THE ROLE OF DIETARY FIBER IN DIVERTICULAR DISEASE AND COLON CANCER

October 1980

Prepared for

BUREAU OF FOODS
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20204

under

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by

John M. Talbot, M.D.

LIFE SCIENCES RESEARCH OFFICE
FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY
9650 Rockville Pike
Bethesda, Maryland 20014
FOREWORD

The Life Sciences Research Office (LSRO), Federation of American Societies for Experimental Biology (FASEB), provides scientific assessments of topics in the biomedical sciences. Reports are based upon comprehensive literature reviews and the scientific opinions of knowledgeable scientists investigating specific areas of biology and medicine.

This technical report was prepared for the Bureau of Foods, Food and Drug Administration (FDA), by John M. Talbot, M.D., Senior Medical Consultant, LSRO, FASEB, in accordance with the provisions of Contract No. FDA 223-79-2275.

The LSRO acknowledges the contributions of the investigators and consultants who assisted with this study. A judicious attempt has been made to incorporate the various viewpoints and opinions expressed by participants in an ad hoc study group that met at the Federation on May 12, 1980. The report was reviewed by these consultants; however, the listing of their names in Section IX does not imply that they endorse the study. The author and LSRO accept responsibility for the contents of the report.

The report was reviewed and approved by the LSRO Advisory Committee (which consists of representatives of each constituent society of FASEB) under authority delegated by the Executive Committee of the Federation Board. Upon completion of these review procedures, the report was approved and transmitted to FDA by the Executive Director, FASEB.

While this is a report of the Federation of American Societies for Experimental Biology, it does not necessarily reflect the opinion of each individual member of the FASEB constituent Societies.

Kenneth D. Fisher, Ph.D.
Director
Life Sciences Research Office
SUMMARY

This report reviews recent research on the character, properties, and definition of dietary fiber as well as its possible action in colonic carcinogenesis and diverticulosis. Considerable progress has been made in analytic methodology, characterization of components and constituents, and determination of physicochemical and biologic properties of dietary fiber. However, issues such as a generally acceptable definition for dietary fiber and precise terminology for components of dietary fiber have been only partially resolved. An accurate, rapid, convenient method for determining total dietary fiber in foods has yet to be developed, but useful modifications of certain analytic methods and development of innovative approaches have been made.

Some effects of different dietary fiber sources and components on gastrointestinal function have been characterized; however, the mechanisms involved, the influence of interactions of fiber components with luminal contents, and the roles of individual fiber components and constituents are incompletely understood. Other unresolved questions concern the physiologic effects of dietary fiber-colonic floral interactions and of fiber-bile salts combinations. Possible untoward effects of dietary fiber include influences on the bioavailability of certain nutrients and drugs, increased risk of volvulus, and erosion of enteric mucosae. Although more information is needed about such possible adverse effects of fiber, most experts appear to regard them as minor.

Although epidemiologic studies suggest that low-fiber intake is associated with increased risk of diverticular disease and colonic cancer, much of the evidence is faulted by genetic, environmental, cultural, dietary, and other uncontrolled variables. Animal studies of chemically-induced colonic cancer indicate that dietary fiber appears to protect against and/or delay the development of colonic tumors; however, the significance of these studies to human colonic cancer is not well established. Furthermore, available data on the total dietary intake of fiber are insufficient to evaluate the adequacy, possible deficiency, or possible excessive consumption of dietary fiber by segments of the United States population. Thus, conclusive evidence for a causal relationship between low-fiber intake and diverticulosis or colonic cancer is not available, and the fundamental question of whether dietary fiber protects against human colonic cancer and/or diverticulosis is not yet resolved.

Nevertheless, clinical trials in which symptomatic diverticular disease is treated with supplementary dietary fiber have generally reported favorable results. While this mode of treatment is widely practiced by the medical community, additional research is needed to establish the role of dietary fiber in human health and disease. Specific suggestions for such research are indicated in the report.
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I. INTRODUCTION

The importance of dietary components with water-holding capacity and limited digestibility as bulking agents in the diet has been acknowledged for many years (Trowell, 1978). Since the turn of the century, alterations in cereal milling practices as well as heightened interest in human nutrition have led to considerable study of the physical and chemical effects of plant fiber in the diet. Indeed, commercial products with high fiber content, such as wheat bran, have been marketed for over 50 years and were originally promoted because of their fiber content (Kellogg, 1923).

During the past several years, public interest in, and scientific study of, dietary fiber in health and disease were reinforced by the reports of Burkitt (1973a,b) and Painter et al. (1972) as well as the rediscovery of the earlier work of Cleave (1956). These and other investigators hypothesized that a restriction of plant fiber in the diet may predispose individuals to a number of diseases and disorders typical of Western cultures. Interest in this hypothesis has led to an expansion of laboratory and clinical research, development of new food products and dietary regimens, revision of nutritional guidelines to include "adequate fiber", suggestions that reduced fiber intake may have adverse health effects, and the call for guidelines and regulations on the fiber content and labeling of food products.

Despite considerable research and clinical use during the past decade, evidence that fibrous components of the diet may promote good health, prevent or ameliorate diverticulosis, and prevent colonic cancer is incomplete and equivocal. The long-term health effects of increasing the fiber content of diets are not fully established; physiologic responses are poorly defined and difficult to measure. A consensus among experts on a definition of dietary fiber and on the most appropriate analytical methodology for identifying and measuring its components and constituents is lacking. Thus, it is clear that important unsolved problems still exist on the exact nature of dietary fiber and its possible significance in health and disease.

These issues have been addressed in a number of recent conferences and reviews (Burkitt and Trowell, 1975; Kelsay, 1978; Mendeloff, 1979; Roth and Mehlman, 1978; Spiller and Amen, 1976; Spiller et al., 1978; True and Heyworth, 1978). In 1976, the Food and Drug Administration requested that the Life Sciences Research Office of FASEB review the basis for the growing interest in increasing the amount of fiber-containing foods in the United States dietary. Based on a literature review and the opinions of an ad hoc group of knowledgeable investigators, the LSRO prepared a synoptic report of the nutritional significance of dietary fiber (Kimura, 1977).
One of the conclusions of the 1976 LSRO ad hoc study group was that few clinical conditions could be identified in which increased dietary fiber had demonstrable medical value. However, since 1977, results of a large number of laboratory and clinical investigations have been published. Because the FDA has a responsibility to evaluate and monitor the safety of foods, establish regulations, and provide nutrition information to consumers, the Associate Director for Nutrition and Food Sciences, Bureau of Foods, requested that the LSRO review and analyze this newer knowledge. FDA indicated that a review and analysis were essential to the development of rational regulatory decisions concerning the declaration of natural and unconventional sources of fiber in foods, the accuracy and adequacy of labeling claims to enable consumers to make informed choices, the accuracy of health claims, and the appropriateness of medical claims for foods if such claims are to be permitted through revisions of the Federal Food, Drug, and Cosmetic Act (1979).

Because public concern and many investigations have focused on the possible role of dietary fiber in preventing human colonic disorders and helping to maintain good health, and because the scientific community has been aware of the need for improvement in analytic methods for plant fiber, FDA requested that LSRO focus its review and evaluation on recently available scientific evidence pertaining to the influence of dietary fiber on the development of colonic diverticulosis and cancer, the treatment of symptomatic diverticulosis, and identify progress since 1977 in the analysis, characterization, and definition of dietary fiber. Recent publications and data are emphasized because the previous LSRO report reviewed the literature through early 1977 (Kimura, 1977).
II. DIETARY FIBER

A. DEFINITION AND COMPOSITION

Despite considerable progress in identification and characterization of the components of various sources of dietary fiber, a generally accepted scientific definition of dietary fiber has not been achieved (Anderson and Chen, 1979; Institute of Food Technologists, 1979; Kelsay, 1978; Mendeloff, 1975, 1977, 1979; Southgate, 1978; Trowell, 1978; Van Soest, 1978). Anderson and Chen (1979) defined plant fiber as portions of foods that are not digested in the human small bowel. Spiller et al. (1978) described dietary fiber as including cellulososes, lignins, water-insoluble hemicelluloses, pectins, gums, and mucilages. In McCance and Widdowson's extensive food composition tables, revised by Paul and Southgate (1978), dietary fiber is defined as

...the sum of the polysaccharides and lignin which are not digested by the endogenous secretions of the human gastrointestinal tract. This fraction has a variable composition as it is made up of several different types of polysaccharides (pectic substances, hemicelluloses, and cellulose) and the non-carbohydrate lignin.

Crude fiber, the term originally applied to analysis of animal feeds and forage, is still used by some investigators because they analyze mixed diets by the generally accepted procedures for crude fiber analysis (Horwitz, 1975). Crude fiber includes primarily the residues of lignin and cellulose obtained after treatment with a fat solvent, hot acid, and hot alkali (Institute of Food Technologists, 1979). This fraction and the term crude fiber are inadequate for characterization of dietary fiber in human nutrition because the reagents and procedures employed may exclude as much as 80% of the hemicellulose, and some of the lignin and cellulose of food plants, components which are actually ingested by man (Mendeloff, 1978a).

1. Major components

Despite its limitations, most authorities use the term dietary fiber or total dietary fiber when referring to cellulose, lignin, hemicellulose, and pectin. Some investigators include the plant gums, mucilages, cuticular substances, tightly bound indigestible proteins and minerals, and other fiber-associated indigestible substances. However, investigators frequently include information on the analytic methodology employed in their studies, thus providing the reader with a basis for comparison with other data. Additional discussion of fiber fractions is presented in the following section on analytic methodology (see page 8).
Fiber is a generic term, and different types of fiber have specific chemical structures and physiologic effects. Components of dietary fiber are indicated in Table 1. For purposes of this report, the term "dietary fiber" is used; it includes both the substances accepted by most investigators and those additional substances accepted as components by many investigators.

Experts have recommended identification and definition of "standard" dietary fibers; however, according to Van Soest (1978), no two sources of plant cell wall are identical, and fiber varies with species, age of the plant, and conditions of plant growth. The standard fiber concept should not be confused with the certified food-grade wheat bran that was prepared by the American Association of Cereal Chemists (Anonymous, 1977b).

A major impediment to universal acceptance of a definition of dietary fiber is the knowledge that while the classes of chemical constituents in plant fibers are well recognized, the exact chemical structures often vary among plant species. Thus, the hemicelluloses of spruce, alfalfa, and bean contain xylans, arabans, and related polymers of four-, five-, and six-carbon saccharides, but have differing compositions of the various polymers. Variations in chemical structure and configuration result in altered physical properties. Because both chemical and physical properties influence physiologic attributes, dietary fibers from different plants may produce variations in experimental results even when isolated by similar methodologies and employed in the same experimental protocols.

2. Fiber-associated substances

In addition to those substances recognized as components of plant fiber, there are several substances that are typically present in plants but are difficult to separate or accurately identify in fiber preparations (Cummings, 1976). They are of interest because they influence the isolation and characterization of fiber from various plant sources, they may interact with components of dietary fiber, and they may play a role in certain physiologic effects of dietary fiber.

Phytates. Phytic acid (inositol hexaphosphate) is present in most plant seeds in association with protein, but typically occurs in succulent tissues and storage tissues as salts complexed with calcium, magnesium, and potassium ions. In the seed and seedling, phytates are a readily available reserve of phosphorus (Van Soest, 1978). Phytates are present in various plant extracts. For example, they are constituents of bran and whole meal flour, but not white flour. Because phytates chelate numerous mineral ions, the phytate content of foods is of interest for its apparent potential to induce deficiencies of calcium as well as copper, magnesium, iron, and zinc in persons whose intakes of these elements are marginal (Institute of Food Technologists, 1979; Reinhold et al., 1973, 1976).
Table 1. Components of Dietary Fiber

<table>
<thead>
<tr>
<th>Fraction</th>
<th>Principal Constituents</th>
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<tr>
<td><strong>Accepted by most investigators</strong></td>
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</tr>
<tr>
<td>Celluloses</td>
<td>cell wall polysaccharides, unbranched glucose polymers</td>
</tr>
<tr>
<td>Lignins</td>
<td>noncarbohydrate cell wall material, phenylpropane polymers</td>
</tr>
<tr>
<td>Hemicelluloses</td>
<td>cell wall polysaccharides derived from various pentoses and hexoses</td>
</tr>
<tr>
<td>Pectins</td>
<td>cell wall galacturonic acid polymers with pentose and hexose side chains</td>
</tr>
<tr>
<td><strong>Additional substances accepted by some investigators</strong></td>
<td></td>
</tr>
<tr>
<td>Gums</td>
<td>non-cell wall, complex polysaccharides containing glucuronic and galacturonic acids, xylose, arabinose, mannose</td>
</tr>
<tr>
<td>Mucilages</td>
<td>non-cell wall, complex polysaccharides some of which are also storage polysaccharides (e.g. guar)</td>
</tr>
<tr>
<td>Algal polysaccharides</td>
<td>highly complex polymers</td>
</tr>
<tr>
<td><strong>Recently suggested additions</strong></td>
<td></td>
</tr>
<tr>
<td>Indigestible storage polysaccharides</td>
<td>Trowell et al., 1976</td>
</tr>
<tr>
<td>Fungal chitins</td>
<td>Trowell, 1978</td>
</tr>
<tr>
<td>Indigestible plant protein</td>
<td>Saunders and Betschart, 1980</td>
</tr>
<tr>
<td>Associated indigestible minerals, waxes, other substances</td>
<td>Spiller et al., 1978</td>
</tr>
</tbody>
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Sandstead and his colleagues (1978) demonstrated that 26 g/d of soft, white, wheat bran added to the diets of well-nourished, young, human adults resulted in slightly negative zinc balance, but did not alter copper or iron balance. However, evidence is insufficient to separate the role of phytates from that of dietary fiber or their possible interactions in altering absorption of various essential minerals. Spiller et al. (1978) noted that there is major disagreement on the effects of the phytates versus those of dietary fiber in wheat bran on mineral balance. In addition, these authors emphasize the importance in mineral metabolism of possible interactions between ingested dietary fiber and other components of the diet. Long-term studies of the mineral-binding properties of dietary fiber are needed, particularly studies of dietary fiber present in commonly eaten items such as fruits and vegetables (Cummings, 1978).

Silicon. Reports of the biologic effects of feeding animals silica and various silicates indicate that these substances are generally nontoxic, are readily absorbed from the bowel when in soluble form, do not elevate blood silicon levels, and are rapidly eliminated via the bowel and kidneys (Select Committee on GRAS Substances, 1979). Voronkov (1975) suggested that silicic acid, released in the body by the metabolism of silicon compounds, forms insoluble complexes with physiologically important cations such as magnesium, copper, and iron. No other evidence was found to indicate that the silica or silicates in dietary fiber influence mineral metabolism. However, there is some evidence that silica may interfere with digestibility and nutritive value of forages in ruminants (Cummings, 1976; Smith et al., 1971). In addition, there is evidence that dietary fiber and silicon interact: 11 male subjects consuming low- and high-fiber diets for 26 d demonstrated negative silicon balances (Kelsay et al., 1979a). The mean silicon balance was significantly more negative on the high-fiber diet.

