

CJON BOOK EXCERPT SERIES

Cancer Prevention

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This excerpt, chapter 1 from the book *Nutritional Issues in Cancer Care*, edited by Valerie J. Kogut, MA, RD, LDN, and Sandra L. Luthringer, RD, LDN, is part of a series of clinically relevant reprints that appear regularly in the *Clinical Journal of Oncology Nursing*.

Overview

Perhaps no subject is more confusing or emotionally charged than food, as it influences our well-being. Eating and taking pleasure in food are central to health (Weil, 2000). The word “cancer,” in contrast, connotes pain, suffering, and death. Cancer causes fear and panic and offers no immunity. Food is our nourishment, associated with comfort and pleasure. Food also is a cancer mediator and deserves closer study.

Michael Sporn, cancer researcher at Dartmouth Medical School, said, “People are obsessed with cures . . . and the (elusive) miraculous cure. They are being . . . selfish by ignoring what could be done in terms of prevention” (Leaf, 2004, p. 88). Andy von Eschenbach, director of the National Cancer Institute (NCI) and a cancer survivor, said we must be on a “mission to prevent the (cancer) process” from occurring at all (Leaf, p. 90). Our society can promote specific behaviors to reduce the risk of cancers. One of the greatest cancer preventions is acting on the knowledge of the benefits and detriments of nutrition.

Early in the 1930s, laboratory studies were conducted that found a correlation between diet and carcinogenesis (Kiple & Ornelas, 2000). Later, human epidemiologic studies were conducted that did not support the relationship. The United States, because of its large number of immigrants, was unique in allowing such an observation to occur. Immigrants showed a variation in cancer incidence compared to U.S.-born citizens. Factors could be genetic makeup, ethnic persona, and specific diets and lifestyles. These ethnic factors gave a control to the studies conducted in the 1930s (Clifford & McDonald, 2001; Weil, 2000; World Cancer Research Fund [WCRF] & American Institute for Cancer Research [AICR], 1997).

Current scientific evidence relates diet and nutrition to cancer risk (WCRF & AICR, 1997). Although factors other than diet can play a role in the development of cancer, health experts know that paying attention to diet and related factors, including weight and exercise, is a proven way to reduce cancer risk.

Research is ongoing, and scientists are beginning to sort out the complex relationships between specific food components and their effects on health. Health and research agencies, such as the American Cancer Society (ACS) and AICR, attempt to summarize the current research in the form of recommenda-

tions that are frequently updated as more data are gathered. A landmark report by Doll and Peto (1981) estimated that 10%–70% of cancer deaths in the United States could be attributed to diet. They concluded that dietary factors could account for 35% of all cancer deaths. The Commission on Life Sciences (1982) reported convincing evidence that diet plays a role in human cancer and included guidelines for risk reduction. Several years later, Willett and Trichopoulos (1996) estimated that one-third of cancers could be completely avoided if specific dietary guidelines were followed. Expert advisory committees used this research as a basis for ACS’s revised nutrition guidelines advocating a plant-based diet with the addition of physical activity (ACS, 1996). More recently, these guidelines were reviewed and revised (Byers et al., 2002). Referenced in these guidelines is the most comprehensive review to date from WCRF and AICR (1997). AICR estimated that 30%–40% of all cancers could be prevented with a healthier diet and exercise. The joint report included 15 specific guidelines for public health goals and advice to individuals. An AICR panel convened in 2003 with the mission of reviewing 10,000 reports from 1997–2003 to further refine the guidelines. The revisions of these guidelines will be completed in 2006. Recommendations of ACS (Byers et al.) and WCRF and AICR (1997) include a plant-based diet to reduce the risk of certain types of cancer.

Diet’s Protective Influence

The Role of Whole Foods Versus Dietary Supplements

Nutrients from whole foods are more beneficial than those obtained from supplements. A single fruit or vegetable contains many nutrients and protective chemicals. These chemicals act together to provide a better defense against disease (Cataldo, DeBruyne, & Whitney, 2003). It is not likely that a person would receive dangerously high doses of any single plant chemical if

From *Nutritional Issues in Cancer Care* (pp. 1–14), edited by Valerie J. Kogut, MA, RD, LDN, and Sandra L. Luthringer, RD, LDN, Pittsburgh, PA: Oncology Nursing Society. Reprinted with permission.

