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Naturally Occurring Carcinogens and Anticarcinogens in the Diet

Frank Bryant, Jr. MD, FAAFP
Chairman
Texas Board of Health

Robert Bernstein, MD, FACP
Commissioner

Bureau of Disease Control and Epidemiology,
1100 West 49th Street, Austin, Texas 78756 (512-458-7455)

NATURALLY OCCURRING CARCINOGENS AND ANTICARCINOGENS IN THE DIET

INTRODUCTION

The increasing prevalence of manmade chemicals has become a major public health concern in recent years. Many of these chemicals are known to be carcinogenic in either laboratory animals or humans. It is not as widely appreciated that many naturally occurring chemicals found in edible plants are believed to have carcinogenic or mutagenic properties. Conversely, other food plants contain chemicals which appear to offer protection against some types of cancers. The natural carcinogens and anticarcinogens are an interesting problem for science and underscore the importance of a healthy diet in helping to prevent cancer.

DIET AND CANCER: IDENTIFYING THE RISKS

For many years there has been indirect, but strong, evidence that certain dietary practices are important risk factors for cancer,[1] perhaps surpassed in impact in the US only by tobacco smoking.[2] Epidemiologic studies of cancer rates in different areas of the world strongly suggest the important role of dietary composition. For example, the Japanese have high incidence rates of cancers of the stomach and esophagus and relatively low rates of colon and breast cancer, when compared to US residents. Japanese immigrants to the US demonstrate, after one to two generations, the high rates of colon and breast cancers and low rates of stomach cancers typical of Americans.[3] The epidemiologic evidence suggests that the high-fat American diet is a significant risk factor for colon and breast cancer.[4,5]

In contrast to tobacco and dietary fat, most naturally occurring carcinogenic chemicals do not yet give evidence of strong association with increased cancer risk.[6] This is due in part to the large numbers of natural carcinogens in many types of food plants and the difficulty of investigating which types of cancers, if any, these chemicals might cause in the amounts typically ingested.

Epidemiologic investigations of dietary carcinogens are at a disadvantage because of the inherent difficulties of determining causes of cancers. These difficulties include: 1) the 20- to 30- year latency period between carcinogen exposure and the appearance of human cancer and 2) the difficulty of connecting cause (a specific carcinogen) with effect (a specific cancer).[7] By contrast, epidemiology has been successful in identifying tobacco smoking as a cause of cancer because there is a control group of nonsmokers, and because smoking causes a characteristic type of cancer (of the lung) which is infrequent in the nonsmoking control group.[7]

The potential harmfulness of dietary and many other environmental carcinogens has been assayed through short-term laboratory tests which measure mutagenicity (DNA damage), the primary event in chemical carcinogenesis. One such test, the Ames test, can detect DNA damage in a species of bacteria which is exposed to a suspected carcinogen in the presence of liver enzymes (this simulates the metabolism of the carcinogen in a live animal or person). The results of such tests can be suggestive of a mutagenic or carcinogenic threat to humans.[7,8]

DISCOVERY OF NATURAL CARCINOGENS

Naturally occurring carcinogens and mutagens were first discovered by observing outbreaks of cancer, birth defects, and other illnesses in livestock. Chemical analyses of certain livestock

forage plants demonstrated the presence of endogenous chemicals which were shown to produce pathological effects.[9] Although chemists have been isolating and describing these chemicals for over 100 years, and new ones are still being discovered, only a small percentage have been subjected to toxicological analysis.

Large numbers of plants in the human diet contain natural toxins, many of which have been identified as carcinogenic or mutagenic in laboratory tests.[2] Fortunately, most plants in the human diet contain negligible quantities of toxins.[10]

NATURAL CARCINOGENS IN THE DIET

Biologists have determined that, in most cases, plants produce toxic chemicals to prevent or reduce predation by insects, fungi, and other organisms which feed on the plants.[9] These chemicals are significant for the human diet not only because they are normally found in many of the plants we eat, but also because agricultural plant breeders are modifying the levels of endogenous toxins in order to increase pest resistance.[13]

Theoretically, using these "natural pesticides" reduces the need for expensive and toxic artificial pesticides. However, this strategy is problematic in that our knowledge of the toxicology and potential carcinogenicity of the natural pesticides is much less extensive than that of the man-made pesticides.[2] Many toxins which occur naturally in food plants have been shown to be mutagenic in short-term laboratory tests (such as the Ames test). Because mutagenicity and carcinogenicity seem to be strongly correlated, some of the plants we eat may be potentially carcinogenic.[7]

The following is a list of food plants which contain chemicals which have been shown to be mutagenic or teratogenic. The list is far from complete and should be viewed as a survey of some familiar foods.[2] It is not meant to suggest that these foods should be avoided.

