

Carcinogens and Anticarcinogens in the Human Diet

EXECUTIVE SUMMARY

From earliest times people have been aware that some plants are poisonous and should be avoided as food. Other plants contain chemicals that have medicinal, stimulatory, hallucinatory, or narcotic effects. The Romans were among the first to enact laws that, over time, have been developed to protect the public from food adulteration, contamination, false labeling, spoilage, and the harmful effects of chemicals added to foods and beverages.

In the past 50 years, great strides have been made in understanding nutrition and the role it plays in human health. This same period has seen vast improvements in the safety and diversity of the diet in the United States, with technological advances in preservation and shipment of foods, and the ability to identify and reduce various food hazards. U.S. laws regulate the safety of the food we eat and the water we drink. Federal agencies, such as the Food and Drug Administration, Department of Agriculture, and Environmental Protection Agency, as well as many state and local agencies, are charged with interpreting and enforcing these laws. As a result, the food supply in the United States is widely recognized as safe, economical, and of high quality, variety, and abundance.

Despite these efforts, concerns remain that some dietary components may contribute to the burden of cancer in humans. For example, the use of pesticides continues to be watched closely, because of indirect exposures of the general public through trace amounts in the food supply (as well as direct exposures of agricultural workers). Yet, by controlling insect vectors, pesticides have profoundly decreased the spread of human diseases, and pesticide usage has increased agricultural yields.

Plants have evolved chemicals that serve as defensive agents against predators. These chemicals may be present in the diet in amounts exceeding the residues of synthetic pesticides used to enhance agricultural productivity. Ames et al. contend that the percentage of naturally occurring chemicals testing positive for carcinogenicity in rodent bioassays does not differ significantly from the percentage of synthetic chemicals testing positive, and that these proportions are likely to hold for untested agents, leading to their conclusion that the cancer risk from natural chemicals in the diet might be greater than that from synthetics. There are, after all, many more naturally occurring chemicals than synthetic. In fact, although the number of naturally occurring compounds in the human diet is certainly far greater than synthetic compounds, the implications concerning health risks—particularly impact on cancer in humans—remain controversial. In addition, it should be noted that synthetic chemicals are highly regulated while natural chemicals are not. This report addresses several elements of this controversy, including the relevance of animal bioassays (including those using the maximum tolerated dose) for identifying human dietary carcinogens, the adequacy and availability of human exposure data, and the complexity of the human diet.

Since the 1930s, scientists have recognized that the occurrence of certain cancers may be related to substances in the diet or to patterns of food consumption. They have also recognized that some chemical constituents of food—either initially present in the food, formed during preparation (especially cooking),

or added for preservation or presentation-are capable of inducing tumors in high-dose rodent tests. Many of the early studies on chemicals that cause cancer were carried out to determine what levels of exposure to specific chemicals, such as polycyclic aromatic hydrocarbons (PAHs) and certain food colors, such as butter yellow (N,N-dimethyl-4-amino-azobenzene), resulted in the formation of cancers in the liver and gastrointestinal tract of rodents. Later it was recognized that a number of naturally occurring chemicals present in some foods, such as mycotoxins (chemicals produced by fungi that often contaminate grains and nuts) and plant alkaloids, could also cause cancer in experimental animals. These findings have stimulated research to better understand the health consequences of naturally occurring chemicals found in our diet.

Doll and Peto, in their 1981 review, concluded that 10% to 70% of human cancer mortality in the U.S. is attributable to the diet, with the most likely figure being about 35%. Epidemiologic studies linking the aforementioned mycotoxins to human liver cancer provide convincing evidence that some constituents of foods can cause cancer. Less firmly established, however, is the contribution to human cancer of other naturally occurring chemicals present at low levels in the food we eat. In addition, the diet is a source of calories derived from fats, carbohydrates, and proteins. Calories and macronutrients (principally fat and oxidation products of fatty acids) in excess of body needs serve as an important risk factor that can contribute to the processes of tumor formation and growth. The observations of Doll and Peto are based on statistical and epidemiologic data which many regard as inconclusive. It is important to note that diet also plays a role in protecting against cancer, since diets rich in fruits and vegetables have been associated with reduced rates of cancer. Although dietary factors are certainly involved in carcinogenesis, the percent of cancer attributable to diet has remained uncertain.

