after preparing it, thus eliminating the need to correct for inedible waste. Average consumption per head was then calculated by dividing total intake by the number of persons in the household. These data have been used to calculate dietary fiber intakes.[15–17]

Tables 2 and 3 summarize the dietary fiber data from this study over a year. The values are slightly higher than those described for the United Kingdom, but the areas were rural. The diets overall had much in common, with white bread as the staple food in most areas. In the southern regions, it was supplemented with pasta and maize flour, while in the north, more brown and rye bread and potatoes were eaten.

It will be noted (Table 3) that only about 1 g/day of lignin was present in the diet, by far the smallest component of the "dietary fiber." This contrasts with animal feeds, where lignin intakes may represent 10–15% of total "fiber." Furthermore, it is more appropriate to call this lignin value "substances measuring as lignin," since isolation of pure lignin from mixed diets for man is difficult. A variety of other materials including protein-condensation products, plant waxes, and cutins come out in this fraction.[7,31] The actual amount of lignin in these diets is probably even less than indicated.

In these 11 regions of the EEC, a greater proportion (on average 45%) of fiber came from cereals and less from vegetables and potatoes (44%) than in the United Kingdom. The Italian regions derived the greatest proportions of their fiber from cereals (51–63%) largely as a result of their liking for pasta.

Table 2. Sources of Dietary Fiber in 11 Regions of the European Economic Community[a]

Area[b]	Cereal	Vegetable	Fruit, nuts	Potato	Total
Friesland (H)	8.2	5.6	2.6	6.3	22.6
Gent (B)	10.9	4.1	1.7	12.3	28.9
Liege (B)	8.0	6.0	2.3	10.5	26.8
Luxembourg	7.3	6.5	2.1	13.2	29.1
Hessen (G)	11.6	4.9	2.6	8.2	27.3
Normandy (F)	9.1	5.7	2.2	7.8	24.8
Bretagne (F)	10.2	4.9	1.8	6.9	23.8
Vendée (F)	10.1	12.7	2.8	4.0	29.6
Fruili (I)	14.7	5.1	1.3	3.8	24.9
Campania (I)	13.4	7.7	4.3	1.6	26.9
Basilicata (I)	13.5	5.7	3.9	0.7	23.8

[a]Values are given as g/person/day.
[b]H, Holland; B, Belgium; G, Germany; F, France; I, Italy.

Table 3. Components of Dietary Fiber Intake in 11 Regions in the European Economic Community[a]

Area[b]	Total	Noncellulosic polysaccharide			Cellulose	Lignin
		Hexose	Pentose	Uronic acid		
Friesland (H)	22.6	8.6	3.2	3.7	5.9	1.1
Gent (B)	28.9	13.5	2.5	4.3	7.5	1.1
Liege (B)	26.8	11.6	2.5	4.4	7.2	1.0
Luxembourg	29.1	13.1	2.4	4.9	8.0	0.8
Hessen (G)	27.3	10.3	4.4	4.2	7.0	1.3
Normandy (F)	24.8	10.5	2.3	4.1	6.9	0.7
Bretagne (F)	23.8	10.6	2.3	3.8	6.6	0.6
Vendée (F)	29.6	10.9	3.8	5.7	8.2	1.0
Fruili (I)	24.9	12.9	1.9	3.7	6.0	0.5
Campania (I)	26.9	10.7	3.6	4.5	6.8	1.3
Basilicata (I)	23.8	9.7	3.1	3.9	6.0	1.1

[a]Values are given as g/person/day.
[b]H, Holland; B, Belgium; G, Germany; F, France; I, Italy.

Fiber from vegetables was highest in the Vendée (45%), where large quantities of beans and peas were eaten in the winter months (about 40 g/day).

2. *Finland and Denmark*

In 1977, the International Agency for Research on Cancer, Intestinal Microecology Group,[32] reported dietary intakes, including dietary fiber intakes, in two selected populations in Scandinavia: Copenhagen (Denmark) and Kuopio (Finland). This was part of a study to relate food intake to bowel cancer incidence. In each area 30 men, aged 55–64 years, were randomly selected from population registers. Menus were kept for 4 days in the spring and autumn of 1975, and in the autumn duplicate portions of food eaten on the last day were collected. Twenty-five of these diets were later analyzed for nitrogen, fat, available carbohydrate, and dietary fiber by the method of Southgate.[12]

A summary of the results is shown in Table 4. The sources of fiber in the diets are not stated in the paper, but it will be seen that fiber intakes of the Finns (Kuopio) were nearly double to those of the Danes (Copenhagen). The composition of the fiber was similar in both areas. The differences in dietary fiber intake between the two areas were due to rye bread and crispbread consumption, which are the staple food of the rural Finns, whereas white bread is more popular in Copenhagen.

3. *Yugoslavia*

In the early 1960s, the food intake of heads of 24 families in villages in Dalmatia and 25 in Slavonia was carefully measured by weighing and collecting duplicate foods.[33] This was part of an international collaborative study,

Table 4. Dietary Fiber Intakes in Denmark and Finland[a,b]

Total and components of dietary fiber	Copenhagen (n = 12)	Kuopio (n = 13)
Dietary fiber (total)	17.2 ± 5.1	30.9 ± 11.3
Noncellulosic polysaccharides (total)	10.9 ± 3.2	19.8 ± 7.9
Hexose	6.12 ± 1.9	11.7 ± 5.0
Pentose	2.39 ± 0.9	4.54 ± 1.6
Uronic acid	2.40 ± 0.8	3.58 ± 1.6
Cellulose	4.94 ± 1.6	7.90 ± 2.5
Lignin	1.42 ± 0.7	3.13 ± 1.7

[a]From IARC Intestinal Microecology Group, 1977.[32]
[b]Values are given as g/day ± SD.

using standardized dietary methods to investigate the effect of diet on the incidence of ischemic heart disease (The Seven Countries Heart Study).[34] Records of the average quantities of foods eaten by the 49 men have been made available to us,[35] and dietary fiber intakes have been calculated from these records.

Total fiber intake was 25.5 ± 7.5 g/day (Table 5), 50% of which was

Table 5. Dietary Fiber Intakes in Africa, India, United States, and Other Countries[a]

Source of data		Total	Cereal	Vegetable	Fruit, nuts
Buzina[35]	Yugoslavia	26	13	9	4
Rottka[37]	Germany	24	12	8	4
Lindgarde *et al.*[38]	Sweden	14	6	NA[b]	NA
Asp *et al.*[39]					
Fielding and Melvin[40]	Ireland	23	NA	NA	NA
Orr and Gilks[41]	Kenya				
	Kikuyu	130	79[c]	54	NA
	Masai				
	Warriors	0	0	0	0
	Women	25	25	NA	NA
Platt (unpublished)	Malawi (foothill village)	55	40[c]	10	4
Jones[42]	Swaziland (middle veld)	60	40	19	1
Ruitishauser[43]	Uganda (Buganda)	150	0	147	3
Mitra[45]	Hos tribe, Bihar state (India)	38	26	12	NA
a. Heller and Hackler[46]	United States	27	8	15	4
b. Southgate[47]	United States	20	NA	NA	NA

[a]Values are given as g/person/day.
[b]NA, Not available.
[c]Calculated assuming maize flour contains 10% dietary fiber.

cereal, mainly white bread. The vegetable dietary fiber was from potatoes, root vegetables, legumes, and green vegetables. The contribution of fruit to the total was small.