Lipids and proteins. Cuticular substances include the complex esters of fatty acids which cover plant surfaces such as those of fruits, seeds, and leaves. Cutin and suberin are the most important groups of complex polymers secreted by plant cells which form the waxy ground substance of exposed plant surfaces. They contain mono-, di-, tri-, and polyhydroxy fatty acids. Cutin and suberin strongly resist digestion, and might possibly impair the digestibility of other cell wall constituents. Whether they should be included within the definition of dietary fiber remains controversial. Proteins of the cell wall structures also are tightly bound and highly resistant to digestion. The question of their possible physiologic effects on the bowel remains to be investigated, and scientists disagree whether these proteins should be included with the definition of dietary fiber.

Lectins. Microorganisms, plants, and animals are known to produce a series of glycoproteins termed "lectins" which play a major role in recognition phenomena. These substances extend
across the lipid bilayer cell membrane and have hydrophilic sugar residues projecting from both membrane surfaces (Lis and Sharon, 1973). Lectins selectively bind to specific saccharide residues of membrane glycoproteins and glycolipids causing agglutination (Sequeira, 1978; Williams et al., 1979). Lectins are distinguished by (a) their ability to bind specific mono- and disaccharides or to bind specific sites on complex oligosaccharides, (b) their multivalent nature or possession of multiple binding sites, (c) their capacity to induce cellular agglutination, and (d) their reversibility of the saccharide binding. Thus, in microbial, plant, and animal systems, cellular recognition phenomena appear to involve a complementary interaction between a saccharide component of a membrane glycoprotein and a lectin-like glycoprotein.

The possible interactive roles of plant lectins with microbial flora, gastrointestinal epithelial cells, nutrients and/or dietary fiber in gut contents are highly speculative. However, several observations are intriguing. Lectins are widely distributed in plant tissues and are known to be associated with plant cell walls (Clarke et al., 1975). Thus plant fiber, derived from cell wall material, can contain glycoprotein lectins which are capable of binding with saccharide components of microbial or intestinal epithelial cell membranes.

Etzler (1979) used several lectins as probes for investigation of the surface properties of intestinal epithelial cells of the rat. Based on previous observations that microvillar cell membranes contain both glycoproteins and glycolipids, she identified three different lectin receptors on the surface of epithelial cells lining the crypts and villi. Furthermore, differences between binding of the three lectins employed in the study suggested that surfaces of crypt and villus cells may contain a receptor substance that varies in the extent of glycosylation as cells move up the villi. These investigations indicate that specific lectin binding sites are associated with intestinal epithelial cells and suggest that if cell wall materials do contain lectins, it is possible that selective binding of components on different types of dietary fiber may occur. In addition, lectins may influence nutrient bioavailability and the metabolic activities of the intestinal flora.

Epidemiologic observations are also suggestive of a possible interaction between lectins and effects of dietary fiber. Spiller et al. (1978), noting that populations consuming diets high in legumes and grains might have a lower incidence of colon cancer, indicated lectins in these dietary components might be a contributing factor. Freed and Green (1975) advanced the hypothesis that responses to lectins in the digestive tract might play a role in protection against intestinal carcinoma. They suggested that lectins might be important in mast cell degranulation, increased mucus production, and increased fecal bulk; in increasing mitotic rate of epithelial cells and cell-turnover rates; in local stimulation of nonspecific lymphocyte activity; and by direct or selective binding to neoplastic cells.
Discussions of the ad hoc group suggested that these topics were receiving only limited investigation. However, they noted that if lectins are present in cell wall material, then diets high in fiber content could also be high in lectin content. It is clear that cell walls, especially those of fresh or raw vegetable materials, may contain glycoproteins with differential and highly selective binding properties. However, there is little evidence that lectins in dietary fiber could reach the large intestine intact or undigested.

If the presence of lectins or lectin-like ligands in dietary fibers were established, a role for lectins in cellular interactions between fiber and other macromolecules during digestion or intestinal transport might be demonstrated. Techniques for investigation of lectin specificity and binding phenomena are available, and there is a need for additional research on possible interactions of lectins and effects of dietary fiber.

B. ANALYTIC METHODOLOGY

Southgate (1976) noted that the analyst faced multiple problems in attempting to measure the complex mixture of polysaccharides and lignin comprising total dietary fiber and that there were no methods then capable of completely analyzing the ranges of fiber components present in a mixed diet. For several years, leading investigators in the dietary fiber field have urged the replacement of the official crude fiber method (Horwitz, 1975) because of its inadequacy for encompassing all components of total dietary fiber, and the proliferation of misinformation that has resulted from its use (Kimura, 1977; Schaller, 1978; Southgate, 1976; Van Soest, 1978). For example, the crude fiber value of wheat bran determined by this method underestimates its true fiber content by a factor of four (Van Soest, 1978). In 1977, frequently used methods for total dietary fiber were (1) an enzyme modification (Schaller, 1978) of Van Soest's neutral detergent fiber (NDF) method (Goering and Van Soest, 1970), (2) Southgate's method (Southgate, 1976), (3) the method of McCance et al. (Southgate, 1976) for indigestible carbohydrate involving measurement of starch in food sample residues insoluble in 80% ethanol, and (4) a method based on the use of amylolytic and proteolytic enzymes developed by Elchazly and Thomas (1976) for determining water-insoluble plant polymers. The Southgate procedure appeared the most practical approach to systematic determination of dietary fiber fractions (Kimura, 1977). However, neither the Van Soest nor the Southgate method adequately isolates and characterizes the soluble polymeric portion of dietary fiber. While these methods reflected progress, they could not satisfy the desired objective of a practical method for complete component analysis of total dietary fiber.

It is generally agreed that those constituents of plant fiber having important physiologic and nutritional properties must be completely identified and characterized to permit systematic
investigation of their physiologic effects, interactions with other fiber components and nutrients, and possible adverse effects. However, the study of dietary fiber effects is complicated by the observed inability of chemically isolated fractions such as cellulose, hemicellulose, and lignin to duplicate the effects of the native plant material (Van Soest, 1978).

Recently, Kelsay (1978) also noted that, "At present, no methods for the determination of total fiber in foods have universal acceptance." Referring to previous studies, Spiller et al. (1978) observed that there had been no major improvements in analytic methods commonly used in plantix (total dietary fiber) analysis. An Expert Panel on Food Safety and Nutrition (Institute of Food Technologists, 1979) suggested that one reason for the variable and conflicting results of dietary fiber studies among different investigators may be related to relatively poor analytic methods available for determining fiber data. However, other reports since 1977 suggest that there has been progress in methodology, characterization, and definition of dietary fiber.

In a review of analytic methodology, Southgate et al. (1978) suggested that use of the Southgate fractionation method, including the Englyst modifications, permits detailed analysis of total dietary fiber and yields more precise information than other available methods. According to these authors, the ultimate goal is a method that will measure and characterize dietary fiber:

in such a way that will predict and explain the physiological effects of the consumption of the mixture in question. It is important, therefore, that methodological studies should be linked to studies of the metabolism of dietary fiber.

Mossberg (1979) suggested that a number of analytic methods should be used, singly or in combination, to elucidate the cause/effect relationships in complex metabolic processes involving fiber. This reflects, in part, the view of Van Soest (1978) who observed that the development of one method to encompass all the substances related to the dietary fiber complex is impractical.

Recently, Collings and Yokoyama (1979) described results of analyzing dietary fiber in delignified feeds and forages; gas-liquid chromatography (GLC) was used to measure the component sugars released by hydrolysis and subsequently derivatized to their corresponding alditol acetates. They also reported the effects of chemical treatment on the ultrastructure of plant cell walls. A modification of the technique of Albersheim et al. (1967) was used, involving predigestion with ammonium oxalate, delignification with sodium chlorite, hydrolysis with trifluoroacetic acid (TFAA), derivatization of the hydrolysed sugars to their corresponding alditol acetates, and gas chromatographic analysis of
the derivatives. From the 16 feeds and forages studied, the hemicellulose-derived sugars included glucose, galactose, mannose, xylose, arabinose, rhamnose, and possibly ribose. Sodium chlorite appears to oxidize the lignin of the plant cell wall without extracting carbohydrates from the cellulose and hemicellulose. The authors compared their values for the principal fibrous fractions of the test substances with values obtained by the following methods: neutral detergent fiber (NDF), acid detergent fiber (ADF), potassium permanganate cellulose, and potassium permanganate lignin determined on the ADF fraction. Ammonium oxalate-derived values for total cell wall material were higher than those obtained by the neutral detergent technique. Permanganate cellulose and TFCA cellulose values were similar in 10 of the 16 substrates, but TFCA hydrolysis yielded higher cellulose values in six substrates. Values of sodium chlorite lignin tended to be higher than with permanganate-oxidized lignin.

It was concluded that detergent methods in fiber analysis of feeds and forages offer quick, relatively easy, and reproducible methodology, albeit with some possible component losses and complications. The aldito acetate derivatization system analyzes for cellulose, hemicellulose, hemicellulose sugars, uronic acids, and lignin (Collings and Yokoyama, 1979). Scanning electron microscopy of wheat-straw cell walls subjected to various methods of analysis revealed open cells with disrupted cell walls after neutral detergent or ammonium oxalate treatment. Sodium chlorite appeared not to disrupt cell walls whereas acid detergent severely ruptured the cell walls. Trifluoroacetic acid did not disrupt the cellulose crystallinity.

Collings (1979) extended these investigations to include analysis of a total of 20 different feeds and forages, measurements of digestibility in cattle, swine, and ponies, and in vitro utilization by rumen bacteria. Sodium chlorite lignin values determined on the ammonium oxalate fractions generally were higher than permanganate lignin values. This resulted from some inaccuracies of the sodium chlorite lignin value. It was suggested that a spectrophotometric method for lignin is needed. Cell wall cytoplasm and some uronic acids were removed by boiling the substrates in ammonium oxalate solution. Values for lignin, cellulose, hemicellulose, hemicellulosic sugars, and uronic acids were determined in the 20 fiber sources. Hemicellulose values were generally higher by the detergent methods than by GLC while TFCA and detergent cellulose values were similar in most substrates, and neutral detergent fiber values were lower than the ammonium oxalate residues.

Collings' (1979) analyses indicated substantial hemicellulose losses in cell walls treated with neutral detergent and recovery of hemicellulose in cell walls treated with acid detergent. Digestibilities of glucose, galactose, arabinose, and xylose derived from NDF, ADF, and GLC fiber analyses were reported as were the fermentation values of two predominant rumen cellulytic bacteria, *Ruminococcus flavefaciens* C94 and *Bacteroides*.
succinogenes S85, cultivated with alfalfa, bromegrass, corn silage, cattle manure fiber, wheat straw, and Whatman No. 1 filter paper as substrates. It was concluded that all these examinations of fiber structure, digestibility, and bacterial utilization were enhanced by GLC analysis and compared favorably with detergent methods (Collings, 1979; Collings and Yokoyama, 1980). Table 2 compares several analytic methods in terms of the fiber components extracted and quantified.

Selvendran et al. (1979) investigated the factors affecting measurement of neutral sugars from vegetable fiber, and recommended a method that consolidates various modifications of the alditol-acetate procedure for estimating neutral sugars. In addition, the investigators adapted the modified carbazole method of Bitter and Muir (1962) to permit measurement of uronic acid content of plant fibers.

Bailey et al. (1978) described a sequential procedure for pectin extraction: use of cold water for 2 h, boiling water for 2 h, and 0.5% ammonium oxalate solution at 100°C for 1 h. The method reportedly provides a useful guide to the solubility of plant pectins. The authors noted that NDF methods remove essentially all plant pectins while ADF treatment extracts pectin from non-leaf tissue, but removes only part of the leaf pectins. They emphasized the care needed in preparing plant material for analysis of structural polysaccharides in view of the high initial losses of pectins in cold, but particularly in hot water.

Saunders and Hautala (1979) compared the "in vivo dietary fiber" contents of wheat milling fractions and wheat foods, as determined in rat feeding studies, with crude fiber, NDF, and dietary fiber values determined in vitro with pronase-α-amylase digestion. They reported close correlations among all values and concluded that the crude fiber, NDF, and in vitro enzymatic fiber methods accurately predict in vivo dietary fiber in rats when the result is adjusted by an appropriate regression equation.

Formulation of a universal method applicable to all plant and food materials may not be possible; however, lack of such a method seems a major obstacle to progress in this area (Furda, 1977).

Participants in the ad hoc group meeting affirmed recommendations of other expert groups that analytic methods are needed for two distinct purposes. One is for rapid quality control on batch ingredients in the food industry. This should be a screening method that will provide at least approximate values. Of the available procedures, the Van Soest NDF method is probably the most suitable; however, this was not a unanimous opinion. One consultant recommended some type of enzyme method even though the state-of-the-art is not far enough advanced. Some of the reagents used in the Van Soest method are harsh, and may alter the structure or chemistry of physiologically significant substances such as pectins, sugars, uronic acids, and most of the cell wall components.
<table>
<thead>
<tr>
<th>Name</th>
<th>Fraction removed by extraction during analysis (soluble fraction)</th>
<th>Fiber components quantified by the assay (undigested)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acid Detergent Fiber</td>
<td>Solubilizes same as neutral detergent plus hemicellulose</td>
<td>Same as neutral detergent fiber, except hemicellulose is solubilized</td>
</tr>
<tr>
<td>Acid Detergent Fiber Ash run on any residue containing silica</td>
<td>All components volatilized by ignition</td>
<td>Silica</td>
</tr>
<tr>
<td>Acid Detergent Fiber Nitrogen run on acid detergent fiber residue</td>
<td>When compared to total protein result, is a measure of percent protein bound in the cell and unavailable due to artifact, lignification, or heat damage</td>
<td></td>
</tr>
<tr>
<td>Collings-Yokoyama method†</td>
<td>Cellulose, hemicellulose; lignin oxidized by sodium chlorite</td>
<td>Cellulose, hemicellulose, hemicellulose sugars, uronic acids, lignin</td>
</tr>
<tr>
<td>Crude fiber</td>
<td>Approximately 80 percent lignin</td>
<td>20 percent total lignin</td>
</tr>
<tr>
<td></td>
<td>Approximately 85 percent hemicellulose</td>
<td>15 percent total hemicellulose</td>
</tr>
<tr>
<td></td>
<td>Approximately 20 to 60 percent cellulose</td>
<td>50 to 80 percent total cellulose</td>
</tr>
<tr>
<td>Lignin (permanganate) run on acid detergent fiber residue</td>
<td>Lignin, acid detergent fiber, nitrogen compounds</td>
<td>Cellulose, cutin, silica (dark specks in residue indicate significant cutin levels)</td>
</tr>
<tr>
<td>Lignin (72 percent sulfuric acid)</td>
<td>Cellulose</td>
<td>Cutin, silica</td>
</tr>
<tr>
<td>a. run on permanganate lignin residue</td>
<td>Cellulose</td>
<td>Lignin, insoluble nitrogen compounds, cutin, silica</td>
</tr>
<tr>
<td>b. run on acid detergent fiber residue</td>
<td>Cellulose</td>
<td></td>
</tr>
<tr>
<td>Neutral Detergent Fiber (total cell wall)</td>
<td>Cellular constituents: starches, sugars, fat, soluble nitrogen compounds, soluble minerals</td>
<td>Cell wall constituents: hemicellulose, cellulose, lignin, bound nitrogen (proteins), cutin, silica</td>
</tr>
</tbody>
</table>

* Modified from Kimura, 1977
† Collings and Yokoyama, 1979 (see page 9)
in some fiber substrates. Van Soest's NDF method will not work well with high-fat or high-starch foods; however, its utility is enhanced when the American Association of Cereal Chemists' (1977) modification is used for removal of fat and starch.