The Charge to the Committee

This report was prepared by the Committee on Comparative Toxicity of Naturally Occurring Carcinogens, which was convened in 1993 by the National Research Council upon the recommendation of its Board on Environmental Studies and Toxicology. The committee was charged to "examine the occurrence, toxicologic data, mechanisms of action, and potential role of natural carcinogens in the causation of cancer (in humans), including relative risk comparisons with synthetic carcinogens and a consideration of anticarcinogens." In addition, the committee was charged to assess "the impact of these materials (natural carcinogens) on initiation, promotion, and progression of tumors." Further, the committee was charged to "focus on the toxicologic information available for natural substances" and to "develop a strategy for selecting additional natural substances for toxicological testing."

In this report, the "initiation, promotion, and progression" stages of carcinogenesis were considered from a mechanistic point of view. However, most of the available carcinogenicity data on the compounds that were reviewed do not provide precise information on the specific stage or stages of the multistage process of carcinogenesis at which these compounds act. Since the terms initiator, promoter, and progressor are especially difficult to apply to specific agents, particularly as they pertain to human carcinogenesis, the committee chose primarily to discuss agents as being genotoxic or nongenotoxic. The committee viewed its charge to address toxicologic issues as limited to cancer.

For this report, the committee adopted the definition of a carcinogen proposed by the International Agency for Research on Cancer (IARC). IARC defines a carcinogen as any agent, the exposure to which increases the incidence of malignant neoplasia. It is recognized that many factors can influence the process of tumor formation and that the application of this definition does not always identify the influence of high dose levels of chemicals used in rodent testing, nor does it identify the uncertainties in extrapolating results from these rodent bioassays to much lower exposure/dose in humans. In this report,

the term "exposure" means the amount of a synthetic or naturally occurring agent (including contaminants) ingested from the diet.

The number of naturally occurring chemicals present in the food supply-or generated during the processes of growing, harvesting, storage, and preparation-is enormous, probably exceeding one million different chemicals. Actions of these chemicals in the complex mixture of our diet may be additive, synergistic, or inhibitory to one another. The observed level of a specific naturally occurring chemical in a food may vary greatly, because, in addition to actual variability, which often is great, such levels can be determined by analysis of the intact plant, analysis of the processed food as consumed, or determined as the form absorbed, distributed, and metabolized in the body for presentation at a target molecule. Further, the concentrations of such chemicals in plant and animal tissues used for food are highly variable, depending on the specific variety of the crop studied, the season of year tested, the geographic location and conditions of growth, the type of harvesting and storage used, etc. Intestinal microflora should also be recognized as important contributors to the availability of chemicals that might be carcinogens.

This report provides a perspective on the importance of chemicals in the diet, in terms of the magnitude of potential cancer risk from naturally occurring chemicals compared with that from synthetic chemical constituents. Also addressed are the protective effects of some chemicals (anticarcinogens) in the diet, which may reduce the risk associated with exposure to cancer-producing agents.

Conclusions

Several broad perspectives emerged from the committee's deliberations. First, the committee concluded that based upon existing exposure data, the great majority of individual naturally occurring and synthetic chemicals in the diet appears to be present at levels below which any significant adverse biologic effect is likely, and so low that they are unlikely to pose an appreciable cancer risk. Much human experience suggests that the potential effects of dietary carcinogens are more likely to be realized when the specific foods in which they occur form too large a part of the diet. The varied and balanced diet needed for good nutrition also provides significant protection from natural toxicants. Increasing dietary fruit and vegetable intake may actually protect against cancer. The NRC report *Diet and Health* concluded that macronutrients and excess calories are likely the greatest contributors to dietary cancer risk in the United States.

Second, the committee concluded that natural components of the diet may prove to be of greater concern than synthetic components with respect to cancer risk, although additional evidence is required before definitive conclusions can be drawn. Existing concentration and exposure data and current cancer risk assessment methods are insufficient to definitively address the aggregate roles of naturally occurring and/or synthetic dietary chemicals in human cancer causation and prevention. Much of the information on the carcinogenic potential of these substances derives from animal bioassays conducted at high doses (up to the maximum tolerated dose, or MTD), which is difficult to translate directly to humans because these tests do not mimic human exposure conditions, i.e., we are exposed to an enormous complex of chemicals, many at exceedingly low quantities, in our diet. Furthermore, the committee concluded upon analyzing existing dietary exposure databases, that exposure data are either inadequate due to analytical or collection deficiencies, or simply nonexistent. In addition, through regulation, synthetic chemicals identified as carcinogens have largely been removed from or prevented from entering the human diet.