4. Germany

In 1973, a dietary survey of 135,000 people was undertaken throughout all the states in Germany.[6] Details of food intake were obtained by a food diary, and fiber intakes were calculated as crude fiber. Dietary fiber has now been calculated and the results are shown in Table 5.[37] Average intakes for men were 25.1 g/day and for women 22.3 g/day. Cereal intakes of dietary fiber were higher than in Britain (51% of the total), largely because of the consumption of rye bread.

5. Sweden

Two recent surveys in Sweden have quantitated dietary and neutral-detergent fiber intakes at 14 g/day. The first[38] was obtained by asking 55 middle-aged men in Malmo to recall all food eaten over the previous 7 days. The men were randomly selected out of a group of 1121 attending a medical health-screening clinic. Dietary fiber intakes, calculated using Southgate's data, were 14.2 ± 4.6 g/day (Table 5), with that from cereals 5.5 ± 3.4 g/day. In this study, the individuals with above-average cereal fiber intakes had "better" glucose tolerance.

In the second study, 35 men and women pensioners were asked to collect replicate portions of a day's food intake, which were then analyzed for neutral-detergent fiber.[39] Daily intakes were 17.8 ± 6.9 g/day for men and 11.1 ± 3.5 g/day for women; analysis as undigestible residues gave higher values (women, 21.1 ± 4.8 g/day; men, 27.5 ± 5.9 g/day).

6. Ireland

In a group of 16 women and 9 men in Dublin, dietary fiber intakes were 22.7 ± 4.3 g/day and 22.6 ± 4.1 g/day,[40] respectively. These intakes were obtained with a retrospective diet history over 1 week, in which data on the portions of food and the frequency with which they were eaten were obtained. Fiber intakes were calculated from published values.[15] No details of the sources of fiber are given.

C. Africa

While much has been written about dietary fiber intakes in Africa, in fact, very little is known about it. No dietary surveys have been done specifically to measure fiber intake and nothing is therefore known of its main sources and composition. Dietary surveys to quantitate intakes of other nutrients have been done, so we have taken data from these and used them as a basis for obtaining

some preliminary figures for fiber intakes. These are summarized in Table 5. The main problem in using these food intake data for dietary fiber calculations is that very few of the staple African foods have been analyzed for fiber. Therefore, the closest approximate figure has to be taken from existing food tables. Notwithstanding these compromises, it is clear from Table 5 that large differences in fiber intakes exist between populations in the African continent and those in the West.

1. *Kikuyu and Masai*

In 1931, the Medical Research Council of Great Britain published a report on the diet and health of two African tribes, the Kikuyu and the Masai in Kenya.[41] A research team had visited the areas and observed the preparation and eating of food. They were able to weigh some foods, but this was limited because of local superstitions, particularly amongst the Kikuyu. Furthermore, food consumed while the tribesmen were at work in the field could not be recorded. The Masai diet was apparently easier to quantitate. Samples of food from both regions were sent back to England for analysis although not for fiber analysis. There were big differences in food intake between men and women, and between warriors and nonwarriors.

The diets of the two tribes were very different, the Masai being a pastoral tribe living mainly on meat, milk, and blood. The Masai warriors live almost entirely on these items, but the rest of the tribe consume bananas, beans, millet, arrowroot, maize, sugar, and honey in addition. Fiber intakes amongst the warriors would usually have been zero and for the rest of the tribe about 25 g/day, mostly from maize.

The Kikuyu, however, have a very different diet, largely vegetarian. It consists of cereals, tubers, plantains, legumes, and green leaves. Meat is rarely eaten. The vegetables are made into a thick porridge or into a gruel, and an average male was observed to eat between 3 and 6 lb of the porridge per day and 2 and 3 pints of gruel. We have calculated this to contain 130 g of dietary fiber.

2. *Malawi*

From 1938 to 1939, B. S. Platt studied the food intakes of two villages and one urban area in what was then Nyasaland. The survey was not published, although the records have been kept by the School of Hygiene and Tropical Medicine in London. The staple diet of villagers living on the shores of Lake Nyasa included cassava, fresh fish, green leaves, and mango, and villagers living in the foothill region ate mainly maize, potato, green leaves, beans, and a little meat. Their intake of dietary fiber was about 55 g/day (Table 5). Interestingly, the diet eaten in urban areas was similar to that of the foothill villages at that time, except that slightly more milk, oil, and sugar were eaten.

3. Swaziland

In a report prepared for the government of Swaziland in the 1950s[42] the food intakes of rural and urban Swazis were recorded, having been studied in detail using the weighing technique. Great diversity exists in climate and land form throughout Swaziland and hence in the diets eaten in rural areas. There was also an abundance of food in spring but shortage and semistarvation in winter. The winter diet of Swazis living in the middle velt was mostly maize, beans, potatoes, and green vegetables and contained about 60 g of dietary fiber (Table 5).

4. Uganda

The staple food of villagers living in the central (Buganda) region of Uganda is the plantain, of which at least 1 kg will be eaten by men at each main meal.[43] This is steamed or boiled and eaten with vegetable and groundnut relishes or very occasionally with meat. The dietary fiber content of plantain is 6/100 g,[29] and total dietary fiber intakes in this region are consequently probably the highest we have found, at 150 g/day.

5. South Africa

A classic paper in 1971 by Lubbe[44] described marked differences in diet between rural and urban Venda males. In the rural areas, maize meal porridge was eaten in large amounts (up to 3.8 kg/person/day). The amount of maize used in the porridge is not reported and its dietary fiber content has not been measured. Nevertheless, an average intake of 1.7 kg/day together with large quantities of vegetable relishes (average intake 586 g/day) suggests dietary fiber intakes of at least 100 g/person/day.

D. India

In 1940–1941, the only method of cooking known to the aboriginal Hos tribe in Bihar State, India, was baking or boiling.[45] The use of spices and oils was unknown to them, and consequently their daily intake of fat is probably the lowest recorded (3 g/day). Legumes and vegetables were eaten in small amounts, 93% of their total energy coming from rice. Rice has a low dietary fiber content and consequently average intakes (Table 5) are only moderate (38 g/day) compared to plantain and other cereal-based diets eaten in Africa.

E. United States

Detailed statistics of the per capita amounts of fruits, vegetables, and cereals available for consumption in the United States have been published recently.[46] These have been used to calculate average dietary fiber intakes using

Southgate's analyses, and the results for 1973–1975 are shown in Table 5. The vegetable and fruit intakes are overestimates, because there is no correction for inedible waste. Cereal fiber intake is equal to that of Britain,[23] and it is likely that vegetable fiber intakes are similar too, since the dietary fiber content of a "typical" American diet analyzed by Southgate was 19.1 g/day.[47]

III. LONG-TERM TRENDS IN FIBER INTAKE

Tables 6 and 7 show long-term trends in total dietary fiber consumption in the United Kingdom and United States. The British data are taken from Southgate *et al.*,[22] supplemented with data on the diet of farm laborers living in southeast England.[48] The American data have been calculated from the food-consumption data of Heller and Hackler.[46]

The trend is for a fall in fiber intakes in both countries.