A second, more exacting method is needed for basic research, and should be capable of analyzing individual constituents such as the monosaccharides of hemicelluloses in dietary fiber. The Southgate method is a possibility, but the method reported by Collings and Yokoyama (see page 9) uses milder reagents and GLC, and may, therefore, yield somewhat more precise and complete data. A method compatible with physiologic reactions occurring in the gastrointestinal tract of animals is needed. It should permit analysis not only of specific components of fiber, but also of the kinds of binding sites available. One problem confounding fiber analysis is that some fibers contain tightly bound starches and proteins, and these carry over in some of the analytic methods. Finally, wide variability of cation binding to various plant fibers, particularly as a function of pH, was emphasized (see also Thompson and Weber, 1978; 1979a,b).

Many fiber chemists tend to restrict the defined scope of dietary fiber to the four major groups of components: celluloses, hemicelluloses, lignins, and pectins, for technical reasons. However, other scientists are convinced that a definition of dietary fiber must also include the gums, mucilages, and cuticular substances despite the fact that these are absent from, or are only trivial components of, more than 90% of foods. Analysis for gums, mucilages, and waxes requires specific methods for each; they are not detected as such by the Van Soest, Southgate, or Collings-Yokoyama procedures.

Another analytic problem is related to the tight binding of some starches, proteins, and minerals to components of dietary fiber. On the one hand, available methods do not completely separate dietary fiber components; however, it remains to be established whether dietary fiber components are essentially free of bound starches, proteins, and minerals as they exert their physiologic actions in the gastrointestinal tract. Another problem is the occurrence of a 5-10% analytic error caused by the increase in moisture content when dried fiber preparations are left exposed to ambient room temperature and humidity conditions for periods as short as 30 min (Collings et al., 1978).

The enzymatic methods show considerable promise for future applications, but are incompletely developed. Microbial enzymes which are not natural to the mammalian species under study should not be used since they would probably not be applicable. With respect to the problem of relating values for celluloses, hemicelluloses, lignins, and pectins to values for their constituent monomers such as the uronic acids and monosaccharides, the consultants were optimistic that practical solutions can be evolved.
For instance, summation of the individual sugar values from GLC analysis of the hemicellulose fraction of a dietary fiber source yields the original hemicellulose content.

The effect of various techniques for isolation of fiber fractions on their biologic properties is a continuing problem; chemically-derived isolates of fiber such as cellulose, lignin, or hemicellulose do not possess the same properties the native materials are presumed to have. For example, chemical isolation of cellulose and hemicellulose makes them enzymatically degradable and renders pectin and hemicellulose essentially water-soluble. According to Van Soest (1978), one cannot reasonably expect that isolating and feeding purified cellulose or other cell wall components will evoke the same physiologic responses as the original plant fiber; physical properties and capacity to be degraded are markedly changed by the preparatory treatments. In addition, some artificial components of dietary fiber may be introduced simply as a result of the methodology. Morrison (1973) concurred in this view, noting that each of the different kinds of fiber is characterized by its method of isolation, making a chemical fiber term of dubious relevance. He suggested that the composition of the plant cell wall ought to be characterized in a more specific way with individual components.

Permanganate delignification of plant fiber may be sufficiently harsh to affect cellulose (Collings, 1979), and NDF treatment of a number of feeds and forages resulted in losses of cell wall hemicelluloses. Thus, it may be more appropriate to use mild solutions such as ammonium oxalate to remove cytoplasm from cell wall preparations.

Matthéé and Appledorf (1978) noted that, of the few publications on the effects of cooking on analytic values for dietary fiber, most reported no marked effects. Short cooking (boiling in water 15-20 min) and long cooking (45-50 min) of carrots, cabbage, broccoli, and okra tended to increase, on a dry weight basis, NDF, ADF, crude fiber, and cellulose values, but had no effect on lignin and hemicellulose values. Changes in cellulose values were observed most frequently. Van Soest (1978) mentioned the formation of the Maillard polymer containing 11% nitrogen, which is a synthetic component found in the crude lignin fraction of cooked, fried, and baked foods, and may influence the exchange and adsorptive properties of dietary fiber.

C. RECENT REPORTS ON CHARACTERIZATION AND PROPERTIES

Despite problems with analytic techniques and with attempts to characterize dietary fiber per se, reports during the past three years indicate some progress in defining properties and characterizing components of dietary fiber. Narrative summaries of some examples are presented below.
1. Chemical characterization

To obtain highly purified pectic polysaccharide for biologic studies, Baig et al. (1980) subjected grapefruit pectin to chromatography using DE-52 cellulose columns. Four chemically distinct pectic polysaccharides were resolved during elution of the column with increasing salt concentrations. The galacturonic acid content of these polysaccharides ranged from 70-80%; the degree of methylation of the galacturonic acid residues in the eluted pectins decreased with increasing salt concentration.

Honig and Rackis (1979) determined the indigestible content of whole soybean, defatted soy flakes, soybean hulls, soy protein concentrate, corn bran, and wheat bran. In vitro pepsin-pancreatin digestions were used to isolate insoluble nondigestible residues, followed by analysis for hemicellulose, cellulose, lignin plus ash, protein, and total carbohydrate. Soluble digests greater than 5000 daltons were isolated by ultracentrifugation and analyzed for carbohydrate and protein content. Total indigestible contents in terms of dry weight were: corn bran 97%, soybean hulls 86%, wheat bran 52%, whole soybean 23%, soy protein concentrate 40%, defatted soy flakes 16%. The large amount of indigestible protein in the soy protein concentrate was unexpected. The composition of the insoluble indigestible fraction from soybean hulls was: cellulose 71%, hemicellulose 20%, and lignin plus ash 9%. Estimated protein digestibilities were: whole soybean 68%, defatted soy flakes 81%, soybean hulls 60%, soy protein concentrate 61%, corn bran 43%, and wheat bran 60%.

Susheelamma and Rao (1978) isolated and defined chemically an arabinogalactan polysaccharide from black gram, a traditional grain legume used in India. Knehans et al. (1979) attempted to characterize an unidentified growth factor in alfalfa and cabbage by fractionating cell wall components and assaying them for biologic activity in guinea pigs. The active compound was associated with the holocellulose fraction (cellulose plus hemicellulose less lignin and extractives) and was destroyed at alkaline pH.

Mod et al. (1978) studied water- and alkali-soluble hemi- celluloses from milled rice and rice bran. Arabinose/xylose ratios, amino acid patterns of associated proteins, and the range of crude and neutral detergent fiber contents of rice bran were determined. Significant amounts of hydroxyproline were found in the water- soluble hemicelluloses, and electrophoretic analysis of one alkali- soluble rice bran suggested the proteins were chemically bound to the carbohydrate. The same investigators (Mod et al., 1979) analyzed water-soluble hemicelluloses from the bran of rice from four growing areas. Rhamnose, arabinose, xylose, mannose, galactose, and glucose were found in all hemicelluloses tested, along with protein, hexuronic, and ferulic acids. Arabinose/xylose ratios were calculated, and amino acid patterns were analyzed. Small compositional differences were observed among the specimens from the different growing areas.
Naivikul and D'Appolonia (1979) isolated the water-soluble and insoluble, nonstarchy polysaccharides from various legume flours, investigated their chemical compositions, identified the sugars in each purified fraction, and compared the results with available data on the nonstarchy polysaccharides found in wheat flour. Fiber sources studied included lentils and navy, pinto, faba, and mung beans.

2. Physicochemical properties

Fiber content, particle size, density, hydrated volume, water-holding capacity (as a function of ionic strength and pH), and temperature effects were determined for 12 commercially available fiber sources, as an aid to selection of the most desirable sources of fiber for use in adding bulk and reducing caloric content of food products (Parrott and Thrall, 1978). The fiber sources included wheat, rice, and soy brans, almond skins, fractionated peanut hulls, coconut residues, and several purified cellulosics. Each fiber source displayed different functional or physical properties, in particular, highly individualized responses to pH, ionic strength, and mono- and divalent cations. Photomicrographs of the fiber sources showed enlargement and elongation of particles and structural damage as a result of increasing temperature in the range 37–100°C.

Rasper (1979) studied relationships among some physical properties of dietary fiber (particle size, density, hydration, and ion exchange capacities) and the distribution of the main insoluble components of a selection of wheat shorts; wheat, rye, corn and rice brans; hulls of barley, rice, and oats; peanut red skins, and soybean hulls. In addition, he compared the following analytic methods: ADF, NDF, buffered acid detergent fiber (Baker, 1977), and enzymatic in vitro fiber (Saunders, 1977). Rasper (1979) emphasized two points in the technique of evaluating dietary fiber: (1) the influence of the isolation method on the nature of the dietary fiber; (2) the effect of particle size on some physical properties. The enzymatic in vitro fiber method (Saunders, 1977) seemed to minimize chemical alteration of the fractions, and was the preferred technique despite some technical disadvantages. Correlation coefficients relating individual physical properties to the measured distribution of the main insoluble fiber components were calculated and discussed. Although cellulose content appeared to dominate the measured physical properties, cellulose correlations alone are insufficient, and may be misleading. Hence, consideration must be given to the other dietary fiber components, and their chemical and physical properties must be better characterized.

The binding capacities of wheat, corn, soy, and rice brans, oat hulls, and cellulose for endogenous copper, zinc, and iron were measured after incubation under three pH conditions: 0.65, 6.8, and a sequence of 0.65 - neutralization - 6.8 (Thompson and Weber, 1979a). Most of the minerals remained bound after the
pH 6.8 and the sequential treatments, but not after the acidic treatment. Recognizing that protein in the fiber sources influenced the hydrogen-ion binding capacity, the investigators repeated the measurements following enzymatic proteolysis of the samples, and found that buffering capacities decreased; however, the results suggested that after removal of the protein, other properties of the fibers may gain in hydrogen-ion buffering capacity (Thompson and Weber, 1979b).

Brodribb and Groves (1978) investigated the effect of wheat bran particle size on stool weight in 21 healthy volunteers whose diets were supplemented daily with 20 g coarse or fine bran. Stool weights were significantly greater (24 g/d, SE ± 6.4 g) with the coarse bran, which also had a higher water-holding capacity. Whether the increased stool weights with coarse bran were solely the result of higher water-holding capacity was not determined.

Kim et al. (1978a,b) studied the chemical composition and gel firmness and strength of sunflower pectins as influenced by pH and Ca++ concentration, as well as the chemical and physical features of ammonia-demethylated preparations. Sunflower pectins showed a high sensitivity to the effects of ionic conditions, particularly Ca++ concentration, on gel firmness and strength, and the demethylated sunflower pectins demonstrated improved gel characteristics.

Stephen and Cummings (1979) measured the water-holding capacities of 17 plant fiber preparations by centrifugation of materials hydrated in simulated ileal fluid, and by a dialysis technique. The gel-forming polysaccharides had the highest water-holding capacities. Tests in human volunteers revealed an overall inverse relationship between water holding and fecal bulking. Bran, with the lowest water-holding capacity, yielded the largest fecal weights while pectin, with the highest water-holding property, produced the smallest change in fecal weight.

Thompson and Weber (1978, 1979b) and Thompson et al. (1980) found the hydrogen-ion buffering capacities to be directly related to protein content and ranked in decreasing order: rice bran, wheat bran, soy bran, oat hulls, corn bran, and cellulose. Following treatment of the fiber sources with neutral detergent or an enzyme, protein levels and buffering capacities were reduced. Fiber sources incubated at pH 0.6 showed iron, copper, and zinc to be substantially released, but at pH 6.8, only minimum amounts were released. Different releasing performance was observed for different fibers. In ion-exchange studies, fiber type affected the mineral binding, and treatment of the fibers with enzymes or neutral detergent caused dissimilar ion exchange patterns. When applied singly, more copper than zinc was bound by all fiber specimens, but in combination, less of each trace element was bound, although again, copper binding exceeded zinc binding.
3. **Biologic properties**

   a. **Animal studies**

   Digestion sequences of lettuce (George et al., 1978) and wheat bran (George et al., 1979) in the alimentary tract of rats were studied by scanning electron microscopy. Little digestion of lettuce occurred in the rat, but gross structure of the lettuce was markedly altered. With wheat bran, epidermal disruption, interior cross tube and aleurone cell distortion, and hydrolysis of protein substances between internal tissues were evident, but little other digestion occurred except for bacterial degradation of endosperm remnants.

   Schneeman (1978) tested several plant and synthetic fiber sources [wheat bran, whole alfalfa, rice bran, safflower meal, cellulose acetate, xylan (from larchwood), a refined cellulose product, and pectin] in vitro for their ability to influence lipase, trypsin, and chymotrypsin activity. Except for pectin, most of the sources caused a significant loss of lipase activity. Both the refined cellulose product and xylan caused partial loss of chymotrypsin activity, and alfalfa and safflower meal had the most potent effect on trypsin activity. A part of the enzyme solution was absorbed into the fiber matrix of all fibers tested, thereby decreasing the availability of total filterable enzyme activity. Rats fed 20% cellulose in the diet had about 20% more intestinal contents than those on fiber-free diets, and trypsin, chymotrypsin, amylase, lipase, and total proteolytic activities per mg of intestinal contents were less than half the control values (Schneeman and Gallaher, 1980). Except for chymotrypsin and leucine amino peptidase, total enzyme activity in the intestinal contents was also lower. Although bile acid levels per mg of contents were lower than in controls, total bile acids were greater. Hence, the availability of enzymes and bile acids in the rat small intestine can be affected by cellulose.

   Other recent contributions from the same research group relating to effects of plant fiber on pancreatic and intestinal enzyme activities in rats include Gallaher and Schneeman (1979) on high-fiber effects; Forman et al. (1979) on pectin; Forman and Schneeman (1980) on pectin; and Sheard and Schneeman (1980) on bran. Results showed that a high-fiber diet (20% cellulose added) fed for 10 d increases pancreatic chymotrypsin, but reduces levels of trypsin, lipase, amylase, total proteolytic activity, and protein in the intestinal contents (Gallaher and Schneeman, 1979). In rats fed for 6 wk a high- or low-fat diet (25 and 5% respectively) with or without 5% pectin added, pectin had no effect on pancreatic amylase activity, but was associated with reduced pancreatic lipase levels at both levels of dietary fat (Forman et al., 1979). In similar studies, Forman and Schneeman (1980) found that pectin had little effect on enzyme levels in the rat pancreas,
but in the small intestine, it increased lipase, trypsin, and amylase activities in the low-fat group, and in the high-fat group, it reduced amylase activity by 60-80% and caused lower trypsin and increased lipase activities. Pancreatic protein and enzyme activities were above control levels in rats fed a diet containing 5% wheat bran for 10 d and then fasted for 12 h before sacrifice (Sheard and Schneeman, 1980). However, pancreata from bran-fed animals sacrificed 3 h after a meal showed no difference from controls in protein content and enzyme levels except for elevated lipase activity.

b. Human studies

Haber et al. (1977) estimated the effects of ingestion of three physical forms of apple on human satiety, blood glucose, and insulin responses. Each test meal provided 60 g of available carbohydrate. Satiety was greatest after whole apple, less after apple puree, and least after fiber-free apple juice. Although plasma glucose levels were similar following all three types of apple meal, a marked fall occurred after the juice, and serum insulin levels were higher after ingestion of juice and puree than following consumption of whole apple.