Third, the committee concluded that it is difficult to assess human cancer risk from individual natural or synthetic compounds in our diet because the diet is a complex mixture, and interactions between the components are largely unknown.

The committee's major conclusions are presented in detail below. They address the complexity and variability of the human diet, cancer risk from the diet, mechanisms and properties of synthetic vs. naturally occurring carcinogens, the role of anticarcinogens, and models for identifying dietary carcinogens and anticarcinogens.

Complexity of the Diet

- The human diet is a highly complex and variable mixture of naturally occurring and synthetic chemicals. Of these, the naturally occurring far exceed the synthetic in both number and quantity. The naturally occurring chemicals include macronutrients (fat, carbohydrate, and protein), micronutrients (vitamins and trace metals), and non-nutrient constituents. Only a small number of specific carcinogens and anticarcinogens in the human diet have been identified (e.g., aflatoxin). However, it seems unlikely that important carcinogens are yet to be identified. In part, this may reflect the limited number of studies performed.
- Human epidemiologic data indicate that diet contributes to a significant portion of cancer, but the precise components of diet responsible for increased cancer risk are generally not well understood.

Carcinogenicity and Anticarcinogenicity

- Current epidemiologic evidence suggests the importance of protective factors in the diet, such as those present in fruits and vegetables.
- Current evidence suggests that the contribution of excess macronutrients and excess calories to cancer causation in the United States outweighs that of individual food microchemicals, both natural and synthetic. This is not necessarily the case in other parts of the world.
- Epidemiologic data indicate that alcoholic beverages consumed in excess are associated with increased risk for specific types of cancer.
- Given the greater abundance of naturally occurring substances in the diet, the total exposure to naturally occurring carcinogens (in addition to excess calories and fat) exceeds the exposure to synthetic carcinogens. Regarding dietary exposure, the committee reviewed data, including those generated by the Department of Agriculture and the Department of Health and Human Services through the Nationwide Food Consumption Surveys, the National Health and Nutrition Examination Surveys, and other related data bases. However, data are insufficient to determine whether the dietary cancer risks from naturally occurring substances exceeds that for synthetic substances (e.g., these databases do not include concentration data on many of the potential carcinogenic constituents found in foods). Indeed, at the present, quantitative statements cannot be made about cancer risks for humans from specific dietary chemicals, either naturally occurring or synthetic.
- Current regulatory practices have applied far greater stringency to the regulation of synthetic chemicals in the diet than to naturally occurring chemicals. The committee reviewed data and findings of IARC, the National Toxicology Program (NTP), and in the general literature to ascertain the status of carcinogenicity testing of naturally occurring versus synthetic chemicals. Only a very small fraction of naturally occurring chemicals has been tested for carcinogenicity. Naturally occurring dietary chemicals known to be potent carcinogens in rodents include agents derived through food preparation, such as certain heterocyclic amines generated during cooking,

and the nitrosamines and other agents acquired during food preservation and storage, such as aflatoxins and some other fungal toxins.

- The human diet also contains anticarcinogens that can reduce cancer risk. For example, the committee evaluated relevant literature on antioxidant micronutrients, including vitamins A, C, E, folic acid, and selenium, and their suggested contributions to cancer prevention. Human diets that have a high content of fruits and vegetables are associated with a reduced risk of cancer, but the specific constituents responsible for this protective effect and their mechanisms of action are not known with certainty. The vitamin and mineral content of fruits and vegetables might be important factors in this relationship. In addition, fruits and vegetables are dietary sources of many non-nutritive constituents, such as isoflavonoids, isothiocyanates and other sulfur-containing compounds, some of which have inhibited the carcinogenic process in experimental animal studies. Foods high in fiber content are associated with a decreased risk of colon cancer in humans, but it is not yet clear that fiber per se is the component responsible for this protective effect.
- Carcinogens and anticarcinogens present in the diet can interact in a variety of ways that are not fully understood. This makes it difficult to predict overall dietary risks based on an assessment of the risks from individual components due to uncertainties associated with rodent-to-human extrapolation and high-dose to low-dose extrapolation. It is likely that there is also considerable interindividual variation in susceptibility to specific chemicals or mixtures due to either inherited or acquired factors.