Digital Object Identifier: 10.1188/06.CJON.649-655

obtained from food sources rather than a pill. Certain dietary supplements can increase cancer risk, and megadosing of some vitamins and minerals can pose unique or unsafe risks from side effects. However, because of the suggestion that plant ingredients might protect against cancer and other diseases, many people are turning to vitamin and mineral supplements or to special diets. Polunin (1999) demonstrated that supplements of beta-carotene and vitamin C showed no protective effect, but eating the actual antioxidant-rich foods had a protective effect on cells. Willett (1999) noted that at least 200 epidemiologic studies suggested that people who consistently consume large amounts of fruits and vegetables have a reduced risk of developing cancer at a number of sites. In a review by Block, Patterson, and Subar (1992) of 156 studies, 82% showed that adequate fruit and vegetable consumption had a protective effect against epithelial types of cancer, including all gastrointestinal, laryngeal, and lung and some skin cancers. WCRF and AICR (1997) reported that vegetable intake decreases one's risk of cancer at 16 cancer sites, and fruits decrease cancer risk at 12 sites, yet the National Health and Nutrition Examination Survey (Patterson, Block, Rosenberger, Pee, & Kahle, 1990) indicated that only 1 in 11 Americans met the guidelines for eating at least three servings of vegetables and two servings of fruit a day.

The Role of Food Components in Carcinogenesis

The cancer process involves three stages: initiation, promotion, and progression (Ruoslahti, 1996). Nutrients and phytochemicals are influences in all stages. Dietary factors influence carcinogenesis directly and indirectly. Nutrients and phytochemicals can inhibit enzymes that activate carcinogens and induce enzymes that detoxify them. Phytochemicals protect plants from insects, disease, and harsh environmental conditions. Research shows that some phytochemicals and nutrients play a role in protecting human cells from cancer. Phytochemicals are non-nutrient chemicals in plant foods that provide pigment and flavor; they give onions and garlic their pungent taste and aroma and other fruits and vegetables their bright and varied colors (Boik, 2001).

In initiation, the procarcinogens enter the cell. Nutrients and phytochemicals can inhibit or block the chemical change by enzyme-driven mechanisms. Vitamin C, for example, inhibits enzymatic activation of chemicals that prevents nitrates from being changed into carcinogenic nitrosamines associated with gastric cancer. Other enzymes induced by phytochemicals, such as glutathione S-transferase, can detoxify and remove potential carcinogens (Health Science Institute, 1997b). If the potential carcinogen compound is not deactivated at this point, it can enter the cell's nucleus, where its DNA can be altered. Once initiation has occurred, the damaged cell cannot be repaired (Health Science Institute, 1997b).

In promotion and progression, latent initiated cells can be transformed into differentiated cells that progress into a tumor (Health Science Institute, 1997a, 1997b). This is a relatively prolonged process that can take several years. Unlike initiation, the processes of promotion and progression can be reversed. Food components can play a vital role in this reversal. For example, certain types of dietary fats act as promoters, and animal research has shown removing fat from the diet can slow the progression of a tumor (Wang et al., 1995).

Phytochemicals and Nutrients

Phytochemicals have the ability to act as antioxidants. Antioxidants work in a variety of ways to stabilize, deactivate, or transform oxygen free radicals (AICR, 1999a). Studies suggested these protective molecules work at all stages of carcinogenesis (Caragay, 1992). Any single fruit or vegetable may contain hundreds or more of the thousands of known phytochemicals (AICR, 1999b). Isolating single phytochemicals does not always demonstrate the same protection as in a combination found in whole food. Chemoprevention trials (Alpha-Tocopherol, Beta Carotene Cancer Prevention Study Group, 1994; Goodman et al., 1993) found that synthetic beta-carotene supplements might increase the risk for lung cancer in a high-risk group of cigarette smokers. Moss (2000) expressed concern over supplementation of carotenoids: "Giving too much of one carotenoid decreases the others, and may paradoxically lower one's resistance to cancer" (p. 32).