1. Potatoes contain alkaloids which are toxic and possibly teratogenic (cause birth defects). These toxins can reach harmful levels when the potato is diseased, damaged, or exposed to light.[14] For this reason it is recommended that potatoes be stored in a dark place.

2. Coffee, tea, and cocoa contain several known carcinogens. Additional carcinogens are produced when coffee is roasted.

3. Some commercial lettuce is being given increased pest resistance by transferring genes from *Lactuca virosa* (poison lettuce), a wild relative of commercially available lettuce. Poison lettuce contains a mutagenic chemical.

4. Rhubarb leaves contain a mutagenic chemical. The leaves are never eaten and should be cut off and discarded (this is often done in the grocery store).

5. Bracken fern is consumed as a delicacy in Japan and to a lesser extent in the US. Extracts of this plant have been shown to be highly mutagenic in the Ames test and may be partly responsible for the high incidence of stomach cancer in Japan.[9] Livestock are known to forage on bracken fern and other poisonous plants. Birth defects have been reported in children whose mothers drank milk from these animals during pregnancy.[2]

Other common foods which contain carcinogens or mutagens are: celery, parsley, and related plants; some herbs and herbal teas; horseradish and mustard products; and common edible mushrooms.[2]

It is estimated that the average dietary intake of natural plant toxins is in the range of several grams per day--probably 10,000 times higher (by weight) than that of manmade pesticides.[2] However, one cannot make relative comparisons of the health risks involved simply on the basis of quantities consumed. Not enough is known about the risks posed by natural plant toxins in the diet. There is no evidence that any of these substances individually makes a major contribution to the total risk of cancer in the US. This should not be interpreted to mean that there is no hazard, in view of the mutagenicity of many of these compounds in non-human tests.[6] In perspective, however, it should be remembered that natural carcinogens and mutagens have

always been a part of the human diet, excessive levels of these chemicals are found chiefly in diseased or damaged plants and in a few species of livestock forage plants or special "gourmet" plants whose overall contribution to the human diet is limited.[2,9] Other aspects of the human diet (such as fat, alcohol, and cured foods) pose more significant risks.

DIETARY ANTICARCINOGENS

Epidemiologic studies relating diet to cancer risk have suggested the possibility of natural inhibitors of carcinogenesis in the diets of low-risk groups.[15] Because the consumption of raw fruits and vegetables has been associated with reduced risk for various cancers, early attempts at isolation of cancer preventative agents were performed using these food groups. Chemicals found naturally in certain foods were purified and found to have the ability to inhibit several forms of experimentally induced cancer (Table 1).[15]

As in the case of dietary carcinogens, much remains to be clarified concerning the specific health effects of individual protective chemicals in the human diet. However, the National Research Council has concluded that there is sufficient evidence to suggest that consumption of certain vegetables is associated with a reduction of risk for certain human cancers.[6] The apparent protective effects have been supported by two main avenues of research: 1) Human epidemiologic studies have shown an association between dietary intake of certain vegetables which contain anticarcinogens (Table 1) and lower cancer rates.[1,6,15] 2) Studies of the biochemistry of these agents in the body indicate that they react with carcinogens to produce "neutralized" or less harmful products.[1,2,15] The optimum dietary levels of these protective factors remains to be determined.

DIETARY GUIDELINES AND CANCER PREVENTION

The components of our diet interact to affect our health in complex ways which are not well understood. However, the evidence of the diet/cancer connection is sufficiently persuasive that dietary guidelines for minimizing cancer risk have been developed and publicized by the American Cancer Society and others (Tables 2 and 3).[6,16] These guidelines incorporate the current state of knowledge and try to modify the unhealthy aspects of the modern American diet. The guidelines typically recommend consumption of fresh fruits and vegetables, and reductions in cured meats, alcohol, and fat.