A. United Kingdom

In the United Kingdom, the fall in fiber consumption was mainly during the 19th century. It has been suggested that this was due to the introduction of roller milling, which allowed cheap white flour to be produced and distributed; previously, it had been relatively more expensive than brown. Roller milling certainly allowed a more effective separation of the various fractions of the wheat grain, enabling the miller to sell the bran for animal feed and thus make cheaper flour. However, little adequate food-consumption data for this period exist, and while it is clear that all types of bread were eaten throughout the 19th century, exactly how much of each was eaten by which social class is difficult to determine. Table 6 also shows that a range of possible dietary fiber

Table 6. Long-Term Trends in Dietary Fiber Available for Consumption: United Kingdom[a,b]

Year(s)	Total	Cereal	Potato	Other
1860	37–47	22–32	10	(5.1)
1880	28.6	(13.9)	9.6	(5.1)
1909–1913	23.9	10.9	7.9	5.1
1938	22.3	9.2	6.1	7.0
1942–1944	32–39.6	18.7–24.6	7.3–8.9	6.0–6.2
1957	23.3	8.7	7.3	7.3
1970	22.7	8.1	7.3	7.3

[a]From Southgate *et al.*[22]
[b]Values are given as g/person/day.
[c]Calculated assuming white bread made from stoneground flour contained 2.7–4.0 g dietary fiber per 100 g.

Table 7. Long-Term Trends in Dietary Fiber Available for Consumption: United States[a]

Years	Total	Cereal	Potato[b]	Other[b]
1909–1913	40.0	17.9	8.9	13.2[c]
1925–1929	37.1	14.2	7.0	15.9
1935–1939	35.3	12.0	6.4	16.9
1947–1949	30.8	9.6	5.4	15.8
1957–1959	26.7	8.0	4.9	13.8
1967–1969	26.4	8.1	5.1	13.2
1973–1975	26.6	7.8	5.2	13.6

[a]Values are given as g/person/day.
[b]No allowance for inedible wastage.
[c]Incomplete.

values has to be given rather than an average for these years since the fiber content of bread varied considerably.

Furthermore, there are no figures on the consumption of fruit, vegetables other than potatoes, or cereals other than wheat in 1860 and 1880. If, however, the consumption of these items in the period 1909–1913 is taken as being similar to that in 1860 and 1880, this can be added to the earlier data. Fiber intakes for these years then become 37–47 g in 1860 and 29 g in 1880. It will be noted that these intakes, although considerably higher than today, are nowhere near those of rural Africa populations. Hughes and Jones[26] estimated that Welsh farm laborers' diets contained around 65 g of dietary fiber in 1870.

A striking, although temporary, increase in fiber intakes occurred in the United Kingdom during the period 1940–1953. From Table 6 it will be seen that this was due mainly to an increase in cereal fiber intake at the time of World War II. This change was the result of alterations in the flour available for breadmaking during the war years.

In 1942, the British government was having difficulty in obtaining sufficient supplies of wheat, which were coming mainly from North America, because of enemy attacks on transatlantic convoys. The government was forced to raise the extraction rate of flour to 85%, thus more than doubling its fiber content. The extraction rate was gradually lowered over the next 3 years, but in 1945–1946 a world shortage of wheat occurred and the extraction rate was once again raised, reaching 90% at one stage. Ultimately, bread itself was rationed and continued so until 1948. Extraction rates were finally decontrolled in 1953. This, together with the relative shortage of other commodities such as meat, sugar, and dairy products, led to an increase in bread intake and in fiber intake.

In addition, as will be seen from Table 8, the composition of dietary fiber changed considerably, with the intake of pentose-containing noncellulosic poly-

Table 8. Long-Term Trends in the Compostion of Dietary Fiber[a]

	Noncellulosic polysaccharides							
	Hexose		Pentose		Uronic acid		Cellulose	
Years	U.S.A.	U.K.	U.S.A.	U.K.	U.S.A.	U.K.	U.S.A.	U.K.
1909–1913	19.2	11.8	3.9	2.5	6.0	3.2	9.3	5.7
1925–1929	15.8	NA	4.5	NA	5.9	NA	9.0	NA
1938–1939	14.3	10.2	4.6	2.6	5.9	3.3	8.6	5.4
1942–1944	NA	12.2–13.8	NA	9.0–9.3	NA	4.5–4.8	NA	8.1–8.7
1957–1959	10.4	10.4	3.7	2.6	4.5	3.5	6.7	5.8
1969–1970	10.5	10.0	3.6	2.6	4.3	3.5	6.5	5.7

[a]Values are given as g/person/day. NA, Not available.

saccharide (NCP) increasing fourfold. This disproportionate increase in NCP-pentose is due to wheat fiber being particularly rich in this type of polysaccharide. It would be interesting to obtain data on changes in fecal weight in this population for the postwar years, since the NCP-pentose fraction of fiber has been shown to be particularly effective at increasing fecal output in man.[49]

B. United States

Data are available for food intakes in the United States from 1909 to 1975.[46] Calculations show that dietary fiber consumption from all sources has fallen over this period, although it has been relatively constant since 1957 (Table 7). Overall total fiber consumption has fallen by 33%, with the fall in that from cereals being relatively greater (55%) than that from potatoes (45%). Dietary fiber from vegetables has probably also fallen, but food consumption figures for all vegetables eaten in the period 1909–1913 are not available.

The underlying trend in both these countries is a fall in cereal dietary fiber intake. In Britain, this has been offset by an increase in vegetable and fruit dietary fiber since 1909; calculations from the National Food Survey confirm this. Total dietary fiber intakes are, however, probably half those of the mid-19th century. In the United States, the fall in total dietary fiber intakes has been more marked over this century and has been caused by a reduced consumption of all sources of dietary fiber, but particularly of cereals.

IV. EFFECTS OF SOCIAL CLASS

Dietary fiber intakes vary considerably among the different populations of the world and, with the passage of time, trends in intake can be seen as food habits change. Within countries, many other factors lead to differences in fiber intakes between selected groups. Gear *et al.*[25] noted that vegetarians have

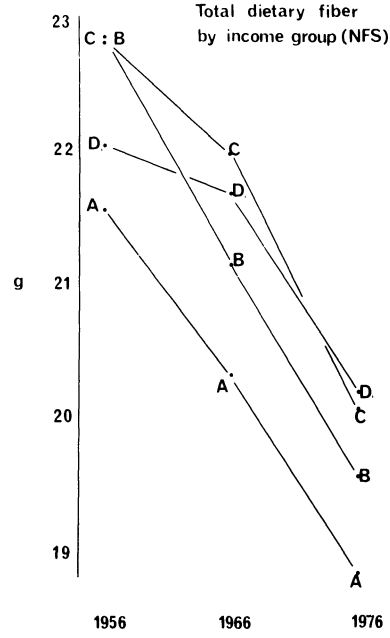

Figure 2. Total dietary fiber intake by income group in 1956, 1966, and 1976 calculated from U.K. National Food Survey.[27] Weekly incomes A, £91+; B, £57–91; C, £33–57; D, less than £33. (g/person/day)

higher intakes than nonvegetarians in Britain. In Sweden, vegan diets were found to contain five times the dietary fiber of average diets on an energy basis.[50] Social class, as defined by income, is also a determinant of fiber intake.