Similar to the evidence that some nutrients are dependent on others for completeness of metabolism and function, the same holds true for phytochemicals. Finding the correct phytochemical that offers protection at a specific cancer site is a tedious process. Several phytochemicals currently are being studied to determine how they influence the cancer process. Some of the phytochemicals of interest and their proposed mechanism of action are listed in Table 1-1.

Fiber

Fiber has been associated with a possible decreased risk for colorectal, pancreatic, and breast cancers (WCRF & AICR, 1997). Proposed mechanisms for fiber in colon cancer reduction include lowering the colonic pH, diluting and binding genotoxic agents, and increasing short chain fatty acids to help to slow cell proliferation (Kiple & Ornelas, 2000; Willett, 1999). Fiber increases the bulk of the intestinal contents, which stimulates intestinal peristalsis and speeds food through the colon for reduced contact time. However, in large prospective studies, total fiber intake has not been shown to reduce the risk of colon cancer (Willett, 1999). Confounding issues include the interactions of nutrients and other phytochemicals in foods that contain fiber. Even though evidence is inconclusive, ACS recommends consumption of high-fiber foods (Byers et al., 2002). The National Academy of Sciences (Hermann, 2002) did not set an upper limit for individuals because of the likelihood that consumption is self-limiting, but specific fiber amounts related to gender and age have been determined. For example, the current guidelines recommend 14 grams per 1,000 calories of adult food intake. More trials are needed to explore the connection between the interaction of nutrients and phytochemicals in foods that contain fiber and the interaction of fat consumption and fiber.

Physical Activity's Protective Influence

In 2001, the World Health Organization reviewed the role of physical activity for cancer risk reduction. This work group reported recent research studies that indicated moderate to vigorous activity decreases the risk of colon and breast cancers independent of an individual's weight (Vainio & Bianchini, 2002). That same work group reported limited evidence suggesting

Table 1-1. Phytochemicals, Food Sources, and Their Proposed Mechanisms of Action

PHYTOCHEMICAL	FOOD	PROPOSED MECHANISM(S) OF ACTION
Allicin, diallyl sulfide, and S-allyl-L-cysteine	Garlic and onions	Inhibit phase I enzymes that activate carcinogens; induce phase II enzymes that detoxify carcinogens
Catechins	Tea: green and black	Antioxidant; prevent lipid peroxidation by inhibiting lipoxygenase enzymes; inhibit cyclooxygenase enzymes
Ellagic acid	Strawberries and grapes	Antioxidant
Flavonoids Citrus: diosmin and hesperidin	Grapefruit and orange juice	Decrease polyamine levels that have a role in cell growth and proliferation
Noncitrus: genistein and daidzein (phytoestrogens)	Soy, red grapes, and apples	Antioxidant; compete with and block estrogens/androgens from binding to their receptors, which retard cell proliferation
Indoles	Cabbage and turnips	Increase conversion of estrogens to inactive forms; induce phase II enzymes (glutathione S-transferase) to increase carcinogen detoxification
Isothiocyanates	Cruciferous vegetables (broccoli, brussels sprouts, cauliflower)	Inhibit phase I enzymes that activate carcinogens; induce phase II enzymes that detoxify carcinogens (Note: phase II enzymes include glutathione S-transferases and NADPH: quinone reductase)
Lignans	Flaxseed and grains	Prevent estrogens and prostaglandins from binding to their receptors, which retard cell proliferation
Lycopene	Tomatoes and watermelon	Antioxidant
Monoterpenes Limonene	Lemon and orange peel	Decrease cell proliferation by decreasing ornithine decarboxylase activity, which is important to the induction of carcinogenesis; decrease activity of growth-promoting <i>ras</i> proteins; increase latent period as inhibitor of promotion; prevent oncogene expression; induce phase II carcinogen detoxification enzymes
Phenols	Turmeric, mustard, tea, berries, grapes, and sesame seeds	Antioxidant; inhibit activity of lipoxygenase and cyclooxygenase enzymes; inhibit formation of carcinogens such as nitrosamines; induce phase II enzymes that detoxify carcinogens
Phytate	Soybeans, grains, nuts, and seeds	Inhibits cell proliferation and metastasis
Polyphenols	Artichokes	Antioxidant; induce phase II enzymes that detoxify carcinogens
Protease inhibitors	Soybeans, dried beans, and lentils	Antioxidant; inhibit malignant cell transformation; inhibit gene amplification; inhibit estrogen- and glucocorticoid-receptor binding; inhibit <i>c-myc</i> oncogene expression and cell proliferation
Saponins	Soy foods, legumes, herbs, and vegetables	Inhibit proliferation of malignant cells
Sulforaphane	Broccoli	Induces phase II enzymes that detoxify carcinogens