Brauer and Marlett (1979) fed six healthy, elderly subjects carefully controlled, "typical American", high- or low-protein diets containing 6.8 to 7.6 g/d of dietary fiber as determined by an α-amylase modification of Van Soest's NDF method. Fiber in stools was estimated by the NDF procedure without amylase. Less than half the dietary fiber could be detected after gastrointestinal transit; digestibility could not be predicted on the basis of wet stool weight or transit time.

Slavin and Marlett (1980) fed seven young women 5.4 g/d or 19.3 g/d cellulose in diets of otherwise constant composition. The high-cellulose diet was achieved by addition of 16 g/d of a commercially available, powdered cellulose product. Mean apparent cellulose digestibility (cellulose in feces:cellulose in diet) during the 30-d, low-cellulose diet was 70.3 ± 10.7%. During the 30-d, high-cellulose study, it was 16.2 ± 15%. Because fecal cellulose during the high-cellulose diet approximated the sum of the amount measured during the low-cellulose diet plus the 16 g/d of added cellulose, the apparent digestibility of refined cellulose was minimal. The authors speculated that refined cellulose was resistant to microbial degradation.

A third study investigated the effects of human digestive processes on three types of bran incorporated into breads used as part of the controlled diets fed to five healthy human volunteers (Dintzis et al., 1979). Dry-milled corn bran was highly resistant to digestion; wheat bran lost about 15% cellulose and 60% of apparent hemicelluloses, while major losses of cellulose and apparent
hemicelluloses were observed with soybean hulls. Scanning electron microscopic observations of fecal residues of these dietary fiber sources showed small effect on corn bran, loss of endosperm and frequently the aleurone layer of the wheat bran, and marked disruption of the soybean hull bran. Large individual differences occurred among the subjects in the degree of digestion of soy hull bran.

During four 4-d tests, eight healthy adolescent males consumed, in random order, a basal diet alone or supplemented with 14.2 g/d of a refined cellulose product, a hemicellulose product, and a pectin from citrus fruits (Gramstorff Fetzer et al., 1979). NDF analysis of feces revealed the apparent disappearance of 45-46% of the cellulose, 76-90% of the hemicellulose, and all the pectin. However, changes in stool characteristics associated with the pectin feedings suggested that the pectin became modified so that it was no longer detectable by standard chemical methods.

Other evidence of degradation of dietary fiber components in the human colon was reported by Vercellotti et al. (1978) who identified the following component soluble sugars of plant polysaccharides in human colonic contents: rhamnose, galactose, mannose, xylose, and arabinose. Fucose, hexosamines, and sialic acids, which are characteristic of mucin, were also identified.

The digestibility of cellulose, hemicellulose, and lignin was investigated in two groups of volunteers -- otherwise healthy persons with an ileostomy and normal subjects (Holloway et al., 1978). Both groups consumed fixed diets of known fiber content for 10 d. NDF and ADF determinations of fecal samples showed 84.5% of ingested cellulose was excreted by the ileostomy subjects but only 22.4% by the normal subjects, indicating digestion of cellulose in the normal subjects of about 80%. Of the water-insoluble hemicelluloses in the diet, 27.5% was excreted from the small bowel of the ileostomy subjects but only 4.0% from the normal subjects, showing approximately 96% digestion of hemicelluloses in the normal subjects. Lignin was undigested in both groups. In similar studies, Holloway et al. (1980) compared the composition of the hemicellulose in the subjects' diet with that measured in excreta from the small and large bowels. Female ileostomy subjects digested an average of 65% of ingested hemicellulose; male ileostomy subjects, 83%. The digestion was 97% in normal female subjects and 95% in the normal males. An arabinoxylan hemicellulose from cereals in the diet appeared to be undigested in the small bowel and only partially digested in the colon. The authors postulated that the majority of hemicelluloses are usually digested in the human small intestine, probably by enzymes from the normal flora, and that arabinoxylans derived from cereals could be important in explaining the effect of dietary fiber on intestinal transit time.
4. Fiber content of foods

Despite numerous studies with various population groups, accurate estimates of dietary fiber intake by the population in this country are not available. Burkitt (1978) stated that Western diets provide less than 5.0 g/d crude fiber while Heller and Hackler (1978) reported that daily crude fiber intake in the United States was 4.9 g in 1957-1959 compared with 6.8 g in 1909. Consumption of vegetables appeared relatively constant during the period 1909-1975, but that of potatoes, fruit (except canned and frozen fruit), whole grains, cereals, dry peas, and dry beans declined. Scala (1974) estimated that during the past century American consumption of fiber decreased about 20% from fruits and vegetables and about 50% from cereals and grains. Based on the Southgate fractionation method (page 9), Johnson and Kolasa (1978) estimated an average daily fiber intake of 14 g in a group of 59 noninstitutionalized women aged 58 to 89. The values for crude fiber intake reported by Heller and Hackler (1978) might be considerably greater if figures for total fiber content had been used for calculations.

The book, Composition of Foods (Paul and Southgate, 1978, 1979) is a major contribution to practical knowledge of total dietary fiber in foods. Dietary fiber values for 461 of 507 foods and food ingredients in 18 categories are given.

Because of limited information on the total and soluble plant fibers of foods, Chen and Anderson (1980), using a modification of the Southgate fiber method (Southgate et al., 1978) analyzed a selection of cereals and vegetables (not specified) for the following fiber fractions and constituents: cellulose, lignin, hexoses, pentoses, and uronic acid. Marked differences in chemical composition of various fiber sources were exemplified by oat bran, described as rich in soluble fiber but poor in cellulose, and by wheat bran, which had a lower soluble-fiber content but was much higher in cellulose. The authors suggested that measurements of the soluble components of total dietary fiber may be necessary to interpret some of the metabolic effects.
III. EFFECTS OF DIETARY FIBER ON GASTROINTESTINAL FUNCTION

Knowledge of the responses of the gastrointestinal tract to dietary fiber has been summarized by a number of investigators including Anderson and Chen (1979), Connell (1978a), Cummings (1978), Cummings et al. (1978, 1979a,b), Eastwood and Kay (1979), Eastwood et al. (1978b), Kelsay (1978), Mendeloff (1977, 1978b, 1979), and Spiller et al. (1978). In addition, recent publications cited elsewhere in this report deal with specific gastrointestinal effects. Despite the highly suggestive epidemiologic data on adverse health effects of fiber deficiency, the basic question of essentiality of dietary fiber in human nutrition has not been answered.

In the upper intestine, fiber acts like a sponge. Its capacities for water holding, gel formation, cation exchange, and adsorption vary with the type of fiber, the pH, osmolality, and electrolyte concentrations of the intestinal contents (Eastwood and Kay, 1979). Connell (1978b) emphasized that addition of fiber to the diet increases the bulk of the meal in the stomach and upper intestine as well as the bulk of the stool, and that interest in the latter has overshadowed the former so that little attention has been paid to the physiologic significance of fiber in the stomach and small intestine.

Investigations of the alleged relationship of fiber-deficient diets to hiatal hernia have revealed little evidence of influence on esophageal motility, lower esophageal sphincter tension, or the secretion of gastrointestinal hormones involved in esophageal motility (Mendeloff, 1979). Guar gum and pectin slow the rate of gastric emptying and small-intestine transit time; however, the influence of other components of total dietary fiber in this regard has not been well characterized.

Amounts of dietary fiber considered advisable may be limited by possible adverse effects on bioavailability of trace metals, electrolytes, and other nutrients in the upper intestine. Obviously, at some measurable point, bulk from dietary fiber can replace or seriously reduce caloric content of food. However, such is not the case in relatively normal dietary patterns. The significance of the binding of cations by certain polysaccharides of dietary fibers and the relative roles of phytates versus fiber components in this regard are not fully established. However, iron deficiency has been documented in Iranian children consuming bread made from high-extraction wheat flour (Haghshenass et al., 1972), and two adult Iranian males studied in a metabolic ward developed negative calcium, magnesium, zinc, and phosphorus balances during a 20-d period in which approximately 50% of their caloric intake was from a high-fiber native bread (Reinhold et al., 1976). The cation exchange capacity, which has been noted by many scientists, appears to result in an irreversible binding of essential minerals, preventing absorption in the upper intestine (Eastwood and Kay, 1979). Kelsay (1978) cited eight human studies
in which absorption of dietary minerals and electrolytes was reduced when foods contained increased amounts of fiber. Mendeloff (1979) suggested that poorly nourished children and other persons whose intake of essential minerals is marginal should probably take mineral supplements if they are ingesting high-fiber diets. Slowed absorption of certain drugs, such as digoxin, may occur with high intake of cereal brans; however, this does not lead to clinically significant reduction in digoxin absorption (Brown et al., 1978; Woods and Ingelfinger, 1979). Pectin reduces absorption of acetaminophen (Welling, 1977).

The amounts of dietary fiber that may be advisable in the human diet in terms of unimpeded upper-intestinal function are unknown. Small-intestine transit times are shortened by whole meal bread, but increased by such gel-forming fibers as guar gum and pectins (Eastwood and Kay, 1979). Gel-forming dietary fibers may delay the absorption of carbohydrates and other nutrients in the small intestine. For example, in normal subjects, consumption of fiber-rich (guar flour and/or pectin) high-carbohydrate meals resulted in lower blood-glucose and serum-insulin levels compared with responses of control subjects ingesting high-carbohydrate meals without added fiber (Jenkins et al., 1977). Nevertheless, the long-term effects of high-fiber diets on absorption of minerals, electrolytes, and nutrients have not been completely investigated (Anderson and Chen, 1979).

Mendeloff (1979) noted that the structure and size of the human colon seem to be related directly to the amounts of fiber in the diet, varying from short and straight in Eskimos whose diets contain little vegetable fiber, to long and wide in rural Africans who consume essentially a vegetarian diet. Among persons consuming a Western-type diet, increased stool bulk and weight result from addition of dietary fiber; for example, daily ingestion of 25 g of moderately coarse wheat bran will increase stool weights from 100-125 g to 180-230 g/d (Mendeloff, 1979). Substitution of the 25 g of bran by an equivalent amount of vegetables with a high soluble-polysaccharide content such as cabbage, brussels sprouts, or beans, quickly leads to increased flatulence. Intestinal transit times usually decrease with increasing intakes of dietary fiber such as coarse wheat bran or bagasse; however, such effects are not consistently observed, and in some studies, added wheat bran, cellulose, or pectin did not influence transit times in normal subjects (Kelsay, 1978; Mendeloff, 1979). In fact, recent studies demonstrated high variability in transit time, frequency of defecation, and fecal weight and volume in normal subjects (Wyman et al., 1978), and in patients with diverticular disease (Eastwood et al., 1978a). Thus, our understanding of the influence of dietary fiber on transit time needs refinement in terms of range and constancy of effects, the question of which components of the fiber complex affect intestinal motility, and of the mechanisms involved.

Addition of pectin to the diet increases fecal bile-acid excretion. This effect is probably initiated in the small bowel because pectin is degraded in the colon (Kay and Truswell, 1977;
Eastwood and Kay, 1979). Microbial enzymes present in the ascending colon degrade certain fiber components, resulting in changes in the matrix structure of the fiber and in the chemical environment of the colon (Eastwood and Kay, 1979). Lignin resists, but other components of fiber yield to degradation in the colon, producing such products as methane, hydrogen, and volatile fatty acids. Changes in the water-absorbing capacity of the colon may result from some of the by-products of fiber degradation (Mendeloff, 1979). The adsorptive surfaces of fiber may hold bacteria and solutes, altering or preventing microbial metabolism of solutes. Fiber in the colon may change the types and amounts of bile acids returning to the liver, and may prevent their bacterial degradation and reabsorption from the colon.

According to Eastwood (1978), 16 g wheat bran or cellulose per day added to a normal diet will nearly double stool weight because of the increased water-holding capacity. This appeared to reduce stool transit times; however, results of the few carefully controlled studies on record are inconsistent (Connell, 1978b). Water-absorption capacity differs among various fiber components; it is greater for hemicelluloses than for celluloses and lignins. The questions of "ideal" stool weight and whether healthy persons with relatively low stool weights should increase their fiber intake merely to increase stool bulk and weight are not settled. One hypothesis in support of increasing fiber intake is that fiber, such as that in cereal bran, increases fecal bulk and adsorption of endogenous and foreign compounds, thereby reducing fecal concentrations of substances which act as initiators and promoters of colon carcinogenesis (Reddy et al., 1978; Weisburger et al., 1980) (see also page 36).

Colonic motor function, as measured by changes in intracolonic pressures, tends to increase as a result of increased fiber intake, with a corresponding reduction in intracolonic pressures. Connell (1978b) noted that the available evidence suggests these effects do not result simply from increased stool bulk, but may be related to possible effects of fiber on gastrointestinal hormone production and/or chelation of calcium, or to action on neurotransmitters of the "enteric nervous system". For example, Morgan et al. (1979) observed that the addition of 10 g of guar to a mixed meal was associated with a 47% decrease in the maximum postprandial levels of gastric inhibitory polypeptide (GIP) in normal subjects and 30% decrease in diabetics. When guar was added to a high-carbohydrate meal, the decrease in GIP levels was 71%.

Table 3 lists known and presumptive physiologic effects of dietary fiber in the gastrointestinal tract.
Table 3. Gastrointestinal Responses to Dietary Fiber