Figures 2, 3, and 4 show total dietary fiber intakes and intakes from cereals and vegetables in the United Kingdom in 1956, 1966, and 1976. The food consumption data were obtained from the British National Food Survey.[27] The weekly incomes of the four groups were A, £91+/week; B, £57–91/week; C, £33–57/week; and D, less than £33/week (in 1976). The highest income group, despite having a greater intake of whole-grain bread, has the lowest total fiber intake and shows a consistent fall in fiber intake over the 20-year period. As a percentage of total energy, income A also has the highest fat intake, which has increased over the same period.[51] The main reason for the variance in fiber intakes is the disparity in cereal fiber intakes (Fig. 3). These contrast markedly, whereas fiber from vegetables is virtually the same in all four groups (Fig. 4). Groups B, C, and D eat fewer vegetables on a weight basis than income group A but obtain slightly more fiber from them because they eat more canned peas and baked beans, which are rich in dietary fiber.

V. SEASONAL VARIATION

It might be expected that since the production of plant foods is closely tied to the seasons, variations in fiber intake would occur from month to month. In

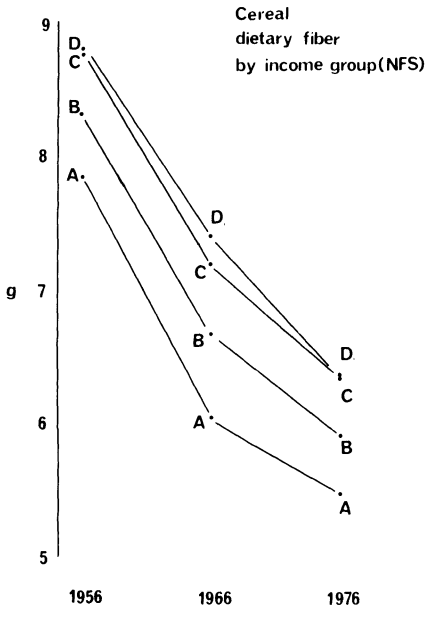

Figure 3. Cereal dietary fiber intakes by income group in 1956, 1966, and 1976. Calculated from U.K. National Food Survey[27] (g/person/day). For details of income groups see Figure 2.

the Euratom study,[30] which covered 11 rural areas of the EEC, monthly information on food intakes was obtained. Table 9 shows the coefficients of variation in each of the 11 areas for total dietary fiber intakes and for fiber intakes from cereals and vegetables. In some areas (Luxembourg, Bretagne, Vendée, Fruili, and Campania) the variation between months was greater than the variation between regions in total dietary fiber intakes. Hence dietary surveys to assess

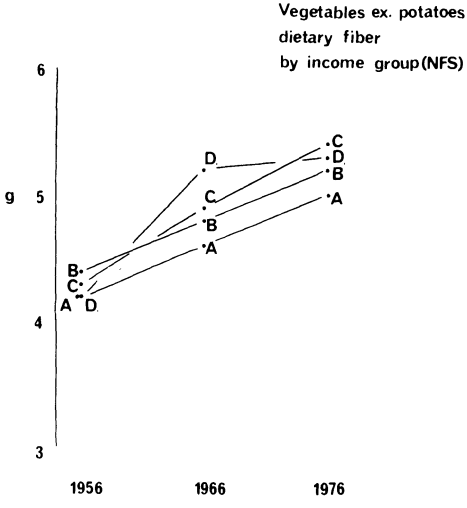

Figure 4. Dietary fiber intake from vegetables, excluding potatoes, by income group in 1956, 1966, and 1976. Calculated from U.K. National Food Survey [27] (g/person/day). For details of income groups, see Figure 2.

Table 9. Monthly Coefficients of Variation in Dietary Fiber Intake in 11 Regions of the European Economic Community[a]

Area[b]	Vegetables[c]	Cereal	Total
Friesland (H)	8.1	13.1	7.3
Gent (B)	8.2	14.3	7.4
Liège (B)	7.2	6.4	4.7
Luxembourg	17.1	6.9	13.7
Hessen (G)	13.6	5.3	5.2
Normandy (F)	10.9	8.9	7.4
Bretagne (F)	17.2	13.1	11.8
Vendee (F)	25.0	6.8	14.8
Fruili (I)	20.8	16.6	12.0
Campania (I)	23.0	13.4	12.3
Basilicata (I)	18.6	5.9	6.4
(Between regions	30.0	26.1	9.1)

[a]Values are given as percentages.
[b]H, Holland; B, Belgium; G, Germany; F, France; I, Italy.
[c]Includes potatoes.

fiber intakes must take into account the time of year. For example, in April, dietary fiber intakes in Fruili were 19 g/day and in Normandy 27 g/day, a difference of 8 g/day. Yet Table 2 shows that average intakes for the whole year were identical.

Figure 5 shows the monthly fiber values for Fruili in Italy, which had one of the biggest overall variations, particularly in cereals, the main fiber source in this area. Total dietary fiber intake was lowest in April (19 g/day) and highest in October (29 g/day). Cereal dietary fiber was also lowest in April but highest in June. However, fruit and vegetable fiber intakes were both highest in October. These seasonal changes in cereal intake are difficult to explain,

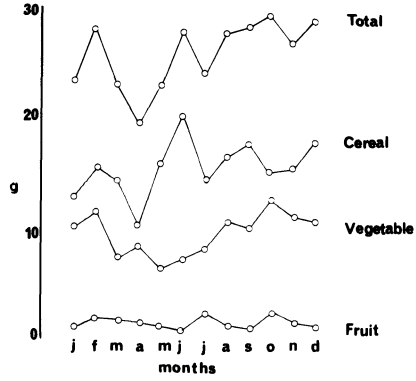

Figure 5. Monthly intakes of total dietary fiber and dietary fiber from cereals, vegetables, and fruit in Fruili (Italy). Calculated from the Euratom study[30] (g/person/day).

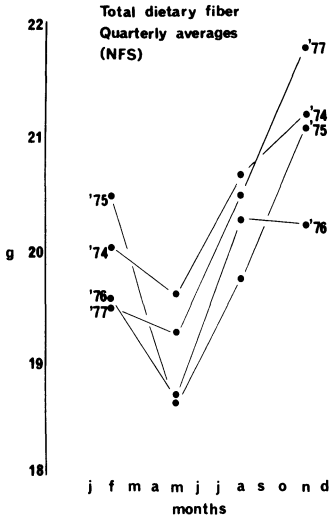

Figure 6. Total dietary fiber intakes for each quarter of the year (January–March; April–June; July–September; October–December) calculated from the U.K. National Food Survey[27] for 1974, 1975, 1976, and 1977 (g/person/day).

since storage of cereals is relatively easy and they are freely available throughout the year. Vegetable fiber intake was lowest in the spring and early summer which would be expected from the normal supply of these commodities. Fruit fiber intake was too low to show any seasonal effects.