Note. Based on information from “Beyond Vitamins,” 1999; Gollman & Pierce, 1998; Health Science Institute, 1997a, 1997b.

a preventive effect of physical activity on endometrial and prostate cancers. Exact amounts for duration and frequency of exercise still are being studied. ACS currently recommends moderate to vigorous activity for 45 minutes five or more days per week to further reduce the risk of breast and colon cancers. The benefit is cumulative, but 20 or more minutes per session are suggested (Courneya, 2002). Physical activity affects different mechanisms that may play a role in cancer risk reduction. It can help with achieving and maintaining a healthy body weight. A healthy body weight could lead to less adipose tissue, which would decrease the exposure of hormones stored in this tissue that play a role in some forms of breast cancer (Wynder et al., 1997). This also may play a role in decreasing circulating insulin and related growth factors (Bianchini, Kaaks, & Vainio, 2002). Physical activity also assists with peristalsis, which shortens the time exposure of mutagens to the bowel epithelial tissues (Duyff, 1998). Evidence suggests that simply not being seden-

tary decreases colon cancer risk. Increased activity has been associated with approximately a 40% risk reduction in colon cancer (Vainio & Bianchini). Breast cancer risk evidenced a reduction of as much as 20%–40% for the most physically active group in one study (Vainio & Bianchini).

Diet as Promoter of Carcinogenesis

Fats and Obesity

Cancer risk-reduction research findings are in conflict regarding the association between fat intake and weight or obesity. Questions to be answered include the interactions and connections of fat in diet to

- Total energy intake
- Type of fat
- Obesity
- Energy expenditure

- Fiber
- Vitamins
- Minerals
- Phytochemicals.

Scientific evidence suggests some relationship between fat intake and lung, colorectal, breast, endometrium, and prostate cancers (WCRF & AICR, 1997). Current research on the effects of the type of fat look promising (Byers et al., 2002). Saturated fats should be limited, with more emphasis on monounsaturated fats (WCRF & AICR). The evidence is still insufficient regarding the role of polyunsaturated fatty acids in cancer development to draw conclusions on intakes for humans (Willett, 2002). Results from intervention trials are needed.

Fat in the diet can play a significant role in excess calories leading to obesity, but there is speculation that fat itself might not be as much of a culprit as originally suggested (Willett, 2002). Obesity from excess calories (fats, proteins, carbohydrates, alcohol) may be more significant than just fat in the diet. Overweightness and obesity are associated with an increased risk of cancer at these sites: breast, colon and rectum, endometrium, esophagus, gallbladder, liver, pancreas, and kidney (Byers et al., 2002). Gender-specific research indicates an increased risk in stomach and prostate cancers for men and in breast, uterine, cervical, and ovarian cancers for women (Calle, Rodriguez, Walker-Thurmond, & Thun, 2003).

Additives, Contaminants, and Cooking Methods

Powerful carcinogens can be created or formed in the preservation and preparation of foods. For decades, the public has been concerned about the possibility of cancer risk from additives or contaminants. However, this has not proved to be as great a factor as has been touted. Additives help to make foods safer and improve their stability. Some of the synthetic chemicals used for sweetening, such as saccharin, once were listed as carcinogenic but since have been proved harmful only in laboratory mice (Kiple & Ornelas, 2000). Nitrate (saltpeter) concentrations can lead to the formation of carcinogenic compounds. Salt used in pickling solutions is associated with a high cancer risk, but these additives increase cancer risk from the carcinogens only when consumed in large quantities. Food safety versus the danger of overuse becomes a question. Moderation of all things is the key element in food consumption (Kiple & Ornelas).