<table>
<thead>
<tr>
<th>Type of Response</th>
<th>Fiber Source</th>
<th>Probable Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased postprandial satiety</td>
<td>apple</td>
<td>pectin</td>
</tr>
<tr>
<td>Delayed gastric emptying</td>
<td>guar flour, purified pectin</td>
<td>guar, pectin</td>
</tr>
<tr>
<td>Delayed mouth-to-cecum transit time</td>
<td>not stated</td>
<td>guar, pectin</td>
</tr>
<tr>
<td>Prolonged glucose absorption</td>
<td>not stated</td>
<td>guar, pectin</td>
</tr>
<tr>
<td>Negative mineral balances</td>
<td>fruits, vegetables</td>
<td>cellulose, hemicellulose, lignin</td>
</tr>
<tr>
<td>Negative zinc balance</td>
<td>cereal bran, whole meal bread</td>
<td>cellulose, lignin</td>
</tr>
<tr>
<td>Disturbed pancreatic, intestinal enzyme activity</td>
<td>wheat bran, alfalfa, others</td>
<td>cellulose, hemicellulose</td>
</tr>
<tr>
<td>Reduced intestinal transit time</td>
<td>wheat bran, purified cellulose</td>
<td>cellulose, hemicellulose</td>
</tr>
<tr>
<td></td>
<td>fruits, vegetables</td>
<td>cellulose, hemicellulose, lignin</td>
</tr>
<tr>
<td>Increased fecal bulk</td>
<td>wheat bran, carrot, alfalfa, purified cellulose</td>
<td>hemicellulose, pectin, cellulose</td>
</tr>
<tr>
<td></td>
<td>fruits, vegetables</td>
<td>cellulose, hemicellulose, lignin</td>
</tr>
<tr>
<td>Apparent increased fecal bile acid, total steroid excretion</td>
<td>wheat bran, bagasse</td>
<td>lignin, pectin, cellulose, hemicellulose</td>
</tr>
<tr>
<td>Reduced intracolonic pressure</td>
<td>wheat bran</td>
<td>cellulose, hemicellulose</td>
</tr>
<tr>
<td>Improved bowel habit</td>
<td>fruits, vegetables, wheat bran</td>
<td>cellulose, hemicellulose, pectin</td>
</tr>
<tr>
<td>Probable Responsible Property</td>
<td>Comment</td>
<td>Reference</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>---------</td>
<td>-----------</td>
</tr>
<tr>
<td>gel forming, bulking, possible effect on GI hormones</td>
<td>mechanism not clear</td>
<td>Haber et al., 1977</td>
</tr>
<tr>
<td>effect on GI hormones</td>
<td>mechanism not clear</td>
<td>Holt et al., 1979; Mendeloff, 1979</td>
</tr>
<tr>
<td>gel forming, increased viscosity</td>
<td>mechanism not clear</td>
<td>Jenkins et al., 1977</td>
</tr>
<tr>
<td>gel forming, bulking, increased viscosity</td>
<td>mechanism not clear</td>
<td>Haber et al., 1977; Jenkins et al., 1977</td>
</tr>
<tr>
<td>ion exchange, mineral binding capacity</td>
<td>—</td>
<td>Kelsay et al., 1979a,c</td>
</tr>
<tr>
<td>ion exchange, mineral binding capacity</td>
<td>decreased zinc levels in Sandstead et al. not stat sig</td>
<td>Reinhold et al., 1976; Sandstead et al., 1978</td>
</tr>
<tr>
<td>bulking, increased intestinal contents</td>
<td>rat studies, mechanism not clear</td>
<td>Forman and Schneeman, 1980; Schneeman, 1978, 1980; Schneeman and Gallagher, 1980</td>
</tr>
<tr>
<td>water holding, bulking</td>
<td>effects of fiber on, and significance of, transit times are inconclusive</td>
<td>Anderson and Chen, 1979; Connell, 1978a; Eastwood et al., 1978b; Kelsay, 1978; Kelsay et al., 1978; Spiller et al., 1980</td>
</tr>
<tr>
<td>water holding, bulking</td>
<td>marked increase stool weight repeatedly demonstrated, coarse and moderately coarse bran</td>
<td>Connell, 1978b; Kelsay, et al., 1978, 1979b; Mendeloff, 1979; Spiller et al., 1980</td>
</tr>
<tr>
<td>water holding, bulking</td>
<td>efficient binding of bile acids results of human studies not consistent, mechanism unclear</td>
<td>Cummings et al., 1976; Eastwood et al., 1973; Jenkins et al., 1975; McLean Baird et al., 1977</td>
</tr>
<tr>
<td>water holding, bulking, possible effect GI hormone secretion</td>
<td>fecal bulking insufficient explanation, mechanism not clear</td>
<td>Connell, 1978b; Eastwood et al., 1978b; Findlay et al., 1974</td>
</tr>
<tr>
<td>water holding, bulking</td>
<td>relieves constipation</td>
<td>Huang et al., 1978</td>
</tr>
</tbody>
</table>
IV. THE ROLE OF DIETARY FIBER IN DISORDERS OF THE COLON

Cumulative information available in 1977 suggested that dietary fiber deficiency was a risk factor in the etiology of such colonic disorders as diverticular disease and cancer. However, the evidence was based on epidemiologic data, most of which lacked the support of controlled clinical studies (Burkitt, 1973a,b; Burkitt and Trowell, 1975; Kimura, 1977; Mendeloff, 1978b). Based on numerous favorable clinical reports, the use of dietary fiber in the treatment of symptomatic, as well as symptomless, diverticulosis had become widely accepted. Again, however, the supporting data were largely anecdotal, and results of controlled clinical trials were conflicting (Connell, 1978a). Knowledgeable experts have repeatedly urged that identification and characterization of the components of dietary fiber be improved, that such components, singly and in combinations, be tested in the diet for physiologic effects, and that controlled clinical trials be conducted to obtain further scientific evidence of the role, if any, of dietary fiber in the treatment and/or prevention of diverticular disease and in the prevention of colonic cancer.

A. DIVERTICULAR DISEASE OF THE COLON

Saccular outpouchings of the colonic wall, most common in the sigmoid colon, are the primary, gross anatomic features of diverticular disease (Austad, 1979; Robbins, 1967; Simonowitz and Paloyan, 1977). A thickened, corrugated bowel wall is a feature in about one-third of colons bearing diverticula. Prevalence of diverticulosis in the general United States population ranges from about 5% of individuals at age 50, to 50% or more at age 80 or older. Uncomplicated colonic diverticulosis is usually symptomless; however, some uncomplicated cases feature abdominal pain and altered bowel habits including diarrhea and/or constipation.

When colonic diverticula develop inflammatory reactions, presumably from fecal impaction and secondary bacterial infection, the condition is known as diverticulitis. It features pain, tenderness, and altered bowel function. When diverticulitis becomes chronic, complications may ensue such as thickening and fibrosis of the bowel wall, sometimes with obstruction, perforation with pericolic abscess formation or peritonitis, or uncommonly, development of pericolic fistulous tracts or massive bowel hemorrhage (Marshak et al., 1980; Robbins, 1967).

Although the etiology of colonic diverticulosis is unknown, a popular hypothesis suggests it is associated with prolonged intestinal transit time, low stool weight, and increased intracolonic pressures which are, in turn, all related to inadequate intake of dietary fiber (Burkitt, 1973a; Burkitt and Trowell, 1975; Painter et al., 1972). Western diets that provide approximately 5 g/d crude fiber are considered fiber-deficient by some authorities (Burkitt, 1978). The hypothesis holds that these effects are
preventable by increasing dietary content of fiber. Additional recent evidence that a low intake of dietary fiber is associated with diverticular disease was presented by Gear et al. (1979), who investigated the prevalence of symptomless diverticular disease in vegetarians and nonvegetarians in southern England. The calculated mean daily fiber intake of the 56 symptomless vegetarians was 41.5 g; that of the 264 patients selected to be broadly representative of the general population, 21.4 g. Twelve percent of the vegetarians had diverticular disease compared with 33% of the nonvegetarians. Similarly, a higher prevalence of diverticular disease in urban than in rural Greece has been reported (Manousos et al., 1977). Intestinal transit times were shorter and stool weights greater in rural Greek populations. Rural inhabitants tended to consume traditional, high-residue diets whereas city dwellers adopted a refined diet.

In view of the reported rarity of diverticular disease in native black Africans, a study by Segal et al. (1977) is of singular interest. Sixteen black Africans ranging in age from 31 to 71 y, who had resided in Johannesburg for over 20 y and had been consuming diets containing highly refined carbohydrates and low levels of fiber were diagnosed as having colonic diverticulosis. Eight of the patients did not eat maize meal, the staple food of the rural South African black, and the remainder ate refined white maize meal. Consumption of fruit was rare, and vegetables were eaten only once per week. Noting a series of prior studies that suggested the rarity of diverticular disease in rural South African blacks, the authors regarded these patients as "... the forerunners of a population group who have almost fully given up their traditional foods and changed from a high to a low residue diet". They considered that these cases confirmed the Painter and Burkitt hypothesis of the etiology of diverticular disease.

However, not all evidence supports this hypothesis. For example, Eastwood et al. (1978a) studied colonic function in 60 untreated outpatients with diverticular disease, and found that stool weights and intestinal transit times were within the same ranges as those in a normal population, raising doubts about the importance of stool weights and intestinal transit times as postulated etiologic factors. The findings suggested that not all diverticulosis cases are attributable to disturbances in colonic motility.

Recent clinical interest has focused on the use of dietary fiber in the treatment of diverticular disease as well as the two rather common problems of irritable colon syndrome and chronic constipation. In striking contrast, a fiber-free, low-residue diet was considered an essential part of conservative clinical management of diverticulosis as recently as 1970 (Mendeloff, 1970). Kelsay's review (1978) of three separate reports of clinical studies involving approximately 130 cases of diverticular disease treated with dietary fiber indicated that symptomatic improvement was reported by a large majority of patients. In addition, intestinal transit times were decreased and stool weights increased in many patients.
However, Brodribb and Humphreys (1976) observed that transit times tended to "normalize" in their patients; that is, to accelerate in those with slow transit times and vice versa. According to Graham and Mettlin (1979), similar effects on transit times were reported by Harvey and associates in 1973, with an additional observation that in subjects with moderate transit times, fiber produced no effect. Two studies were conducted on a total of 82 patients with irritable bowel syndrome. Addition of fiber to the diet was reported to be effective in one study, but not in the other. Kelsay (1978) concluded that the available data on the effectiveness of dietary fiber in alleviating the symptoms of diverticular disease and irritable bowel syndrome were difficult to evaluate, partly because of the self-selected, uncontrolled dietary intakes of the subjects.

Connell (1978b) noted that the ability of some types of natural fibers to increase stool bulk and reduce intracolonic pressures together with the fiber-deficiency theory of diverticulosis formed the basic rationale for the use of fiber in treating diverticular disease and irritable bowel syndrome. He stated, "It seems reasonable to treat persons with irritable bowel, constipation, and mild forms of diverticular disease with increased amounts of dietary fiber." However, he observed that, "No satisfactory explanation of the mechanism of the possible beneficial effects of fiber in disease states has emerged."

Spiller et al. (1978) reviewed clinical studies of diverticulosis and concluded that, while "no final conclusion on the correlation of diverticular disease and plantix (dietary fiber) is possible at this time, it appears that plantix has a favorable effect in the prevention as well as in the relief of the disease." An editorial in The Lancet (Anonymous, 1978) stated that, although the question of fiber deficiency as the cause of diverticular disease remains to be answered, the number of operations done for uncomplicated diverticular disease has decreased markedly since the "dietary-fibre boom".

Brodribb (1977) treated nine patients who had uncomplicated, symptomatic diverticular disease by substituting bran crispbread (containing about 6.7 g dietary fiber) for ordinary bread in the daily diet. As compared with a control group of patients who consumed wheat crispbread (provided about 0.6 g dietary fiber daily), relief of symptoms was significantly greater in the bran-consuming group, and the effectiveness of the bran treatment increased during the 3-month period of the study.

Results of studies that are not well controlled are frequently difficult to interpret with certainty. Devroede (1978) described studies that showed no significant differences in ranges of stool weights when normal human subjects consumed diets containing 14.4 g crude fiber or fiber-free diets; however, stool frequency decreased when subjects consumed fiber-free, elemental diets. He found the limited data on the effects of dietary fiber on bowel
habits of healthy persons to be inconsistent. In addition, he emphasized the importance of the placebo effect in dietary studies, noting a recent study in which wheat bran was reported to relieve symptoms of irritable bowel syndrome in 52% of patients in a double-blind trial, while a placebo resulted in improvement in 65% of the control group. In a preliminary survey of a random trial of the effects of wheat bran on diverticular disease, 50% of the patients reported subjective improvement while taking a placebo.

Thus, colonic diverticulosis occurs most often as a symptomless, benign alteration of the large bowel featuring saccular herniations of the bowel wall, particularly in the sigmoid colon. However, it may become symptomatic and lead to dangerous bowel complications in a small percentage of cases. Of unknown etiology, its prevalence is high in older persons. The popular hypothesis that fiber deficiency results in diverticulosis is based primarily on global epidemiologic data that correlate low-fiber diets with an increased prevalence of the disease. Presumed etiologic factors thought to be associated with low-fiber intakes are prolonged intestinal transit time, low stool weight, and increased intracolonic pressures. Results of studies aimed at demonstrating a causal relationship between disturbances of colonic motility and the development of diverticulosis are equivocal. On the other hand, dietary fiber supplements taken by patients with symptomatic diverticulosis seem to have alleviated symptoms in a majority of reported clinical studies. The significance of such studies is difficult to assess because of such factors as the placebo effect and lack of dietary controls.

The participants at the LSRO ad hoc meeting tended to link irritable bowel syndrome, chronic constipation, and diverticular disease together in a time continuum measurable in years. Although diverticulosis of the colon is clearly associated with advancing age, more cases have recently been identified in persons under 50 years of age. While it was generally agreed that the epidemiologic evidence associating diverticular disease with low-fiber diets should not be ignored, a causal relationship has not been proved. At best the evidence is equivocal. Some participants with experience in conducting nutrition surveys in the field questioned the reliability of data from certain underdeveloped countries, and cited gross inadequacies of morbidity and mortality data even in countries with relatively sophisticated medical care systems. Others noted the futility of attempts to derive the prevalence of diverticular disease in Western societies by extrapolation from clinical studies of patients with irritable colon and painful diverticular disease. However, most of the participants were of the opinion that colonic diverticulosis is widespread in Western societies and that it was rare in these societies until some time in the 20th century.

Studies suggest that a great majority of people with colonic diverticulosis have no symptoms, have normal intracolonic pressures, and do not have thickened bowel walls. Inconsistencies
abound in the results of recent clinical trials of dietary fiber in treating diverticular disease, and of related clinical studies -- lack of correlation of elevated intracolonic pressures and/or colonic muscle thickening with the presence or absence of symptoms in diverticular disease; failure to relate stool bulk to diverticular disease; and confusion about the significance, if any, of intestinal transit times in the etiology of diverticular disease. Difficulties of conducting meaningful clinical studies were cited such as the placebo effect of different diets and the fact that, even in clearly diagnosed cases of irritable bowel syndrome and symptomatic diverticular disease, symptoms tend to fluctuate, and patients usually are asymptomatic part of the time in the absence of any treatment.

The participants noted a lack of accurate dietary-fiber consumption data in the United States, but judged that average daily intakes may be between 10-20 g while vegetarians may consume about twice that much. Although recommended doses vary among clinicians, 25 g total dietary fiber daily was suggested as a target dose for maintaining normal bowel function. Finally, there was concern that some people who have been consuming ample quantities of dietary fiber may now be ingesting too much as a result of promotional advertising of fiber-supplemented foods. This is particularly important for patients on certain types of medication (see page 24). However, the notion that some Americans may be consuming excess fiber as a result of commercial promotion was not unanimous.

Low-fiber diets may have metabolic or endocrine effects that might lead to disorders of the gastrointestinal tract, and increases in dietary fiber may modify such influences. An unpublished study was mentioned in which the administration of dietary fiber caused a significant decrease in the postprandial levels of vasoactive intestinal polypeptide. Gastric inhibitory polypeptide is a potent inhibitor of gastric secretion and motility. In contrast, vasoactive intestinal polypeptide is a potent stimulant of intestinal secretion and motility (see also Morgan et al., 1979, page 25). It remains to be clarified whether the effects of dietary fiber on transit time and intestinal motility are direct effects or secondary to changes in gastrointestinal hormones and whether disturbances in gastrointestinal motility, which may be associated with irritable bowel syndrome and diverticular disease, are consequences of disturbances in gastrointestinal hormones.

Thus, the scientific evidence on whether low-fiber diets contribute to the development of diverticular disease remains equivocal. However, the results of numerous clinical trials seem to support the use of added dietary fiber for persons on low fiber intakes who are suffering from irritable colon, chronic constipation, or symptomatic diverticular disease. Dietary fiber may influence other, unknown environmental or intrinsic factors that may indeed be causally related to the etiology of diverticular disease. In view of the marked differences in distribution of diverticular disease in different populations, the likelihood
that some dietary component is the source of the difference, and the known effects of dietary fiber on colonic function, investigation of dietary fiber appears a logical approach to elucidation of the etiology of diverticular disease and in therapy of the irritable bowel syndrome.