Figure 6 shows fiber intakes for the United Kingdom as a whole for each quarter of the year from 1974 to 1977. In contrast to the EEC areas, total variation is much less, although fiber intakes are significantly lower in the second quarter and highest in the fourth. Vegetable fiber intakes (Fig. 7) are low in the summer months. Lower vegetable consumption in the second quarter is expected because of normal growing patterns, the exhaustion of winter stores,

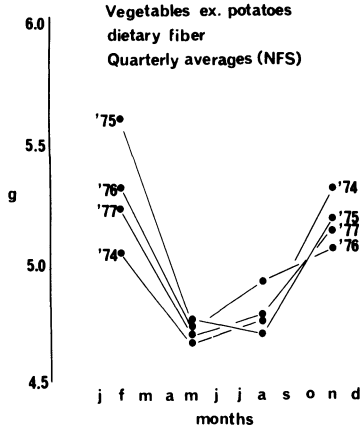

Figure 7. Dietary fiber intake from vegetables (excluding potatoes) for each quarter of the year calculated from the U.K. National Food Survey[27] (g/person/day). See Figure 6 for details.

and the high cost of imports, but the low values for the third quarter are more difficult to explain. However, the type of vegetable eaten in the winter (root vegetables, brussel sprouts) contain more fiber than traditional summer salad vegetable (tomatoes, lettuce, cucumber, etc.). Overall, however, differences are small and reflect the wide availability of frozen and imported vegetables the year round.

Total dietary fiber intake measured in a small survey of individuals in East Anglia, England,[52] were lower in May (16.9 ± 5.5 g/day) than in June (21.8 ± 4.7 g/day) but not significantly so in July or August (20.9 ± 5.8 g/day, 20.8 ± 4.2 g/day).

VI. INDIVIDUAL VARIATION

Even with the low dietary fiber intakes seen in the United Kingdom, the United States, and so forth, the range of individual intakes is large. Figures 8 and 9 show dietary fiber intakes in individuals from two dietary surveys; Fig. 8,[23] of 63 adults randomly selected from the population in Cambridgeshire and including men and women; and Fig. 9,[25] of 56 vegetarians and 264 nonvegetarians in Oxfordshire. In the nonvegetarians, the range of intakes is from 6 to 60 g/day and in the vegetarians from 6 to 87 g/day. In the study by Morris *et al.*[24] of 337 healthy middle-aged men, fiber intakes ranged from 5.6 to 56.1 g/day.

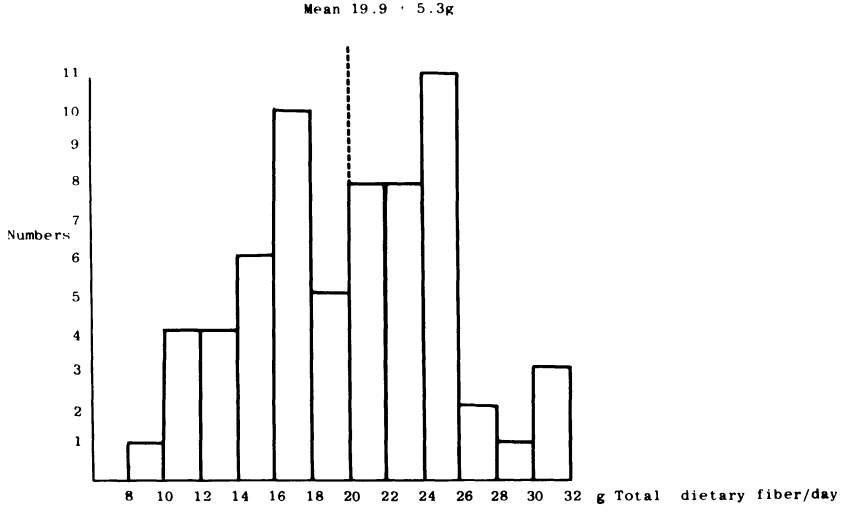

Figure 8. Distribution of individual dietary fiber intakes from survey of 63 adults in Cambridgeshire, England, 1977. From Bingham *et al.*[23] with permission.

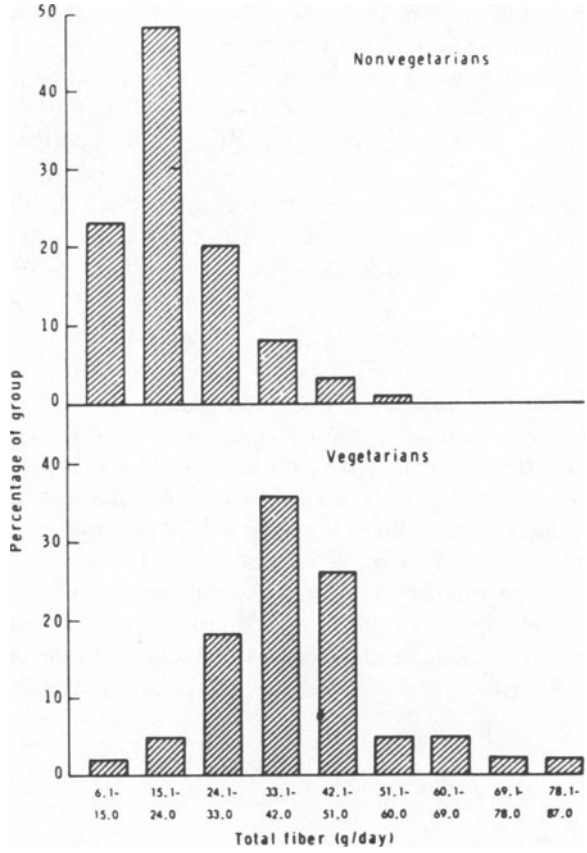

Figure 9. Distribution of individual dietary fiber intakes from survey of 264 members of a general-practice population in Oxfordshire, England, and 56 symptomless members of the U.K. Vegetarian Society. From Gear *et al.*[25] with permission.

One would expect some of the individual differences to be explained on the basis of sex and age, as in energy intake. Sex and age differences in fiber intake are, however, not always large.

A. Sex

In the Food Report Study from Germany,[36] differences in fiber intakes between the sexes were only 3 g/day, women consuming less.[37]

In the Cambridgeshire study,[23] fiber intakes were 20 g/day in men and 20 g/day in women. The largest difference in published data is that from Sweden, when neutral-detergent analyses of pensioners' diets were 18 g/day in men,

and 11 g/day in women.[39] In a study of 16 men and 9 women in Wales,[53] who weighed their food for 2 days, dietary fiber intakes were 24 g/day and 21 g/day, respectively.[54]

Eastwood *et al.*[55] measured total dietary fiber intakes in a group living in a suburb of Edinburgh, Scotland. Food consumption data were obtained using a diet history and a diet diary. Fiber intakes in 41 men were 15.9 g/day and 12.5 g/day in 42 women.