It is interesting to note that not all chemicals in foods are disease protective. Some phytochemicals are naturally occurring carcinogens produced possibly to ward off insects, disease, and/or a harsh environment (Shils, Olson, Moshe, & Ross, 1994). In rodent studies, the doses required to cause cancer in humans exceeded dietary intake (Shils et al.). Other chemicals in foods that are not naturally occurring include pesticides and additives, such as artificial sweeteners. Carcinogenic or mutagenic compounds in plants are formed during cooking, such as polycyclic aromatic hydrocarbons, heterocyclic amines (HCAs), and possibly acrylamide (Tareke, Rydberg, Karlsson, Eriksson, & Tornqvist, 2000). The best method for cooking muscle meat is under 400°F (212°C) to reduce these compound formations (Mayo Clinic, UCLA, & Dole Food Company, 2002). Other effective methods are baking, boiling, braising, steaming, and poaching. The effect

on cancer rates from these cooking methods is extremely difficult to determine.

AICR (2002) stated that no convincing evidence shows that eating foods containing trace amounts of chemicals such as fertilizers, pesticides, herbicides, and drugs used on farm animals changes cancer risk. AICR (2002) reported environmental pollutants cause less than 1% of all cancers. Byers et al. (2002) stated that pesticides and herbicides can have a health risk if not used properly, but at low doses, pesticides and herbicides do not increase cancer risk. The benefits of a plant-based diet far outweigh any harm from exposure to trace amounts of chemicals that may be found in these foods.

Pesticides are regulated by the following government organizations: Environmental Protection Agency, the U.S. Food and Drug Administration, and the U.S. Department of Agriculture (USDA). These agencies are responsible for approving pesticide levels in food, setting the tolerance levels, and inspecting domestic and imported foods for compliance. They work together to regulate substances and determine the status of "Generally Recognized as Safe." If a concern is raised, the substance must go through a food additive premarket review and approval process (Thompson, 2000).

Genetically modified foods also must satisfy safety requirements. The pros and cons of these foods currently are being researched (Thompson, 2000). A number of valid concerns arise with altering genetic makeup by gene splicing, such as violating dietary restrictions and/or religious beliefs or introducing altered genes to the human food supply. Genetic changes can alter the plant to make it more frost resistant, for example (Beringer, 1999). A plant may be modified so that it is less susceptible to insects with the possible benefit of requiring fewer pesticides (Thompson). Research regarding the safety of consuming genetically modified foods will continue well into the future.

Organic Versus Conventionally Grown Produce

A review by Williams (2002) indicated few compositional differences comparing organically grown vegetables and fruits to conventionally grown produce. Another study stated there is not strong evidence that organic and conventional foods differ in nutritional quality (Bourn & Prescott, 2002). However, some differences in these comparisons include variation in the groups studied as well as differences in growing conditions: organic versus conventional. Organic does not necessarily mean pesticide-free (Baker, Benbrook, Groth, & Benbrook, 2002). A Consumer Union report on unwashed produce indicated 25% of the organic produce contained residues, compared with 77% of the conventional produce (Neville, 1999). The organic foods may be exposed to chemicals carried in the wind or water. The USDA (2002) developed new criteria to receive the stamp of "Certified Organic" in 2002. Farmers must use only government-preapproved, plant-based chemicals; pesticides and herbicides are prohibited. Farmers also must use land that has been free of pesticides or herbicides for several years and be open to inspections, including samples of soil, water, and plant tissue. Individual steps to reduce pesticide residue would include scrubbing fruits and vegetables under running water, removing outer leaves, choosing produce free of holes, eating a

variety of foods to lower exposure to any one pesticide, and, if affordable, choosing organic (AICR, 2002). Variety is key, and this will ensure exposure to a number of protective chemicals present in various plant-based foods while decreasing exposure to chemicals that may be used on any one specific crop.