B. CANCER OF THE COLON

The most common internal cancer among Americans is large bowel (colon and rectum) cancer. In 1977, it accounted for approximately 110,000 new cancer diagnoses and about 50,000 deaths per year (Anonymous, 1977a), more recently, in excess of 116,000 new cases and more than 52,000 deaths annually (Texter, 1981). Cancer of the colon was said to cause about 20% of all deaths from malignant diseases in the United States (LaMont and Isselbacher, 1977). The peak incidence of colonic cancer occurs in persons in the age range 40–70 y. Liu et al. (1979) reported the mortality rate from colonic cancer in the United States averaged 36.4 deaths per 100,000 per year among persons in the 35–74 y age range. The American Cancer Society (Anonymous, 1977a) estimated the 1977 mortality from cancer of the colon and rectum to be 15% of all cancer deaths in women and 12% in men. Burkitt (1971) reported a low, age-adjusted incidence of colonic cancer in men in rural Africa; for example, 3.5 cases per 100,000 per year in Uganda, but a high incidence in Western Europe and the United States, with a maximum of 57.8 cases per 100,000 per year in Connecticut. During the period 1940–1973, age-adjusted incidence rates per 100,000 Connecticut men and women rose from 32.7 to 48.4 cases (Snyder et al., 1977).

About 15% of all colorectal cancer occurs in the cecum or ascending colon, 10% in the transverse, and 75% in the descending colon, sigmoid, and rectum. By far the most common type of large bowel cancer is the adenocarcinoma (LaMont and Isselbacher, 1977).

1. Hypotheses on cancer of the colon

The etiology of large bowel cancer is unknown. Mendeloff (1979) has estimated that less than 5% of colonic cancers have a genetic basis; however the number of investigations of familial occurrence of colonic cancer is limited. The prevalence of adenomatous polyps of the colon, considered to be precursors of cancer by some authorities, ranges from 2 to 15% of adult Americans, but the incidence is unknown. Although the question has been controversial, some experts regard adenomatous polyps as neoplasms that are destined to become malignant (LaMont and Isselbacher, 1977; Riddell, 1981). Results of an ongoing bowel-cancer screening project in about 7500 asymptomatic people indicate that 16% of 160 persons with positive occult blood tests had early, asymptomatic colon or rectal cancer (Texter, 1979, 1981).
Burkitt (1978) believed there was a constant positive relationship between the prevalence of colon cancer and the economic development and cultural characteristics of Western societies. He stated, "Its prevalence is invariably lowest in communities where the traditional way of life has altered minimally and is highest in affluent Western societies." Studies of migrant groups suggest the variation in colon cancer prevalence is probably not related to genetic differences; that is, colon cancer frequency in such groups tends toward that of their adopted locale (Sherlock et al., 1980).

Many experts agree that the etiology of colonic cancer is probably multifactorial, and that the causal agents are environmental (Burkitt, 1978; Gori, 1979; International Agency for Research on Cancer, 1977; Mendeloff, 1979; Sherlock et al., 1980; Spiller et al., 1978). Environmental factors have been described as those originating largely outside the host's body, and may include nutrition, carcinogens, cocarcinogens, procarcinogens, promoters, and other potentially toxic substances (Visek et al., 1978).

One of the two principal current hypotheses on the etiology of colonic cancer is based on dietary fiber deficiency. As in the case of diverticular disease of the colon, epidemiologic evidence such as that reported by investigators in Africa, India, and Israel (Burkitt, 1978; Burkitt et al., 1974; Malhotra, 1974; Modan et al., 1975) forms the main basis for the concept that fiber-deficient diets are associated with excessive prevalence of large bowel cancer. This is supported theoretically, to some extent, by results of studies of the effects of dietary fiber on stool bulk, intestinal transit time, colonic microflora, and excretion of bile acids and associated sterols. However, the International Agency for Research on Cancer (1977) noted:

The dietary-fibre deficiency hypothesis (Burkitt, 1971) postulates that a refined diet, low in fibre, leads to slow intestinal transit-time, reduced faecal volume, and increased concentration of carcinogens. So far there has been little supportive evidence.

The other major hypothesis (Hill, 1975), suggests that high dietary fat may facilitate growth of intestinal bacteria which are capable of converting dihydroxy-bile acids to carcinogenic polynuclear hydrocarbons. There is no experimental evidence to indicate that dihydroxy-bile acids undergo bacterial metabolic conversion to carcinogenic polynuclear hydrocarbons (Reddy et al., 1975). If this hypothesis is correct, levels of fecal bile acids could affect the risk of colonic cancer. Both hypotheses require rigorous experimental testing (Story and Kritchevsky, 1980). However, Reddy and coworkers (1975) have theorized that high-fat diets enhance the production of bile acids, some of which have been shown to act as colon tumor promoters.
Postulated mechanisms whereby dietary fiber could reduce the risk of colonic cancer involve a reduction of colonic mucosal exposure to carcinogens by such properties as adsorption and/or dilution of carcinogens (the chemical-binding, water-holding, stool-bulking capacities); shortened colonic transit times; direct modification of bile-acid metabolism; and metabolic alteration of bacterial flora so as to decrease conversions of dihydroxy-bile acids to carcinogenic polynuclear hydrocarbons (Gori, 1979; Huang et al., 1978; Reddy et al., 1978; Story and Kritchevsky, 1980). In addition, participants in the ad hoc study group suggested the following properties of dietary fiber might influence colonic carcinogenesis: antitoxic effects including direct action on carcinogens, cocarcinogens, promoters and precursors, acidulant effect, chelating effect, cation exchange capacity, and interference with free radical formation. The chelating property of fiber may decrease the ability of procarcinogens or proximal carcinogens to interact with the colonic epithelium.

2. **Influence of dietary fiber on colonic carcinogenesis**

   a. **Epidemiologic data**

   Notwithstanding certain methodologic difficulties, several dietary case-control studies and other investigations suggest a low colonic cancer risk for persons who consume relatively high-fiber diets (Dales et al., 1979; Graham and Mettlin, 1979; Graham et al., 1978; International Agency for Research on Cancer, 1977; Modan et al., 1975; Phillips, 1975; Reddy et al., 1978).

   Modan and his associates (1975) compared the dietary histories of 198 Israeli colonic-cancer patients with those of two matched control populations: a neighborhood group and a hospital noncancer surgical group. Fiber consumption (diets with at least 0.5% fiber) was significantly lower in the cancer patients. According to the authors, these data lend support to the hypothesis that low-fiber diets influence the etiology of colonic cancer.

   Bjelke (1973) found a relatively low frequency of vegetable consumption in the dietary histories of colon and rectal cancer patients in Minnesota and Norway. Similar results were reported by Graham et al. (1978), who studied the dietary histories of 470 colon and 512 rectal cancer patients and 1411 control subjects who were noncancer patients. Frequent consumption of vegetables, particularly cabbage, Brussels sprouts, and broccoli, was associated with decreased risk of colorectal cancer. These findings were consistent with experimental results in which the carcinogenicity of chemicals such as dimethylenbenzanthracene and benzo(a)pyrene was inhibited by feeding these and other cruciferous plants to laboratory animals (Wattenberg, 1971; Wattenberg and Loub, 1978; Wattenberg et al., 1976; Welsburger, 1979). These studies have led to an hypothesis for the etiology of colon cancer that inducers of aryl hydrocarbon hydroxylase activity, including natural indoles in cruciferous plants, initiate a metabolic barrier
to noxious chemicals in the tissues of the major portals of entry including the alimentary canal (Wattenberg et al., 1976). This protective effect is not directly related to the fiber content of cruciferous plants and other vegetables and fruits which contain inducers of aryl hydrocarbon hydroxylase activity (Weisburger, 1979). Participants at the ad hoc group meeting noted that cruciferous plants are also known for their production of goitrogenic substances, but they drew no inference from this observation.

Data from a comparative study of dietary patterns and fecal characteristics in a high-colonic-cancer-risk Danish, and a low-risk, rural, Finnish population indicated higher intakes of dietary fiber and milk in the low-incidence area, thus suggesting a possible protective effect (International Agency for Research on Cancer, 1977). Intestinal transit times were not correlated with colonic cancer incidence. A study of 99 black, San Francisco Bay area adults with colonic or rectal cancers indicated that they tended to report less frequent consumption of foods containing at least 0.5% crude fiber than control subjects who comprised three sets of matched controls per cancer patient (Dales et al., 1979). In addition, more colon cancer patients reported eating high-saturated-fat, low-fiber foods (> 5% saturated fat, < 0.5% crude fiber) than controls. Lyon (1978) emphasized the importance of the cited reports by Dales and Modan and their colleagues (see page 36) in terms of careful assessment of dietary fiber as a variable.

In a case-control study of colon and breast cancer, Seventh-Day Adventists consuming lacto-ovo-vegetarian diets had fewer colon cancers than those whose diets included beef, lamb, or a combined group of highly saturated-fat foods consisting of cheese plus cheese and eggs plus all meats and poultry (Phillips, 1975). However, the negative association with colon cancer of the lacto-ovo-vegetarian group was not statistically significant.

Dietary factors and certain fecal characteristics of a New York City area population with a high risk of colon cancer were compared with those of a low-risk group in rural Finland (Reddy et al., 1978). While mean daily intakes of fat and protein were comparable in the two groups, more of the fats were derived from dairy products and dietary fiber intakes were higher in the Finnish diets. Stool weights and frequency as well as fecal excretion of fiber, bile acids, neutral sterols, bacterial β-glucuronidase, and nuclear dehydrogenase activities were reported. The data suggested that reduced bile acids in the feces would be accounted for by dilution resulting from the bulking effect of the fiber in the Finnish diets.

Other investigations do not necessarily support the association of fiber-deficient diets with increased prevalence of colonic cancer. For instance, Hill et al. (1979) reported that large bowel cancer mortality rates per 100,000 Hong Kong residents per year in the age range 35–64 y were more than twice as great in patients from the highest, compared with those from the lowest,
socioeconomic groups. The high-income group consumed more food of all types, including high-fiber foods, than those in lower-income groups.

Modan's (1977) review of the problems of scientific investigation of the role of diet in the etiology of cancer listed the following criticisms of dietary case-control studies: inaccurate information based on deficient recall, poor estimates of dietary quantities, inability to specify the diet at the time of origin of the carcinogenic process, and difficulty in determining adequate control cases. Graham and Mettlin (1979) reviewed the capabilities and limitations of various techniques of measuring dietary habits, and concluded that, while diet interviews and questionnaires have proved useful, few large scale studies of their validity have been conducted.

With regard to possible effects on the large bowel of urbanization, cultural change, and Westernization of diet among South African blacks (Segal et al., 1977), the statement of Walker (1978) is of interest: "... the true frequency of colon cancer in urban blacks is very low and is not increasing." He suggested that an unrecognized protective factor is prevalent among urbanized South African blacks that affects susceptibility to colon cancer and appendicitis.

Bowel transit time studies aimed at exploring the concept that prolonged transit times are involved in the etiology of colonic cancer have yielded divergent results. Despite shorter transit times, Japanese Hawaiian men (nisei) had the same risk of developing large bowel cancer as Caucasian Hawaiian men of the same age (Glober et al., 1974). The authors concluded that bowel transit times did not appear to be related to the etiology of colonic disease in their 63 nisei and 23 Caucasian subjects. In an extension of these studies, Glober et al. (1977) found similar bowel transit times in native Japanese men who were reportedly at low risk for developing colonic cancer, and Hawaiian nisei men. Mower et al. (1979) indicated that ratios of primary/secondary fecal bile acids in native Japanese and Hawaiian Japanese were the same, suggesting similar modes of metabolism. Glober et al. (1977) reported the unexpected finding that stool weights of the nisei men were lower than those of the native Japanese, leading to speculation that a possible bowel transit-time factor in Hawaiian nisei men, independent of stool weight, might act directly on the intestinal mucosa or on secretion of enteric hormones which regulate intestinal water balance and motility.

In summary, most of the epidemiologic information on which the fiber-deficiency theory is based was derived from national and international demographic correlations and qualitative circumstantial relationships. Despite the simplicity, logic, and common sense of the fiber-deficiency theory, the supporting data tend to be incomplete. Case controls are lacking, and generally it has not been feasible to evaluate the possible influences of a number of variables that may affect cancer susceptibility such as race,
cultural or ethnic background, lifestyle, and physiologic and psychologic stress factors, as well as the presence of parasitoses and impaired or marginal nutrition. Thus, while the epidemiologic evidence supporting the fiber-deficiency theory cannot be ignored, it should be regarded cautiously in terms of a suggested causal relationship.

However, at least six recently reported case-control studies, some of which included extraordinary attempts to obtain reliable dietary fiber intake data, indicated an inverse relationship between amounts of fiber in the diet and the prevalence of colonic cancer. Moreover, a majority of participants in the LSRO meeting agreed that most of the epidemiologic evidence and the results of carcinogenesis studies in animals strongly suggest that dietary fiber exerts some type of a protective effect against colonic cancer.

b. Animal models of human colonic cancer

Rats and other laboratory animals given known chemical carcinogens parenterally develop tumors of the colon and rectum (Newberne and Rogers, 1973; Weisburger et al., 1977). Among the known carcinogens tested on animal models are 1,2-dimethylhydrazine (DMH), azoxymethane, methylazoxymethanol acetate, 3,2'-dimethyl-4-aminobiphenyl, and 3-methylcholanthrene (the latter in hamsters). Others, given intrarectally, can act directly on the bowel mucosa to induce cancer; examples are N-methyl-N'-nitro-N-nitrosoguanidine and methylnitrosourea (Reddy et al., 1975).

Many recent reports from animal studies indicate that dietary fiber influences the carcinogenesis of known chemical carcinogens (see Sections VII and VIII, pages 55-74). An example is the study of Bauer et al. (1979), who investigated the effect of wheat bran, carrot fiber, or citrus pectin on induction of colorectal tumors following subcutaneous injections of DMH in rats. Groups of rats were fed a fiber-free diet or diets containing wheat bran from 3 d prior to the first DMH injection until 14 d after the last injection. They were then transferred to standard rat-pellet diet for about 10-12 wk before sacrifice. The frequency of colorectal tumors was high in all groups including the basal diet control group, but considerably higher in the animals fed the pectin-supplemented diet. Differences in tumor frequency of the bran, carrot fiber, and control groups were not significant. However, it is possible in this study that not only the high tumor yield, resulting from large doses of DMH, but also a switch from the high-fiber diet to low-fiber standard diet during the post-carcinogen period failed to show any protective effect of fibers tested.

These results differed from those in several previously reported studies that showed a protective effect of fiber. Fleiszer et al. (1978) found that increasing amounts of fiber in the diet [rat chow (sic) 5 g, special chow (sic) 15 g, or bran fiber 28 g/100 g diet] reduced the frequency of DMH-induced colon carcinomas.
that was inversely proportional to the levels of fiber intake compared with rats consuming a fiber-free, chemically-defined diet (Flexical®). In similar experiments, Freeman et al. (1978) found that fewer rats injected subcutaneously with DMH and fed diets containing highly purified microcrystalline cellulose developed colonic neoplasia (and with a lower frequency per animal) than did rats similarly treated but fed a semipurified, fiber-free diet. Thirty percent of the group fed cellulose had grossly detectable tumors compared with 70% of those not consuming cellulose. The protective effect was apparently time dependent because differences in tumor frequency between the two experimental groups did not become statistically significant until the final 8 wk of the 44-wk study. The cellulose-fed group showed an apparent proximal to distal shift in tumor distribution. The authors concluded, "This study strongly supports the hypothesis that fiber is an important protective agent against colonic neoplasia development."

