The Need for Comprehensive Diet Studies to Assess the Relation of Lipids to Cancer

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Abstract

Dietary lipids have been linked by both basic research and epidemiological evidence to the etiology of some cancers. It is yet unclear which lipid(s) may be active in the carcinogenic process, but one promising hypothesis concerns the interaction of cholesterol metabolites, considered a risk factor for colon cancer, and dietary fiber which may have a protective role. A multidisciplinary case control study currently underway is investigating the relationship and possible mode of action of fiber and bile acids on colon cancer. The study has epidemiological, biochemical, and pharmacological components that have been designed to integrate data on the intake and fate of lipids, dietary fiber, and other nutritional parameters in colon cancer cases and matched controls and in animal models. Subcomponents of the study deal specifically with the characterization of dietary fiber constituents and their in vivo effect on lipid metabolism.

The role of diet in cancer may be related to an overall complex nutritional pattern rather than individual nutrients, foods, or food groups (12). When consumption differences are seen in one food group, there is almost always a compensatory difference in other components of the diet (2). The effects of diet can also be altered by the combination of foods consumed at one time (2). Unfortunately, when evaluating one nutrient parameter, it is difficult to isolate it from other dietary factors because of the complex interactions among them. Therefore, considerable attention in nutrition research should be directed to the synergistic and inhibitory effects of food components upon each other or other substances which have carcinogenic potential (17). When feasible, diet and cancer studies should examine the entire diet pattern over time. It is unlikely that any one dietary factor is responsible for colon cancer or that the natural food components produce the carcinogenic effect. Rather, those substances which have a slow or cumulative effect are likely to be more important in defining the relationship of diet to cancer etiology.

Lipids and Cancer

Clinical trials and animal studies have linked colon cancer to dietary habits which affect bowel sterols, bile acids, and bacteria (10). Much evidence supports the theory that a major dietary association with several cancer sites is due to high dietary fat consumption (3, 9).

A number of specific lipids including triglycerides, steroids, trans-fatty acids, and lipoproteins have been associated with cancer induction (6). However, it is still unclear whether an individual lipid type(s) or the effect of total fat is of greater importance in cancer etiology. Furthermore, the degree of association and the interaction of intrinsic and extrinsic lipids has yet to be determined. Several studies have shown that there are differences in the amount of circulating and adipose unsaturated fatty acids between high- and low-risk populations (2) which raises the question of antioxidant adequacy in such high-risk groups.

In addition to dietary lipids, some attention must also be given to the probable occurrence in food lipids of various fat-soluble chemical carcinogens, including thermal autooxidation products of fats and representative agents of the environmental pollution problem. Many such candidate chemicals have been identified as weak carcinogens and might be associated with lipid-related disease trends.

Possible Modes of Action of Lipids in Carcinogenesis

Since dietary fat is known to influence adipose fatty acid composition (9) and serum lipid content (1, 16) and to affect hormone responses, several modes of carcinogenic activity linking fat to cancer etiology have been suggested. Fats may mediate a carcinogenic process via hormonal responses, altering membrane permeability (8), influencing DNA repair potential, and/or interfering with immunocompetence (2, 5). Some researchers have become interested in bile acids and cholesterol as possible carcinogenic precursors because of their structural and steric similarity to the potent polycyclic hydrocarbon carcinogens (4, 7, 11).

Animal experiments have shown that steroid metabolites such as bile acids and taurodehydroxycholic, lithocholic, and glucuronide conjugates are not carcinogenic but may become cocarcinogenic when deconjugated and/or oxidized to products like deoxycholate (13, 14).

Some evidence supports the hypothesis that both carcinogen-producing bacteria and steroids must be present for development of bowel cancer. Though many nutrients are linked to cancer etiology, a postulated interrelationship of lipids with dietary fiber is currently one of the most promising fields of research. Bacterial populations vary not only with the type of overall dietary fat but also with the type of dietary fiber (19).