Synthetic Versus Naturally Occurring Carcinogens

- Overall, the basic mechanisms involved in the entire process of carcinogenesis—from exposure of the organism to expression of tumors—are qualitatively similar, if not identical, for synthetic and naturally occurring carcinogens. The committee concluded that there is no notable mechanistic difference(s) between synthetic and naturally occurring carcinogens. To assess relative potency, the committee compiled and analyzed data on over 200 carcinogens—65 of which were naturally occurring. The data set included agents identified by IARC as having sufficient evidence of carcinogenicity in humans or animals, or by the NTP as known or reasonably anticipated to be human carcinogens. Based in part on this limited sample, the committee concluded that there is no clear difference between the potency of known naturally occurring and synthetic carcinogens that may be present in the human diet. Of the selected agents tested, both types of chemicals have similar mechanisms of action, similar positivity rates in rodent bioassay tests for carcinogenicity, and encompass similar ranges of carcinogenic potencies. Consequently, both naturally occurring and synthetic chemicals can be evaluated by the same epidemiologic or experimental methods and procedures.
- Although there are differences between specific groups of synthetic and naturally occurring chemicals with respect to properties such as lipophilicity, degree of conjugation, resistance to metabolism, and persistence in the body and environment, it is unlikely that information on these properties alone will enable predictions to be made of the degree of carcinogenicity of a naturally occurring or synthetic chemical in the diet. Both categories of chemicals—naturally occurring and synthetic—are large and diverse. Predictions based on chemical or physical properties are problematic, due in part to the likely overlap of values between the categories.

Models for Identifying Carcinogens and Anticarcinogens

- The committee evaluated current methods for assessing carcinogenicity and concluded that current strategies for identifying and evaluating potential carcinogens and anticarcinogens are

essentially the same. The methods can be grouped into epidemiologic studies, in vivo experimental animal models, and in vitro systems. The committee recognized the value and limitations of each approach for identifying dietary carcinogens and anticarcinogens.

- In its assessment of traditional epidemiologic approaches to identifying dietary carcinogens and anticarcinogens, the committee concluded that these can be beneficially expanded by incorporating into research designs more biochemical, immunologic, and molecular assays that use human tissues and biologic fluids. Furthermore, incorporating the identification of biologic markers into these approaches may provide early indicators of human carcinogenicity-long before the development of tumors.
- The committee analyzed the applicability of rodent bioassays-specifically the long-term bioassays conducted by the National Toxicology Program-for identifying dietary carcinogens and anticarcinogens. The committee concluded that, despite their limitations, rodent models (involving high-dose exposures) have served as useful screening tests for identifying chemicals as potential human carcinogens and anticarcinogens. Concerns about the use of data generated from these models for predicting the potential carcinogenicity and anticarcinogenicity of chemicals in food arise from the fact that they do not mimic human exposure conditions, i.e., we are exposed to an enormous complex of chemicals, many at exceedingly low quantities, in our diet.

Recommendations

Numerous and extensive gaps in the current knowledge base were apparent as the committee endeavored to examine the risk of human cancer from naturally occurring versus synthetic components of the diet. These gaps are so large-and resources are so limited-that careful prioritization of further research efforts is essential. The following recommendations emphasize the need for expanded epidemiologic studies, more human exposure data, improved and enhanced testing methods, more detailed data on dietary components, and further mechanistic studies, if these gaps are to be filled. These research endeavors may prove inadequate, however, when the complexity and variability of diets and food composition, as well as human behavior, are considered.

Epidemiologic Studies and Human Exposure

- Improved methods are needed to enable the incorporation of relevant cellular and molecular markers of exposure, susceptibility, and preneoplastic effects (DNA damage, etc.) into epidemiologic studies.

While existing markers are useful, additional molecular markers of exposure and susceptibility need to be developed, and their relevance and predictivity to the carcinogenic process need to be evaluated. These markers should then be incorporated into epidemiologic studies. In particular, methods are needed to identify high- and low-risk populations. Biologic markers for both genotoxic and nongenotoxic agents need to be developed and validated.

- Additional data on the concentrations of naturally occurring and synthetic chemicals in foods and human exposures to them are needed.

To determine exposures to specific dietary chemicals, it is necessary to know the concentration of a specific chemical in individual food commodities, as well as the patterns of consumption of those food commodities. At present, the concentrations are known for relatively few chemicals. In addition, more information is needed on the factors that modify these concentrations.