B. Age

The available data suggest that only small changes in dietary fiber intakes occur with age. In Cambridge, England, average total dietary fiber intakes were lowest (16 g/day) in women (but not men) over the age of 60 yr and highest (21 g/day) in both sexes at middle age.[52] In Edinburgh, Scotland,[55] average intakes in the 65+ age groups were about 4 g/day less than in the 16- to 35-year-olds. In the United States, average dietary fiber intakes for women aged 58–89 yr were low, 14 g/day, but there was no relation to age.[56]

C. Other Factors

The variations in individual dietary fiber intakes are not entirely explained on the basis of age or sex, since they are still present when these factors have been eliminated, as in the busmen study[24] and in the Swedish study of middle aged men.[38]

Very high intakes of dietary fiber are usually associated with greater intakes of unrefined cereal products (Figure 1) but, in general, the composition and sources of fiber vary little from person to person. Differences in fiber intake are usually due to differences in total food intake. Positive associations between individual energy intakes and dietary fiber were found in the bank clerks and busmen[24] and in Sweden.[38] In the study of Bingham *et al.*,[23] the lowest fiber intake was found in people attempting to slim by reducing energy intake. Not surprisingly, slimmers often find constipation a major drawback to prescribed diets, which usually specifically exclude bread and potatoes. Within a given community, therefore, the factors controlling energy intake will strongly influence individual fiber intakes.

VII. CONCLUSIONS

Different populations of the world consume widely varying amounts of dietary fiber. Some, such as the Masai warriors in Kenya, may go for long periods without any dietary fiber, while other African tribes consume around

150 g/day. Fiber intakes in Western Europe and North America are relatively low (20–40 g/day).

Such differences can readily be explained by markedly contrasting food consumption patterns. The unrefined-cereal- and vegetable-based diets of Third World countries contrast with the highly processed and more varied food of the West. Differences in the type and amount of bread consumed explain some of the differences between countries, particularly in Europe.

Equally large variations occur in fiber intake among individuals within a given community. These differences relate mainly to contrasting energy intakes, although seasonal influences, income, age, sex, and ethical beliefs contribute.

These generalizations, however, are based on relatively little reliable data. A great deal more work is needed to document the type and amount of fiber eaten across the world and to improve the accuracy of dietary fiber analytical methods. Nevertheless, the large differences in fiber intake will probably stand up to more critical examination. If these differences can be separated from the effects of other dietary components on human physiology, it is possible that a start can be made in ascertaining the exact role of fiber, or its lack, in the etiology of disease.

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Glossary

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with the assistance of Gene A. Spiller and Ruth McPherson Kay

Absorption. The process in which a nutrient (or other component of the diet) passes from the lumen of the intestine across the intestinal mucosa and into the organism.

Acid-Detergent Fiber (ADF). Obtained by heating the food with hot dilute sulfuric acid containing cetyl trimethylammonium bromide (CTAB). The residue filtered off and weighed is a measure of the *cellulose* and *lignin* in the sample.

Adsorption. Occurs at the surface of a solid or liquid when substances are taken from the surrounding medium. The forces that bind the adsorbed layer to the surface may be physical or chemical in nature. Physical adsorption is often followed by a gradual diffusion of the adsorbed molecules from the surface into the interior of the solid.

Agar. Occurs as a cell-wall constituent of the red marine algae Rhodophyceae, from which it can be extracted with hot water. It sets on cooling to a jelly at a concentration as low as 0.5%. It is a mixture of two polysaccharides, agarose and agaropectin. Agarose, the main constituent, is a neutral polysaccharide containing 3,6-anhydro-L-galactose and D-galactose as the repetitive unit. Agaropectin contains carboxyl and sulfate groups of native agar.

It is not hydrolyzed by mammalian digestive enzymes and is, therefore,

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part of dietary fiber. Its chief uses are as a solid medium for cultivating microorganisms, as a thickener in the food industry, and as a laxative.

Agal Polysaccharides. Extracted from the tissues of algae; divided into two groups: (1) reserve polysaccharides which are water soluble and (2) structural polysaccharides which are not. They are not hydrolyzed by the mammalian digestive enzymes and are, therefore, part of dietary fiber.

Alginates. Algal polysaccharides not hydrolyzed by mammalian digestive enzymes and, therefore, part of dietary fiber. Alginic acid is insoluble in water but readily soluble in aqueous solutions of alkali metal hydroxides and carbonates. It is obtained as a highly gelatinous precipitate by treating a sodium carbonate extract of certain dried seaweeds with acid. Commercial algin is the sodium salt and is slowly soluble in water, forming an extremely viscous solution. It is used as a stabilizer for ice cream and other food products.

Apparent Digestibility. Based on measurements of intake and fecal excretion of a constituent and defined as intake minus fecal excretion, expressed as a proportion (or percentage) of intake.

Although *unavailable carbohydrates* in the diet are not hydrolyzed by the endogenous secretions, they are apparently digested. The extent to which this occurs varies greatly from individual to individual, perhaps because of differences between the intestinal flora and also the transit times in different individuals. *Hemicelluloses* are apparently digested to a greater extent than *cellulose.*

Arabinans. Polysaccharides that give L-arabinose on hydrolysis. They are present in wood cellulose, are associated with *pectin,* and have been isolated from the *pectic substances* of mustard seed and sugar beet.

Arabinogalactans. Substituted galactans that form part of the *hemicellulose* complex in many tissues. Although most emphasis has been given to arabinogalactans from woody tissues, polymers of this type are widely distributed. The water-soluble arabinogalactan of larch has received considerable study.

Arabinoxylans. Have a main chain composed of (1 → 4) β-D-xylopyranosyl units with an occasional branching in some preparations. The arabinose is present as single- or double-residue side chains. Arabinoxylans are widely distributed in the cell walls of many materials, although they are uncommon in woody tissues; they have been isolated from the husks of many grains.

Available Carbohydrates. All carbohydrates digested by the endogenous secretions of the human digestive tract and *absorbed:* the sum of glucose, fructose, lactose, maltose, sucrose, dextrins, starch, and glycogen.

Carrageenan. An *algal polysaccharide* chiefly composed of polymerized sulphated D-galactopyranose units, but with other residues also present. It is the

dried extract from the edible seaweed *Chrondus crispus* (carragheen, Irish moss).

The ability of carrageenan to react with milk protein has led to its widespread use in preparations containing milk and chocolate. It has been shown to be a potent cholesterol-lowering agent but, unlike almost any other plant polysaccharide, has an adverse effect on the gut. Ulceration of the cecum of both rats and guinea pigs has been demonstrated when carrageenan was added to the diet.

Cation Exchange. The ability of a material to exchange some of the cations (positively charged ions) it contains for others in solution. Polysaccharides, by virtue of their acidic sugars, possess this property.

Species of plants have characteristic cation-exchange capacities that are relatively independent of external nutritional factors in the soil. Most vegetable fibers act as weak monofunctional cation-exchange resins, while maize, oatmeal, bananas, cereal bran, and new potatoes act as very weak polyfunctional exchangers. The physical properties of fiber may be affected by the presence of ions. Divalent metals have a considerable effect on the *gel* formation and precipitation properties of sodium alginate, for example. Also, there is a linear relationship between the *water-holding capacity* and the cation-exchange capacity of fiber.

Cellulose. The best known, most widely distributed and only truly fibrous component of the plant cell wall. It is a polymer of glucose and the glucoside linkage is β, whereas in starch it is α. The cellulose molecules contain about 10 000 β-D-glucose units (giving a molecular weight of about 1 million).

The α linkages in starch can be broken by enzymes present in man, but the β linkages in cellulose are not hydrolyzed by the enzymes endogenous to man; thus cellulose is *unavailable carbohydrate* and so part of dietary fiber.