Prepared by: Randy Norwood, Public Health Technician, Cancer Registry Division, Texas Department of Health.

References available upon request.

Table 1. Dietary anticarcinogens[15]

Chemical Compounds	Tumor Site Inhibited	Dietary Source
Ascorbic acid	Colon	Citrus fruits
Carotenoids		
β-carotene	Breast	Carrots, melons
Indoles		
Indole [3] carbinol	Forestomach	Cruciferous vegetables
Indole [3] acetonitrile		
Isothiocyanates		
Benzylisothiocyanate	Liver	Cruciferous vegetables
Phenolic acids		
Caffeic acid	Stomach	Apples
Cinnamic acid	Stomach	Many fruits and vegetables
Chlorogenic acid	Colon	Coffee beans
Ellagic acid	Lung, skin	Grapes, strawberries, nuts
Sinigrin	Liver	Cruciferous vegetables
Sulfides		
Diallyl sulfide	Colon*	Garlic
Propenyl sulfides		Onions
Tocopherol		
α-tocopherol	Lung	Nuts

*Studies in progress.

Table 2. Summary of interim dietary guidelines from the Committee on Diet, Nutrition, and Cancer, and the American Cancer Society[16]

Committee	ACS
. . . reduce intake of fat from its present level (approximately 40%) to 30% of total calories	Avoid obesity
	Decrease total fat intake
Include fruits, vegetables, and whole-grain cereals in the daily diet	Eat more high-fiber foods, such as whole-grain cereals, fruits, and vegetables
	Include foods rich in vitamins A and C in the daily diet
Minimize consumption of food preserved by salt-curing (including salt-pickling) or smoking	Include cruciferous vegetables such as cabbage, broccoli, brussels sprouts, kohlrabi, and cauliflower in the daily diet
Minimize contamination of foods with carcinogens from any known source	
Identify mutagens in food and test for their carcinogenicity	Be moderate in consumption of alcoholic beverages
Alcoholic beverages, if consumed, should be in moderate amounts	Be moderate in consumption of salt-cured, smoked, and nitrite-cured foods

Table 3.
Summary of findings of the Committee on Diet, Nutrition, and Cancer[6]

Dietary Components	Findings
Fats	. . . increasing intake of total fat increases the incidence of cancer at certain sites, particularly the breast and colon, and conversely, risks are lower with lower intakes of fat
Cholesterol	The relationship between dietary cholesterol and cancer is not clear. . . . the evidence is not conclusive
Dietary fiber	. . . no conclusive evidence to indicate that dietary fiber (such as that present in certain fruits, vegetables, grains, and cereals) exerts a protective effect against colorectal cancer in humans
Vitamins	
Vitamin A	. . . foods rich in carotenes or vitamin A are associated with a reduced risk of cancer
Vitamin C (ascorbic acid)	. . . limited evidence suggests that vitamin C can inhibit the formation of some carcinogens and that consumption of vitamin C–containing foods is associated with a lower risk of cancers of the stomach and esophagus
Minerals	
Selenium	. . . studies suggest that selenium may offer some protection against the risk of cancer; however, firm conclusions cannot be drawn from the limited evidence
Inhibitors of carcinogenesis	. . . consumption of certain vegetables, especially carotene-rich (ie, dark green and deep yellow) vegetables and cruciferous vegetables (eg, cabbage, broccoli, cauliflower, and brussels sprouts), is associated with a reduction in the incidence of cancer at several sites in humans
Alcohol	When consumed in large quantities, alcoholic beverages appear to act synergistically with inhaled cigarette smoke to increase the risk for cancers of the mouth, larynx, esophagus, and the respiratory tract
Naturally occurring carcinogens	. . . certain naturally occurring contaminants in food are carcinogenic in animals and pose a potential cancer risk to humans
Other	
Protein Carbohydrates Vitamin E (α-tocopherol) Vitamin B complex Other minerals Mutagens in food Food additives Environmental contaminants	The committee did not find enough evidence, either epidemiologic or laboratory, to make a positive statement regarding the protective or contributory role of these dietary components to cancer

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