Current methods for assessing food consumption based on personal recall or food diaries have limitations; they may entail a substantial degree of error and lack of reproducibility. Furthermore, the sample sizes of existing food consumption surveys are limited, particularly when subpopulations such as infants and children or the elderly are considered. To minimize the resources needed to acquire these data, consideration should be given to building on other large population-based studies, such as the Women's Health Initiative Study currently supported by the National Institutes of Health.

Testing

- Improved bioassay screening methods are needed to test for carcinogens and anticarcinogens in our diet.

The rodent bioassay currently used in screening chemicals for potential carcinogenicity or anticarcinogenicity has major problems and uncertainties, especially in providing quantitative estimates of dietary cancer risk to humans or the magnitude of protection by anticarcinogens. These uncertainties relate to the variability of the composition and caloric content of the human diet and the bioassay's inability to mimic this range of variability. In addition, human exposures to individual naturally occurring or synthetic chemicals are far lower than experimental test conditions. (The committee recognized that of the NTP bioassays netting positive results, only 6% were from test levels exclusively at the maximum tolerated dose.) Uncertainties also result from variation in responses among species. The factors causing these and other uncertainties should be further evaluated and minimized wherever possible. New methods are needed for assessing complex mixtures such as those present in food. Because some chemicals may produce or prevent cancer in animals by mechanisms not relevant to humans, or do so only at high doses, information on the mechanisms of action of chemical carcinogens and anticarcinogens is crucial to improving the science of human risk assessment.

- Further testing of naturally occurring chemicals in the food supply for carcinogenic and anticarcinogenic potential should be conducted on a prioritized basis.

At present, only a limited number of naturally occurring substances present in the human diet have been subjected to testing for carcinogenic and anticarcinogenic potential. Selected additional substances should be subjected to appropriate testing in order to develop a more comprehensive database on which to base comparisons of the potential cancer risks or protective effects of naturally occurring and synthetic chemicals in the diet. Because resources for toxicological testing are limited and because there is a vast number of naturally occurring dietary chemicals, further testing of appropriately selected naturally occurring food chemicals requires the establishment of selection criteria. For potential carcinogens, priority should be assigned to those suspected naturally occurring nonnutritive chemicals that occur at relatively high concentrations in commonly consumed foods, and/or those whose consumption is associated with diets or life styles known to be deleterious. Research should be conducted only when there is substantial evidence that an important problem exists and when there is a reasonable expectation of a meaningful result. Unless a suspected carcinogen or anticarcinogen occurs at high and measurable levels in a diet, its risk to humans cannot be predicted using present methods (experimental animal studies or human epidemiologic investigations).

Additional criteria should be based on knowledge of known carcinogens and anticarcinogens. For example, naturally occurring chemicals could also be accorded a higher priority for testing if they 1) fall in the same chemical class as known chemical carcinogens or anticarcinogens; 2) contain chemical groups also found in known chemical carcinogens or anticarcinogens; 3) are likely, based on structural comparisons with known chemical carcinogens or anticarcinogens, to form reactive intermediates, in

vivo; 4) are known to be mutagenic and/or to bind to DNA; 5) share biologic effects similar to those of known nongenotoxic carcinogens; or 6) are likely, based on structural comparisons with known chemicals, to be unusually stable (i.e., long lasting) in vivo.

High priority for identifying potential anticarcinogens might be considered, in view of the fact that they do offer the possibility of new approaches to cancer control and prevention.

- *To help fill the data gaps on the cancer risk of dietary constituents, improved short-term screening tests for carcinogenic and anticarcinogenic activity should be developed, especially for detecting nongenotoxic effects that are relevant to carcinogenesis.*

Currently available short-term screening tests, usually employing cell-culture systems, often provide useful information, but new methods need to be developed and validated. Emphasis should be placed on developing systems that use human genes, enzymes, cells, or tissues. Because most present short-term tests detect DNA-reactive compounds, new methods are needed for screening chemicals for nongenotoxic end points, such as cell proliferation, hormonal effects, receptor-mediated events and effects on cell-cell interactions, gene expression, differentiation, and apoptosis (programmed cell death). Great promise exists for the use of transgenic mice.