Some members of the ad hoc group were critical of many animal studies, primarily because the protocols lacked uniformity, precluding direct comparisons among tests. The aggregate of animal-model colorectal cancer studies was described as uninterpretable because of divergent results; in many cases experimental variables differed so much among studies that useful comparisons often could not be made. Such factors as the following were cited: control of the quantity of carcinogen administered, animal strains, numbers of animals, background diet, type, dose, and route of administration of the carcinogens, duration of experiment, and types and amounts of dietary fiber fed. There is an urgent need for animal-model studies to be standardized to the greatest feasible extent.

Nevertheless, there is good evidence that some types of dietary fiber protect against chemically-induced colon carcinogenesis in the animal model. A key question is whether any of the results in the animal studies approximate the human response. Whether it will be possible to extrapolate such results accurately to humans is unknown. However, the animal model is useful to investigate mechanisms of carcinogenesis, possible interactions between chemical carcinogens and components of dietary fiber, and dietary fiber inhibition of large-bowel carcinogenesis.

c. Dietary fiber-colonic flora interactions

It has been estimated that the contents of the human colon contain from 200 to 400 billion bacteria per gram, comprising 400 to 500 different species, mostly obligate anaerobes, with greatly differing metabolic activities (Moore, 1978). A basic assumption about the fecal flora has been that it represents only the luminal colonic flora, excluding the flora associated with the mucosal epithelial surfaces (Bornside, 1978).

Because of marked technical difficulties, only preliminary analysis of the effects of the intestinal flora on the physiology and nutrition of the host and on caloric and nutrient sources in the intestine has been accomplished. Indeed, some microbiologists
are convinced that searching for differences in species or genus in the quest for causal relationships with colonic carcinogenesis is unproductive; they suggest that studying metabolic activities of fecal material is more likely to yield useful data (Moore et al., 1978).

An important part of the fiber deficiency—colon cancer hypothesis is the concept suggested by Aries et al. (1969) that colonic bacteria may convert bile salts to potential carcinogens or cocarcinogens. These investigators postulated that carcinogen-producing bacterial species depend upon a high-fat diet and elevated bile acid concentrations in the bowel, factors which would disappear as a result of low-fat, high-fiber diets. Enzyme studies of cultures of intestinal bacteria have detected dehydrogenases that convert sterols to compounds similar to known chemical carcinogens and cocarcinogens (Moore et al., 1978).

Some components of dietary fiber undergo bacterial degradation in the digestive tract (Williams and Olmstead, 1936), yielding such products as soluble sugars, short-chain fatty acids, methane, hydrogen, carbon dioxide, and alcohols. Disappearance of pectin and structurally similar, soluble fibers is nearly complete during passage through the alimentary canal (Anderson and Chen, 1979; Cummings, 1976); digestion of hemicellulose varies between 56–80%, and cellulose was about 40% (Cummings, 1976); however, the lignins and chitins are essentially indigestible (Van Soest, 1978). The products of microbial action on the degradable fiber fractions probably play a role in establishing the microbial environment of the lower digestive tract (Van Soest, 1978). Savage (1978) suggested that dietary fiber may affect the gut flora inhabiting the epithelial surfaces by altering peristaltic rate, amount and composition of mucus, oxygen tension, oxidation-reduction potential, and by providing nutrients.

Supplements of raw cabbage or alfalfa holocellulose fed to weanling guinea pigs for 28 d resulted in abundant growth of fusiform-type organisms in the small intestines and ceca compared with an infrequent occurrence of fusiforms in the basal diet controls (Knehans and O'Dell, 1980). Large quantities of mucus observed on the intestinal epithelia of the controls were nearly eliminated by the cabbage supplement. In addition, alfalfa and alfalfa holocellulose supplements appeared to have stripped off some microvilli and occasionally to have punctured a villus.

Finegold and Sutter (1978) reviewed the literature on the influence of relatively short-term (1 mo or less) dietary manipulation on the fecal flora. They concluded that the flora tends to be constant despite such nutritional interventions as starvation; administration of fiber-free, defined-formula, vegetarian, or nonvegetarian diets; and administration of ordinary diets supplemented with bran, pectin, guar, plantains, or other bananas. From a review of recent literature on the effects of diet on human fecal flora, Bornside (1978) concluded that neither fiber-free nor
fiber-supplemented diets altered the major groups of bacteria or their numbers (per gram of feces), but daily fecal mass is approximately doubled with added dietary fiber (banana, plantain, bran), and is halved in the absence of fiber (chemically-defined, liquid diets). It has been estimated that about half the human fecal mass consists of bacterial cells (Moore, 1978).

Finegold and Sutter (1978) noted a lack of knowledge of the mucosa-associated flora in man, and that significant changes in metabolic activity of intestinal bacteria may occur in response to dietary manipulation, without accompanying changes in the bacteriolog of the fecal flora. For instance, polysaccharide-degrading enzymes from several Bacteroides species from the human colon were mostly inducible rather than constitutive (Salyers et al., 1978), suggesting that the metabolism of the flora could be altered by the amount and type of fiber in the diet but without a change in the composition of the flora. Statistically significant differences have been found in the frequency of certain organisms or groups of fecal organisms in various populations around the world, reportedly at high or low risk of developing colonic cancer (Bornside, 1978). However, the results of such studies have not been fully confirmed, and the significance of these differences in terms of the etiology of colonic cancer has not been established.

Goldin et al. (1976, 1978) studied the effect of dietary variation and age of the test animal on fecal bacterial enzymes that have been implicated in the etiology of colon cancer. Activities of β-glucuronidase, azoreductase, and nitroreductase increased 1.5- to 2.5-fold in young male Fischer rats within 20 d on a high-beef diet, and a further increase of β-glucuronidase activity on this diet was observed in rats over 20 mo of age. Grain-fed rats 8-14 mo of age had increased levels of all three enzymes compared with levels in the same animals at 10-18 wk of age. Human subjects consuming mixed, Western style diets supplemented with 30 g defatted wheat bran or wheat germ daily showed no significant changes in fecal enzyme activity compared with activities measured in the pre- and postsupplemental test periods (Goldin et al., 1980).

In additional human studies in the same laboratory, the effect of diet and Lactobacillus acidophilus supplements on human fecal enzymes known to catalyze reactions that may lead to proximal carcinogens was determined (Goldin et al., 1980). Omnivorous subjects had higher fecal levels than vegetarians of β-glucuronidases, nitroreductase, azoreductase, and steroid α-dehydroxylase. Removal of red meat or addition of bran or wheat germ for 30 d did not affect levels of these enzymes except for a decrease in steroid α-dehydroxylase. Supplements of viable L. acidophilus reduced β-glucuronidase and nitroreductase activities.

Reddy and Wynder (1973), Reddy (1975), and others have reported a positive correlation between fecal steroid metabolite concentrations and risk of human colon cancer. However, there is evidence that certain human intestinal bacteria produce specific
steroid dehydrogenases. These types of bacteria are as frequent in populations with low colonic cancer risk as in high-risk groups (Moore et al., 1978). The total metabolic activity of bacteria in dehydrogenation and dehydroxylation of steroids is a more significant factor in colonic carcinogenesis than determination of individual strains of bacteria that have the capacity to modify steroids. Moore et al. (1978) noted that other intestinal microbial products that have been suggested as possibly carcinogenic, cocarcinogenic, or procarcinogenic include indole, skatol, amines, and branched-chain alcohols; as with the steroid degradation products, their possible role in the etiology of colon cancer has not been established.

In summary, the recent literature on relationships between the fecal flora and cancer of the colon suggests that while differences in the frequency of certain bacteria and bacterial groups have been identified in members of populations with high and low risks of colon cancer, such observations have not been confirmed and their significance is unclear. Various severe dietary interventions can alter the concentrations of the fecal flora, but it tends to remain qualitatively stable. Neither fiber-free nor fiber-supplemented diets change the major groups of colonic bacteria, but these diets change the metabolic activity of colonic bacteria as indicated by changes in the activity of key enzymes. Despite reports of positive correlations between fecal steroid metabolite concentration and risk of human colon cancer, the frequencies of those human intestinal bacteria that produce specific steroid dehydrogenases are similar in populations with low and high risk of cancer of the colon.

Unpublished data presented at the meeting indicate that a low-fat diet supplemented with 30% beef fat, fed to rats resulted in a two-fold increase in fecal β-glucuronidase, nitroreductase, and an azoreductase compared with activities of these enzymes in animals fed low-fat diets. β-Glucuronidase was selected because many toxic compounds, including many carcinogens, are conjugated with glucuronic acid in the liver. A certain percentage of these, especially polyphenyl compounds, are secreted in the bile, depending on their aglycone structure. These are then deconjugated in the intestine to form potential carcinogens or carcinogen precursors. Similar data were reported by Reddy et al. (1977).

There is some evidence that substrates from certain fiber sources are essential for the growth of certain bacteria (Collings and Yokoyama, 1980). This and other observations (see Lectins, page 6) suggest that additional studies are warranted on the mechanism of bacterial attachment to dietary fiber substrates.

Participants in the ad hoc meeting noted that vegetarians have low levels of fecal floral enzymes that are associated with carcinogenicity in experimental animals, such as β-glucuronidase, nitroreductase, and an azoreductase. However, studies from microbiologists actively engaged in research in the fiber field have not led to any clear conclusions relating colonic cancer risk to quantitative and qualitative aspects of the flora.
Some members of the ad hoc group believed that, despite major technical problems, investigations of diet-induced metabolic alterations of the colonic flora appear more promising than taxonomic identification of the flora in determining relationships between dietary fiber (and other dietary components) and colonic cancer. However, other members recommended continuing bacteriologic investigations of associations between fecal flora and colonic cancer, and Moore et al. (1978) observed, "... if and when significant metabolic products or activities are discovered, we will want to know which bacteria are responsible." It is of interest that while the great majority of colonic microbial inhabitants are bacteria, other microorganisms are known to be present. Their role in interactions with dietary fiber is essentially unknown.

d. Dietary fiber, bile acids, and sterol excretion

Dietary fiber influences bile acid excretion although the reported effects are not easily summarized because of inconsistencies in experimental results (Story and Kritchevsky, 1980). In 3-wk, adult, human feeding studies: (1) diets supplemented with 16 g bran per day resulted in increased fecal acidic steroid excretion; after returning to their controlled diet, the subjects excreted increased amounts of secondary bile acids (Eastwood et al., 1973); (2) 36 and 40% increases (neither statistically significant) in neutral and acidic fecal steroid excretion occurred after 36 g bran daily (Jenkins et al., 1975); and (3) no change took place in fecal neutral steroid, but a slight reduction of acidic steroid excretion occurred after 3 wk of 39 g bran per day; however, the same subjects showed a 50% increase in acidic steroid excretion during 12 wk of sugar cane bagasse dietary supplementation (McLean Baird et al., 1977). Increases in fecal bulk resulting from such dietary fiber supplementation may mask the true concentrations of total acidic fecal steroid excretion (Story and Kritchevsky, 1980).

Dietary fiber can affect the relative sizes of the bile salt pools not only in the colon, but in the ileum and jejunum as well (Story and Kritchevsky, 1978). The adsorption affinities of most of the bile acids and bile salts in humans vary markedly with different types of dietary fiber sources and components such as alfalfa, bran, lignin, and cellulose (Story and Kritchevsky, 1976). Interactions among the bile salts, dietary fiber, and the intestinal flora are considered responsible, at least in part, for the observed changes.

Kay and Truswell (1977) reported that human subjects consuming carefully formulated and controlled diets supplemented daily with 15 g citrus pectin for 3 wk demonstrated 44, 17, and 33% increases in fecal excretion of fat, neutral steroids, and bile acids, respectively. Excretion of fecal bile acids and total steroids increased in nine nonlipidemic and hyperlipidemic subjects whose diets were supplemented with 40-50 g pectin per day (Miettinen and Tarpila,
1977). Inconsistent decreases in fecal secondary bile acids and sterols occurred. The authors suggested that the observed serum cholesterol reduction by pectin was caused by increased cholesterol elimination as fecal bile acids.

Ullrich et al. (1980) reported that, in human volunteers fed normal foods of high- or low-fiber content, high-fiber diets (41 g/d NDF) resulted in no change in neutral fecal steroids (cholesterol and coprostanol) and total steroids whereas the percent of primary bile acids (chenodeoxycholic and cholic) increased markedly. The secondary bile acids, lithocholic and deoxycholic acids, decreased during the high-fiber diet. The authors suggested, as other investigators had done previously (Kritchevsky et al., 1974), that fiber binds bile acids, decreasing conversion of primary to secondary forms and increasing fecal steroid excretion.

In recent animal studies, rats fed a cholesterol-supplemented diet containing softwood lignins showed less absorption of taurocholic acid than animals given extra cellulose; however, the lignin diet did not lower serum or liver levels of cholesterol (Chang and Johnson, 1978). Yorkshire swine were fed for 2-wk periods diets containing 1 g cholesterol, added fat, and one of the following dietary fiber sources: hog mash (10% fat), wheat bran cereals (10-40% fat), or Alphacel® (40% fat) (Kim and Lee, 1980). The wheat-bran-containing diets resulted in markedly less fecal excretion of neutral and acid steroids than did mash; the effect of Alphacel® was similar to that of the bran. Steroid excretion was significantly less in the high-fat/bran group than in the other bran groups.

After consuming a semipurified diet supplemented with 1% cholesterol for 4 wk, young male rats were fed cholesterol-free diets with no dietary fiber or with 5% pectin (Thomas et al., 1980). During cholesterol feeding, liver cholesterol increased more than four-fold compared with control values (14.86 ± 2.74 vs 3.72 ± 0.34 mg/g). After 2 wk of cholesterol-free diet, liver cholesterol declined to 4.47 ± 0.25 mg/g in the pectin-fed and 5.31 ± 1.12 mg/g in the fiber-free groups; however, after 8 wk, there was no significant difference in liver cholesterol between the two groups. Fecal bile acid excretion was greater in the pectin-fed group during the first 2 wk of cholesterol-free diet. The authors noted that the removal of tissue cholesterol was apparently accelerated via a pectin-induced increase in fecal bile acid excretion.

In other studies, male Sprague-Dawley rats were fed basal diets supplemented with various sources of dietary fiber to compare their effects on fecal bile acids, sterols, and fatty acids (Peifer and Karp, 1978). Analyses of 3-d pooled fecal samples from each rat, taken near the end of the 43-d test period, indicated that pectin and pectin-rich citrus pulp promoted the highest excretions of total and primary bile acids, and of neutral sterols. Soy hulls promoted less excretion of neutral sterols. Total fecal bile acids were not influenced by soy or rice hulls or wheat bran.
Participants in the LSRO meeting agreed that increased intake of dietary fats leads to higher levels of bile acids in the colon, and that there is some evidence that bile acids may promote colonic cancer in experimental animals. It is possible that the promotion of colonic cancer with bile salts can occur independently of interactions of the bile acids with the colonic flora.

Finally, it was suggested that one should not overlook the possibly abnormal or adverse effects of dietary fiber such as delayed gastric emptying, interference with bioavailability of some essential minerals via its mineral-binding and ion exchange properties, adsorption and slowed or reduced absorption of therapeutic drugs, volvulus with intestinal obstruction, reduction in food intake as a result of its bulking effect, and intestinal irritation. In addition, there is evidence that bile salt-binding substances such as cholestyramine fed to rats at a level of 2% of a fiber-free diet result in erosive damage to the enterocytes that occupy the tips of the jejunal and colonic folds (Cassidy et al., 1980). This epithelial damage apparently includes disruption of the continuity of the mucosal barrier, and has been correlated with increased risk of chemically induced colon cancer in rats. Other data suggest that the dietary fiber-bile acid "unit" damages the colonic mucosa of rats in direct proportion to the bile acid-binding capacity of the fiber (Kritchevsky et al., 1980). The significance of these findings in terms of human tolerance for dietary fiber remains to be elucidated.