For clarification, a number of researchers have defined dietary fiber as a complex group of polymers in the diet which is not appreciably degraded by the action of the digestive enzymes or intestinal bacteria (15). These groups include cellulose, hemicellulose, pectins, lignins, and the less frequently described gums, mucilages, subgroups of hemicelluloses, plant cutins, and other substances, although these may be quantitatively as significant in some diets as the former. It is generally agreed that different fiber components have different modes of action in vivo (14, 18).

1 Presented at the Workshop on Fat and Cancer, December 10 to 12, 1979, Bethesda, Md.
A Multidisciplinary Research Model

The complexity of the relationships of dietary components to cancer and other multietiological diseases make it difficult to plan and execute studies that yield valid data. Besides the problem of determining nutritional status (i.e., dietary intake, biochemical measures, and clinical assessments), studies of human populations must account for as many other confounding variables as possible. Demographic, health, and risk factors must be considered. Extrapolations of clues found in humans to animal research present further complications. Such holistic concepts require a multidisciplinary research effort.

"Diet and Cancer in Man: The Effects of Fiber," a joint study between the Department of Family and Community Medicine at the University of Utah Medical Center and the Departments of Animal, Dairy, and Veterinary Science and Nutrition and Food Sciences at Utah State University, illustrates a multidisciplinary project that includes the evaluation of dietary lipids. This casecontrol study concerns the 2 most often suggested dietary links to colon cancer, fiber and lipids. This study is being supported by Grant 1 R01 CA 25580-01 from the diet and cancer section of the NIH.

The Utah population, which is at low risk for colon cancer, does not conform to either the high-fiber or low-fat theories as they are presently stated. According to limited data, Utahns consume relatively high amounts of animal fat and protein but a relatively low amount of less than 100 mg of crude fiber per kg of body weight. However, one must keep in mind that "crude fiber" is not equivalent to dietary fiber. The intake of total dietary fiber is probably higher than average because of the large consumption of produce, i.e., fruits and vegetables. Dietary fiber or one or more of its components may be protective for colon cancer, but the scanty amount of food composition data on fiber in terms other than crude fiber has made it difficult to determine how the protective mechanism may work.

Epidemiological, biochemical, and pharmacological components have been integrated in the Utah project. One part of the study has been designed to determine the relative levels of lipids and specific fiber components in the diets of the Utah population, while also determining the possible correlations of these factors to morbidity and clinical evaluation of the disease risk for colon cancer.

By assaying home-preserved and commercial foodstuffs available to the Utah population, a data base can be established for the specific fiber composition of high-fiber foods commonly consumed. Once these data are available, the fiber intake of the Utah population can be more precisely determined. The intake of these control groups can then be compared to colon cancer patients in Utah. Serum and fecal samples are being collected from a subsample of cases and controls and will be chemically assayed for serum lipids and fecal steroids, respectively.

Fiber in food samples will be chemically characterized and quantified in terms of defined constituents: cellulose, xyloligocan hemicellulose, pectic acids, gums, and "lignins." These analytical values will be compared to the empirically defined classical fiber categories: crude fiber, NDF, ADF, pectin, and lignin.

The basic research component of the study is the investigation of pharmacological effects of purified fiber components on model xenobiotics in laboratory animals. These data will be used to interpret the effects of specific fiber components and patterns of dietary fiber identified in cases and controls in relation to chemical carcinogenesis of the colon and cholesterol-related disease processes.

Metabolic effects of the fiber constituents relating to chemical carcinogenesis and cholesterolemic diseases will be investigated in laboratory animals dosed with model drugs. Investigation will cover hepatic and intestinal drug metabolism activities, drug absorption, distribution, elimination (i.e., carcinogen activation and elimination), and cholesterol and bile acid turnover rates.

By comparing the serum lipid profiles to the composition of dietary fiber and lipid intake of the experimental subjects and by examining the pharmacological action of fiber on drug distribution and metabolism and on cholesterol and bile acid turnover, it is expected that some clue will be found to help explain the low incidence rates of colon cancer in the Utah population.

References

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