Dietary Factors

- *The risk of cancer from excess calories and fat should be further delineated vis-a-vis naturally occurring and synthetic substances in the diet.*

There is considerable evidence that excessive calorie (energy) intake (i.e., in excess of body needs and including fat) is associated with increased cancer risk for several sites. In rodents, and especially in humans, mammary cancer is associated both with excess calories and with high proportion of calories as fat. The mechanisms responsible for this effect have not been clearly identified. Possible mechanisms that have been implicated include increased cell proliferation, decreased cell death, changes in hormonal status, and alterations in the activity of enzymes which metabolize endogenous and environmental agents, and increased oxidative stress. Further studies are needed to elucidate the precise mechanisms and to better define what is optimal or excess caloric intake. Dietary fat has also been associated with increased risk of some forms of cancer, but it is not clear if this is related to the high caloric contribution of fat, to specific constituents in foods high in saturated fats (such as specific fatty acids or other lipid oxidation products), or heterocyclic amines produced in cooking. These relationships and the underlying mechanisms need further study and clarification.

- *The specific chemicals that provide the protective effects of vegetables and fruits should be identified and their protective mechanisms delineated.*

The consumption of diets rich in fruits and vegetables is associated with reduced incidence of several forms of human cancer. The specific factors accounting for this relationship are not known with certainty and require further investigation. A number of vitamins, minerals and non-nutritive components of fruits and vegetables may contribute to the protective properties of these foods. Further research is needed on the independent and interactive effects of these compounds and on the identification of additional protective components. At present, a sound recommendation for cancer prevention is to increase fruit and vegetable intake. Concerning specific plant derived chemicals, we do not have adequate information to recommend supplementation beyond the recommended daily requirements for particular vitamins or other nutrients.

Future Directions

New research approaches and enhanced resources are needed to address the precise roles of both naturally occurring and synthetic dietary chemicals in human cancer causation and prevention. Multidisciplinary efforts in food chemistry, analytical chemistry, toxicology, nutrition, carcinogenesis, biochemistry, molecular biology, and epidemiology are needed. Such understanding would improve our ability to apply, with greater confidence, results of animal studies to the estimation of human risk. Mechanistic understanding will also improve our ability to foresee and interpret the effects of mixtures. As noted earlier, our diets are one of the most complex mixtures to which we are exposed. As an example, epidemiologic studies will become far more informative when they routinely employ improved biologic markers for exposure, individual susceptibility, and early cellular response. (The NRC addressed biologic markers in a recent series of reports.) The use of human tissues in cell systems has been limited by the obvious fact that they are not the entire organism and that there have been many technical difficulties in maintaining them. Improved techniques from biotechnology can permit us to employ human tissues and cell systems with greater confidence in how the results will relate to responses in the living person. Also, greater mechanistic knowledge will support and expand our understanding of structure-activity relationships.

Closing Remarks

At the present time, cancers are the second leading cause of mortality in the United States, resulting in over 500,000 deaths per year. It is agreed that smoking-related lung cancer is a major contributor to this statistic. However, it appears that dietary factors play an important role in the causation of a major fraction of these cancers. Current knowledge indicates that calories in excess of dietary needs, and perhaps fat or certain components of fat, as well as inadequate dietary fruits and vegetables, have the greatest impact. Most naturally occurring minor dietary constituents occur at levels so low that any biologic effect, positive or negative, is unlikely. Nevertheless, a significant number of these chemicals have shown carcinogenic or anti carcinogenic activity in tests. Overall, they have been so inadequately studied that their effect is uncertain. The synthetic chemicals in our diet are far less numerous than the natural and have been more thoroughly studied, monitored, and regulated. Their potential biologic effect is lower.

The subject of this report is, therefore, of major relevance to public-health protection and disease prevention. The assessment by this committee indicates that our current knowledge of the specific naturally occurring chemicals (or mixtures) that are involved in cancer causation or prevention, the mechanisms by which they act, which types of cancer they affect, and the magnitude of these effects, is inadequate. New research approaches at the fundamental and applied levels are urgently required to address this important problem.

Coupled with the requirement for research efforts in these areas is the need to better characterize the chemical composition of our diet and its variations in the American population. Advances in analytic and survey techniques should facilitate this endeavor.

Finally, as advances are made in identifying with certainty specific naturally occurring dietary chemicals that either enhance or inhibit cancer risks in humans, it will be possible to formulate rational dietary guidelines for the American public. It may also be possible to use this information to modify the composition of our food sources through breeding methods, genetic engineering, and other advances in biotechnology, so as to optimize the quality of the diet with respect to cancer prevention. Above all, a

major effort will be needed to educate the American public regarding appropriate life-style modifications if we are to achieve these goals.