An important property of cellulose is its ability to take up water and swell. Cotton fiber is, for example, able to take up 0.4 g water per gram of fiber. This water-imbibing property of cellulose is the explanation for its ability to increase fecal weight in human subjects.

Crude Fiber. The residue left after boiling the defatted food in dilute caustic and then in dilute acid. Despite its established place in the history of human nutrition, deficiencies in this method have been recognized for over 100 years. It is not a good predictor of the nutritive value of food; moreover, it measures a variable proportion of the total plant cell-wall constituents. The method recovers 50–80% of *cellulose,* 10–50% of *lignin,* and 20% of *hemicellulose.* The proportion of the total cell-wall constituents recovered depends to a large extent on the amount that the *hemicellulose* fraction contributes to the overall cell wall. The *hemicelluloses* are largely lost during the crude-fiber procedure and, therefore, plants such as wheat or banana, that have a high proportion of

hemicellulose in the cell wall, give a low recovery of cell-wall constituents in the crude-fiber fraction.

Cutin. A complex polymer of mono-, di-, tri-, and polyhydroxy fatty acids. It is a lipid component of the waterproof covering and cuticle of the outer cellulose wall of plants.

Cuticular substances are extremely resistant to digestion and in turn are thought to impair the digestibility of the other cell-wall constituents, somewhat as does *lignin.* While they represent only a very small proportion of the fat content of the diet, their resistance to digestion means they appear in the feces, where they may constitute a much larger proportion of the fecal fat and may account for a substantial part of the increase in fecal fat that is seen in subjects taking a high-cereal-fiber diet.

Dietary Fiber. Includes all the polymers of plants that are not digested by endogenous secretions of the human digestive tract, i.e., *cellulose, pectins, hemicellulose, gums, mucilages,* and *lignin.* (See *plantix* and *unavailable carbohydrates.*) This definition should not be confused with *neutral-* or *acid-detergent fibers,* which are only a portion of dietary fiber.

Galactans. Polysaccharides which, on hydrolysis, give galactose. They occur in wood and in many algae. The most important galactan is *agar.*

Galactomannans. Polysaccharides that have both galactose and mannose in the chain. These polymers vary in the proportion of the two constituent sugars but belong to the same structural group. *Guar gum (guaran)* is a representative example. Galactomannans are part of the *hemicellulose* fraction of the plant cell wall.

Gels. Long-chain polysaccharides that have linked up by means of H^+ bonds to form an entrapping network for water.

Gels are sometimes solid and sometimes an easily deformable mass or jelly. They are thus divided into elastic and rigid gels. Gelatin is an example of the first type and silica gel the second. Gelatin gel may be converted back to the solution on heating and is thus a reversible gel; silica is irreversible.

Glucofructans. Linear polymers with both fructose and glucose in the chain. They are found in the *hemicellulose* part of the cell wall and form the storage polysaccharides in many temperate-climate grasses.

Glucomannans. Appear to be linear polymers with both mannose and glucose in the chain. The ratio of mannose to glucose is between 1:1 and 2.4:1. Hardwood glucomannans appear to contain no galactose and are relatively insoluble, but the glucomannans from gymnosperms have galactose side chains and a higher mannose:glucose ratio (3:1). The presence of side chains tends to make these polysaccharides more soluble in water, possibly because the side chains

prevent the formation of intermolecular hydrogen bonding. Glucomannans are part of the *hemicellulose* fraction of the plant cell wall.

Glucuronoxylans. Have a main "backbone" chain of (1→4) linked β-D-xylopyranosyl residues, containing side chains of 4-*O*-methyl-α-D glucopyranosyluronic acid and, in some annual plants, unmethylated D-glucuronic acid. Glucuronoxylans are found in the *hemicellulose* fraction of all land plants and most plant organs.

Glycans. The generic name for a polysaccharide. Progress towards a systematic nomenclature has produced the ending "an" to designate a substance as a polysaccharide. The term glycan has evolved from the generic word glycose, meaning a simple sugar, and the ending -an signifying a sugar polymer.

Glycuronans. A generic name for polymers of uronic acids. For example, galacturonan is a polymer of galacturonic acid and mannuronan is a polymer of mannuronic acid, and both are glycuronans.

Guar Gum (guaran). A neutral polysaccharide, a D-galacto-D-mannan, that is isolated from the ground endosperm of a leguminous vegetable cultivated in India for animal feeds. In small amounts, it finds widespread use in the food and pharmaceutical industries, being included as a thickener and stabilizer in salad dressing, ice cream, soap, medicinal tablets, and toothpaste.

Gums (exudates and seed gums). Complex polysaccharides, each containing several different sugar molecules and *uronic acid* groups. The true plant gums, e.g., gum acacia and gum tragacanth, are the dried exudates from various plants obtained when the bark is cut or the plant is otherwise injured. They are soluble in water to give very viscous colloidal solutions, sometimes called *mucilages,* and are insoluble in organic solvents. These are not part of the plant cell-wall structure but are generally indigestible and so are considered a part of dietary fiber. Guar and locust bean gums are examples of gums derived from seeds.

Hemicelluloses. A wide variety of polysaccharide polymers, at least 250 of which are known. The largest chemical group are the *pentosans, xylans,* and *arabinoxylans;* a second group consists of *hexose* polymers such as the *galactans;* a third group are the acidic hemicelluloses, which contain galacturonic or glucuronic acid.

Hemicelluloses are those polymers extractable from plants by cold aqueous alkali. They are not precursors of *cellulose* and have no part in *cellulose* biosynthesis but represent a distinct and separate group of plant polysaccharides. Together with *pectin,* the hemicelluloses form the matrix of the plant cell wall in which are enmeshed *cellulose* fibers. The hemicelluloses are not digested in the small intestine but are broken down by microorganisms in the colon more readily than *cellulose.*

Heteroglycans. Polysaccharides that hydrolyze to two, three, or more monosaccharides. They have prefixes of di-, tri-, and so on to designate the number of different types of sugar residues.

Hexoses. Monosaccharides with each molecule containing six carbon atoms. Glucose, fructose, galactose, and mannose are all hexoses.

Homoglycan. Polysaccharide that contains only one type of sugar unit and hence on hydrolysis gives only one monosaccharide type. The most abundant polysaccharides are of this type, e.g., starch and cellulose. Cellulose is present in the world in a quantity equal to or greater than all the other polysaccharides, and is a homoglycan.

Hydrocolloid. A dispersion of particles in water, generally larger than molecules, but not large enough to be seen by the naked eye. Colloidal solutions of proteins and carbohydrates are very stable. This stability is due to the existence of a sheath of dispersion medium (usually water), which protects the hydrophilic particles. Hydrophilic solutions are characterized by a high viscosity and often set to a gel on cooling. They can be prepared so as to contain a large proportion of the dispersed colloid. Gelatin and starch form colloidal dispersions when they are brought into contact with water and warmed.

Hydrophobic Bonding. Occurs when nonpolar molecules or groups associate together in water, a result of the tendency of water molecules to exclude nonpolar groups.

Indigestible Residue. Residue left after digestion by the endogenous secretions of the human digestive tract and further fermentation in the large intestine. Resistance to digestion by animal enzymes is not synonymous with indigestibility. Carbohydrates that escape animal digestion and reach the lower bowel are subject to microbial fermentation, the extent of which is dependent upon the type of fiber, its potential fermentation rate, and residence time.