While dietary fiber influences bile acid excretion, inconsistencies in experimental results make summarization difficult; however, most recent studies suggest that excretion of fecal acid steroids and, less frequently, of neutral steroids tends to increase in experimental animals and humans given diets supplemented with various dietary fiber sources or components. Adsorption affinities of most known bile acids and bile salts vary markedly with different fiber sources. Dietary fiber affects the size of bile-salt pools in both the small and large bowels. While this review is not directly concerned with the lipidemias, recent studies with rats consuming cholesterol-supplemented diets show that lignins added to the diet do not reduce serum or liver cholesterol concentrations while pectins seem to retard cholesterol accumulation in the tissues.

Notwithstanding the suggestive epidemiologic and animal model data, the question of whether dietary fiber protects against human colonic cancer remains debatable; some investigators have produced scientific evidence that it does; others maintain that adequate data to support this concept are not available. Future investigations may show that dietary fiber by itself, or in combination with other exogenous or endogenous substances, has a significant role in preventing large bowel cancer.
V. CONCLUSIONS

ANALYSIS, CHARACTERIZATION, COMPOSITION

- As has been recognized repeatedly by expert groups, there is a requirement for two main types of analytic methodology: a rapid screening system for estimating the primary fiber components (or total dietary fiber, should an acceptable definition be achieved) for use in quality control in the food industry; and a research method that will identify and quantify the component carbohydrates and other constituents of fiber. Currently, the best approach for quality control purposes appears to be the Van Soest neutral detergent fiber method although it does not adequately isolate and characterize the soluble polymeric portions of dietary fiber.

- Development of better methods for the determination of total fiber in foods remains a critical challenge in view of reported inadequacies of the available methods. The problems of improving the methodology are aggravated by lack of agreement on a definition of dietary fiber and terminology, including the question of which portions of indigestible food residues should and should not be included.

- Significant development has occurred recently in an analytic method that includes derivatization of hydrolyzed sugars from plant fibers to their corresponding alditol acetates and gas chromatographic analysis of the derivatives. The delignification and predigestion steps employ milder reagents than other methods, and this method appears to offer advantages of a more nearly comprehensive analysis of dietary fiber.

- Of the indigestible substances that are associated with plant fiber, such as phytic acid, cuticular substances, and tightly bound proteins and minerals, phytic acid and phytates are known to form insoluble complexes with trace elements and macroelements. The relative importance of this property of phytic acid as compared with the mineral binding and ion exchange capacities of various plant fiber components has not been established.

- Lectins are glycoproteins with special reactive properties that might influence the bioavailability of drugs, nutrient proteins, and carbohydrates and affect the normal intestinal flora. Little information is available about the lectin content of plant fibers and whether it may account for any of the biologic effects of dietary fiber.
GASTROINTESTINAL FUNCTION

- Significant progress has been made during the past three years in characterizing dietary fiber components and defining their physiologic effects in the gastrointestinal tract, but little is known about the mechanisms involved and the fractions or subfractions of total dietary fiber which are responsible for a given effect.

- While fecal mass may readily be doubled in monogastric species by addition to the diet of plant fiber such as wheat bran, the bulk of evidence from relatively short-term studies on dietary fiber—colonic flora interactions suggests that the flora tends to remain qualitatively constant despite consumption of increased amounts of fiber.

- Dietary fiber influences fecal bile acid and steroid excretion, with a tendency to increase total acidic steroid excretion. However, the effects vary among different fiber sources and with fat content of the diet; inconsistencies in experimental results make the effects difficult to summarize, and the long-term effects of altered bile salts metabolism resulting from binding of the salts to fiber constituents are not yet clear.

DIVERTICULAR DISEASE AND COLONIC CANCER

- Epidemiologic evidence that low-fiber intake is associated with an increased risk of diverticular disease and cancer of the colon seems persuasive; however, definitive proof of a causal relationship is lacking. Available data fail to account for such variables as genetics, physiology, life-style, stress responses, marginal or impaired nutrition, environmental factors, parasitosis, and, in Western diets, the possible adverse effects of excessive dietary fat, meat, refined carbohydrates, and salt as well as total calories.

- Clinical experience with the use of dietary-fiber supplements such as wheat bran has resulted in their routine use in treatment of diverticular disease of the colon, irritable bowel, constipation, and hemorrhoids. However, validation of the apparent therapeutic effectiveness of such fiber supplements in diverticular disease or in irritable bowel syndrome is still needed. The validity of the conclusions in many reports of the clinical effectiveness of dietary fiber in such disorders as symptomatic diverticular disease of the colon is impaired by failure to control basal diets and by the strong placebo effect that plagues dietary intervention studies.
Despite incompatibilities of data resulting from lack of standardization of experimental protocols, the majority of rat-model studies suggests that certain dietary fiber supplements significantly reduce the risk of colonic cancer from administration of known chemical carcinogens. Whether the results of such animal studies approximate the human response and may be extrapolated to man are unanswered questions.

The fundamental question of whether dietary fiber protects against human colonic cancer is debatable; while some investigators are convinced it does, others maintain that adequate scientific data to support this concept are not available.

A majority of the consultants for this review considered studies of intestinal bacterial enzyme activity and fecal floral metabolites and their effects on the large bowel and its contents more promising than fecal bacteriologic taxonomy in the elucidation of the dietary fiber-fecal flora-colonic carcinogenesis question.
VI. SUGGESTIONS FOR FUTURE CONSIDERATION

A majority of the research recommendations contained in the report of the 1977 dietary fiber workshop held at the National Institutes of Health (American Journal of Clinical Nutrition 31:S1-S291, October 1978) remain valid and are of direct interest to this review. In addition, the following specific suggestions were submitted during the ad hoc group meeting:

ANALYSIS, CHARACTERIZATION, COMPOSITION

• Analytic methods should be developed to permit complete identification and characterization of the constituents of dietary fiber. Further development of nonbacterial enzymatic methods is warranted. A schedule for formal, periodic review of fiber analytic methodology and terminology should be established.

• More research is warranted on the effects of various food preparation procedures on the physiologic properties of dietary fiber.

• Estimates of dietary fiber intakes of Americans and appropriate population subgroups are needed to determine levels of fiber intake. As an aid to this process, better data are required on the fiber content of foods consumed in the United States. A possible model for this is the British set of food composition tables published in 1978.

• Questions concerning the possible lectin content of plant fibers and their physiologic significance in human nutrition should be reviewed in detail.

• The interactions of dietary fiber with fats in the diet are poorly understood but potentially significant. They warrant substantial additional investigation. In animal models, a suitable endpoint for such studies might be chemically-induced colonic cancer.

GASTROINTESTINAL FUNCTION

• Additional investigations of the influence of dietary fibers on the long-term bioavailability of trace minerals and therapeutic drugs are necessary to address questions of the practical significance, if any, of the reported effects. Such investigations should include tests designed to differentiate between phytate and fiber effects.

• Upper and lower limits of dietary fiber intake that are compatible with optimal health need to be established for human consumers of both sexes and all age groups.
Studies are needed to compare the gastrointestinal physiologic effects of individual fiber constituents such as cell wall polysaccharides with those of major fiber components (lignin, cellulose, hemicellulose, pectin) and with the total dietary fiber source as normally consumed. Such research should attempt to determine mechanisms of action and the synergistic or antagonistic relationships of the various fiber components and constituents.

Mechanisms of action of dietary fiber in the gastrointestinal tract are poorly defined. In addition to extending investigations of the physicochemical interactions of fiber with the gut and its contents, efforts should be made to develop techniques to determine the influence of fiber on the production and secretion of gastric acid, such enteric hormones as cholecystokinin-pancreozymin, vasoactive peptide, gastric inhibitory polypeptide, somatostatin, glucagon, and various neuroendocrine transmitters as well as the composition and rate of release of bile and pancreatic secretions.

Standardization of diets used in human metabolic studies on the gastrointestinal effects of dietary fiber should be undertaken.

Colonic function may be influenced by alterations in upper gastrointestinal physiology; consequently, investigations of the effects of dietary fiber on gastric and small intestinal physiology should be expanded. For example, the significance of the bulking effect of certain fiber components in the stomach and upper intestine is incompletely understood.

Improved marker techniques are needed to facilitate tracking dietary fiber through the gastrointestinal tract and measuring effects at different anatomic levels.

The physiologic and nutritional significance of gels resulting from hydration of certain fiber components should be investigated in both upper and lower intestines, with particular reference to effects on digestion and absorption of nutrients and energy balance, and in the colon, on availability of other fiber components, bile salts, and nutrients for microbial metabolism.

The human nutritional significance of products of microbial degradation of dietary fiber substrates in the colon such as short-chain fatty acids should be assessed.

Studies should be conducted on the influence of different dietary fiber sources on colonic bacterial growth and metabolism under anaerobic conditions designed to simulate the in vivo environment. Mechanisms of attachment of colonic bacteria to different fiber substrates should be investigated as part of such research.
DIVERTICULAR DISEASE AND COLONIC CANCER

- Research is needed on the influence of various dietary fiber sources and components on the neuromuscular physiology of the colon as an approach to elaborating the mode of action of fiber in alleviation of symptomatic diverticulosis and its possible prevention. A key question concerns what, if any, constituents of dietary fiber prevent the abnormal muscle responses that have been associated with colonic diverticulosis or the irritable bowel syndrome.

- Consideration should be given to the feasibility of conducting human studies of a possible role of dietary fiber on development of colonic polyps, and the relationship, if any, between fecal steroid excretion and polyps.

- More epidemiologic investigations of possible relationships between low-fiber intake and development of diverticular disease and colonic cancer are needed. Methodology should be improved, if possible, to provide for better dietary estimates of surveyed populations and to account for other variables that could influence the development of diverticulosis and colonic cancer such as general environmental, genetic, physiologic, lifestyle, and stress factors as well as excess consumption of calories, fats, protein, and refined carbohydrates.

- Carefully controlled clinical investigations are required to establish whether dietary fiber supplements truly influence symptomatic diverticular disease of the colon.

- Research should be continued using the animal model to elucidate the role of the type and amount of dietary fiber in inhibiting chemically-induced colonic carcinogenesis. Conversely, additional research is essential to expand the evidence that bound dietary fiber-bile acid units may damage enteric mucosae and increase susceptibility to carcinogens.

- The comparability and usefulness of data from animal model studies of colonic carcinogenesis would be significantly improved by developing a consensus on standardization of experimental protocols to minimize variation in such factors as animal strains, background diet, type of carcinogen, dose, route of administration, and duration of experiments.

- In studies of interactions of dietary fiber and human intestinal flora, emphasis should be placed on determination of bacterial metabolites as they may relate
to carcinogenesis. Investigation should be expanded on the influence of various dietary fiber sources on the production by the colonic flora of putative carcinogens and on their adsorption and/or binding, dilution, and excretion.
VII. LITERATURE CITED


VIII. LITERATURE NOT CITED

(Additional pertinent literature reviewed in the course of this study)


IX. STUDY PARTICIPANTS

A. ATTENDEES, AD HOC MEETING, MAY 12, 1980

CO-CHAIRMEN

Kenneth D. Fisher, Ph.D.
Director
Life Sciences Research Office
Federation of American Societies for Experimental Biology
Bethesda, Maryland 20014

John M. Talbot, M.D.
Senior Medical Consultant
Life Sciences Research Office
Federation of American Societies for Experimental Biology
Bethesda, Maryland 20014

CONSULTANTS

George F. Collings, Ph.D.
Nutritionist
Ralston Purina Company
900 Checkerboard Square
St. Louis, Missouri 63188

Juan M. Munoz, Ph.D.
Fargo Clinic
737 Broadway
Fargo, North Dakota 58102

Barry R. Goldin, Ph.D.
Assistant Professor of Medicine
New England Medical Center Hospital
171 Harrison Avenue
Boston, Massachusetts 02111

Bandaru S. Reddy, D.V.M., Ph.D.
Member and Head, Division of Nutrition
American Health Foundation
Dana Road
Valhalla, New York 10595

June L. Kelsay, Ph.D.
Research Nutritionist
Beltsville Human Nutrition Research Center
Science and Education Administration
U.S. Department of Agriculture
Beltsville, Maryland 20705

Daphne A. Roe, M.D.
Professor
Division of Nutritional Sciences
Cornell University
Ithaca, New York 14853

Albert I. Mendeloff, M.D., M.P.H.
Physician-In-Chief
Sinai Hospital of Baltimore
Belvedere Avenue at Greenspring
Baltimore, Maryland 21215

Gene A. Spiller, Ph.D., D.Chem.
Principal Scientist
Syntex Research
2375 Charleston Road
Mountain View, California 94043
E. Clinton Texter, Jr., M.D.
Professor Medical Physiology
and Biophysics and Director,
Division of Gastroenterology
University of Arkansas
College of Medicine
4301 W. Markham
Little Rock, Arkansas 72201

Charles W. Weber, Ph.D.
Professor, Department of
Nutrition and Food Science
Agricultural Science Building
University of Arizona
Tucson, Arizona 85721

BUREAU OF FOODS, FDA

Allan L. Forbes, M.D.
Associate Director for
Nutrition and Food Sciences
Bureau of Foods
Food and Drug Administration
200 C Street, S.W.
Washington, D.C. 20204

Barbara Harland, Ph.D.
Research Biologist, Division
of Nutrition
Bureau of Foods
Food and Drug Administration
200 C Street, S.W.
Washington, D.C. 20204

Victor P. Frattali, Ph.D.
Deputy Director, Division of
Nutrition
Bureau of Foods
Food and Drug Administration
200 C Street, S.W.
Washington, D.C. 20204

John E. Vandermeer, Ph.D.
Director, Division of Nutrition
Bureau of Foods
Food and Drug Administration
200 C Street, S.W.
Washington, D.C. 20204

OTHER PARTICIPANTS

George Kitzes, Ph.D.
Health Sciences Administrator
Digestive Diseases Program
National Institute of Arthritis,
Metabolism, and Digestive
Diseases
National Institutes of Health
Bethesda, Maryland 20205

Donald H. Luecke, M.D.
Chief, Special Programs Branch
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20205

LIFE SCIENCES RESEARCH OFFICE

Richard G. Allison, Ph.D.
Staff Scientist

Herman I. Chinn, Ph.D.
Senior Staff Scientist

Sue Ann Anderson, Ph.D., R.D.
Staff Scientist

Frederic R. Senti, Ph.D.
Associate Director
B. SPECIAL CONSULTANTS

Tyron E. Huber, M.D.
Medical Consultant
6002 Roosevelt Street
Bethesda, Maryland 20014

David Kritchevsky, Ph.D.
Associate Director
Wistar Institute Anatomy and Biology
36th & Spruce Streets
Philadelphia, Pennsylvania 19104

C. OTHER CONTRIBUTING LIFE SCIENCES RESEARCH OFFICE STAFF

Philip L. Altman
Senior Staff Scientist

C. Grace Gurtowski
Bibliographer, Librarian

Cynthia Claypoole
Secretary

Beverly Keder
Literature Retrieval/
Technical Report Specialist

Elizabeth M. DeWitt
Administrative Aide

Anne Rhames
Secretary

Sandra Ferman
Administrative Aide