Lignin. Highly polymeric substance occurring in woody plant tissues; an aromatic polymer of molecular weight about 10,000, based on coniferyl and sinapyl alcohols. Virtually indigestible, it is usually classified as part of dietary fiber. It is of commercial value as a source of vanillin and other aromatic chemicals.

Mannans. Polysaccharides made up of mannose units, found in the *hemicellulose* fraction from many cell walls. They seem to be storage polysaccharides. The best known is mannin A from the endosperm of the ivory nut.

Middle Lamella. Develops from the cell plate that forms between the daughter nuclei of the plant cell wall and extends to meet the existing wall, and therefore is the structure between the cell walls of adjacent cells. It appears to be rich in galacturonans, which are characteristically part of the *pectic substances.*

Mucilages. Polysaccharides usually containing galactose, galacturonic acid residues, and often xylose and arabinose. Structurally, they resemble the *hemicelluloses* and are water soluble, being obtained as slimy, colloidal solutions. They are found mixed with the endosperm or storage polysaccharides or in special cells in the seedcoat of many seeds. They retain water and so protect the seed against desiccation.

Neutral-Detergent Fiber (NDF). That part of a food that remains after extraction with a hot neutral solution of the detergent sodium lauryl sulfate. It is a measure of the cell-wall constituents of vegetable foodstuffs. The method for determining NDF was designed to divide the dry matter of feeds very nearly into those constituents which are nutritionally available by the normal digestive process and those which depend on microbial fermentation.

Noncellulosic Polysaccharides. Another term for *hemicelluloses,* includes all the matrix polysaccharides from the cell wall other than cellulose; a large number of different structural types of polysaccharides, ideally divided on a structural basis.

Nonnutritive Fiber. A term used in food labeling, where it is usually applied to *crude fiber* or *acid-detergent fiber* values. It is ambiguous and should be avoided in scientific writing.

Oligosaccharides. Collective term for disaccharides, trisaccharides and tetrasaccharides. These yield two, three, and four monosaccharide residues on hydrolysis, respectively.

Pectic Substances. Mixtures of acidic and neutral polysaccharides that can be extracted with water from plant tissues. They are characteristically rich in galacturonic acid and are galacturonans with a variable degree of methyl esterification.

Pectin. General term designating those water-soluble *pectinic acids* of varying methyl-ester content and degree of neutralization which are capable of forming gels with sugar and acid under suitable conditions. Pectin is found in the *primary cell wall* and intracellular layer. It changes from an insoluble material in an unripe fruit to a much more water-soluble substance in the ripe fruit. Its ability to form gels and its ion-binding capacity may be important in human nutrition.

Pectinic Acid. Groups of *pectins* in which only a portion of the acidic groupings are methylated.

Pentoses. Monosaccharides with each molecule containing 5 carbon atoms. Pentose sugars most commonly present in human foods are L-arabinose and D-xylose, which are widely distributed in the polysaccharides in plants. Pentoses are present in small amounts in all cells whether animal, plant, or bacteria.

Dietetically, the 5-carbon sugars are of little or no importance as a source of energy for the body.

Plantix. A term coined from "plant" and "matrix" to replace *dietary fiber* to avoid the uncertain and diversified meaning of the term *fiber.* It includes the same polymers found in *dietary fiber* from plants. It has not yet found widespread acceptance.

Primary Cell Wall. Is polysaccharide in nature and is built of individual sugars like glucose. The *cellulose* fibers of the primary cell wall are laid down in a random network on the *middle lamella.* The fibrils are surrounded by an amorphous matrix of *hemicellulose.*

Protopectin. Term applied to the water-insoluble parent *pectic substance* which occurs in plants and which, upon hydrolysis, yields *pectinic acid.*

Sclerenchyma. Tissue forming the hard parts of plants such as nutshell or seed coat.

Secondary Cell Wall. Is polysaccharide in nature and apparently amorphous. It is formed after the cell has reached maturity and is laid down inside the *primary cell wall* either as a continuous layer or as localized thickenings or bands.

Silica. Is deposited in the plant cell wall, usually in the aerial part of the plant. The amount varies according to the species, the silica content of the soil, and the maturity of the plant. The ash content of the plant cell wall, particularly of wheat, may be as high as 10%; of this the principal element present is often silicon.

It is an important element in plant growth. The nutritional significance of silica relates to its capacity to impair the digestibility of cell-wall materials.

Suberin. *Cutin*-like substance found in cork. It is a plant lipid that cannot be extracted with a simple solvent but needs saponification before extraction.

True Digestibility. A measurement of the intake of a diet minus fecal excretion, corrected for endogenous losses expressed as a proportion (or percentage) of the intake.

It is obtained by measuring a constituent in the intake and in fecal excretion and then applying a correction for endogenous fecal excretion of the constituent on a diet free (or virtually so) of that constituent.

Unabsorbable Plant Polysaccharides. Polysaccharides not hydrolyzed by endogenous enzymes of the mammalian digestive tract.

Unavailable Carbohydrates. Term originally used to distinguish between *available carbohydrate* and *dietary fiber.* It comprises all those polysaccharides not digested by the endogenous secretions of the human digestive tract, i.e., *pectins, hemicelluloses,* and *cellulose.* These are therefore not available as car-

bohydrate to man but are fermented in the large intestine to yield fatty acids. As originally defined, *lignin* was included in this fraction.

Uronic Acids. Are present in the *pectic substance* and the *hemicellulose* portion of the plant cell wall. They are found in about half the known plant polysaccharides, the commonest being D-galacturonic and D-glucuronic acids. Uronic acids are derived from sugars by oxidation of the terminal CH_2OH to COOH and, when present as glycosides, behave like simple hydrocarboxylic acids, forming metal salts, amides, and alkyl and methyl esters.

Water-Holding Capacity. Amount of water that can be taken up by unit weight of dry fiber to the point at which no free water remains.

Methods of determining water-holding capacity require the separation of the free or unadsorbed water phase from the entrapped water. Several alternative procedures have been used to measure this property, but no general agreement on the best method has been reached.

A close relationship exists between *acid-detergent fiber* content of vegetable dietary fiber and water-holding capacity, but there is no such relationship between *lignin* content and water-holding capacity. This suggests that the polysaccharide content of a plant determines the ability to hold water.

Water-Soluble Fraction. Fraction of dietary fiber soluble in water; it includes *pectic substances, gums, mucilages,* and some polysaccharide food additives. The amounts extracted depend on the state of division of the sample and on the precise conditions used; comparisons between the results obtained by different authors are therefore difficult.

Xylans. Group of polymers having a main chain of (1 → 4) β-D-xylopyranosyl residues. Few D-xylans are neutral molecules containing D-xylose residues only, and most bear side chains of other sugars; arabinose and 4-*O*-methyl glucuronic acid are the most usual substituents. Xylans are found in the *hemicellulose* portion of the plant cell wall in all land plants and in most plant organs.

Xylem. Water-conducting elements of plant tissues, usually made up of cells with lignified walls. In mature woody tissues, the walls of the xylem vessels are completely lignified; in less mature tissues, the lignification is partial and localized in distinct areas in the wall.

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