Alcohol

Alcohol's proposed mechanisms in the cancer process include source of free radicals, solvent to carcinogens, and, if abused, depleted nutrient intake (Physician Oncology Education Program, 2001). Molecules in alcohol are being researched for their beneficial effects with reducing the risk of heart disease, but this research has not yet been shown to carry over to cancer risk reduction. Alcohol has been associated with an increased risk of head and neck cancers and gastrointestinal cancers, especially if combined with tobacco (Bal, Woolam, & Seffrin, 1999). Alcohol also has been associated with an increased risk of cancers of the lung, liver, and breast (WCRF & AICR, 1997). Currently, both ACS and AICR suggest moderate consumption of no more than two drinks per day for men and no more than one drink per day for women (Byers et al., 2002; WCRF & AICR). Typically, a serving size for one drink is the equivalent to 12 oz. of beer, 5 oz. of wine, or 1.5 oz. of liquor (Byers et al.).

Food Preparation

American culture includes meat preparation in the form of barbecuing, grilling, and frying, which involve cooking foods at a high temperature. Heat greater than 374°F (212°C) in contact with muscle meat produces HCAs (AICR, 2002; Lan & Chen, 2002). HCAs are associated with gastrointestinal (stomach, pancreatic, colon), breast, and prostate cancers (Lan & Chen; Sugimura, Wakabayashi, Nakagama, & Nagao, 2004). Other sources of protein, such as dairy products, eggs, or organ meats, do not have significant HCA amounts naturally or when cooked (NCI, 1996). Microwaving briefly (one to two minutes) or marinating the meat before placing it in contact with a high heat source reduces the formation of HCAs (Kiple & Ornelas, 2000; Mayo Clinic et al., 2002; Salmon, Knize, & Felton, 1997).

The Promotion of Prevention

Public Campaign

Education of the public about the need for cancer prevention as a priority is paramount. NCI recognizes the key role of prevention in the War on Cancer, and prevention has been one of ACS's primary concerns. Funding for prevention trials must be lobbied.

Knowledge of the prevention and protection benefits of foods must be brought to the public. The 2002 revised ACS guidelines included recommendations for community action for the first time (Byers et al., 2002). Current lifestyle trends related to adverse effects on the long-term health of children include sedentary lifestyle, increased use of electronic entertainment, increased reliance on automobiles, reduced leisure time, consumption of high-calorie convenience foods, and declining levels of physical activity. Recommendations include a challenge

to healthcare professionals to be active in their communities to promote lifestyle changes. A unique challenge for communities includes implementation of community and work-site health promotion programs and policies for planning to ensure that all groups have access to healthful food choices and opportunities for physical activity (Byers et al.).

Counseling

With respect to reducing cancer risk, the role of the healthcare professional is that of a counselor in assessing baseline and guiding clients in making healthy behavior changes. The thinking is that "the combined effects of nutrients as contained in the mixtures commonly known as whole foods seem to be more effective in reducing cancer risk than are nutrients contained in supplements. This simple conclusion can be a sound basis for broad nutritional advice to the population, as well as for clinical counseling of individual patients" (Bal, Woolam, & Seffrin, 1999, p. 328).

Common Foods and Their Cancer-Fighting Activity

Research continues to identify numerous anticancer activities from the established essential nutrients as well as from phytochemicals (non-nutrient chemicals that help to ward off disease). The mechanisms of protection still are being studied, but experts have grouped these foods and herbs according to their level of cancer-fighting activity. The following foods and ingredients are thought to decrease cancer risk (Craig, 1997).

Highest anticancer activity

- Garlic
- Soybeans
- Cabbage
- Ginger
- Licorice
- Umbelliferous vegetables (carrots, celery, cilantro, parsley, and parsnips)

Modest anticancer activity

- Onions, flax, citrus, and turmeric
- Cruciferous vegetables (broccoli, brussels sprouts, and cauliflower)
- Solanaceous vegetables (tomatoes and peppers)
- Brown rice and whole wheat

A lesser but still measurable amount of protection

- Oats and barley
- Mint, rosemary, thyme, oregano, sage, and basil
- Cucumber, cantaloupe, and berries

Summary

The full connection between diet and cancer still is incomplete. Results from ongoing control trials are needed. Unfortunately, these trials are time consuming and costly. Patients desire nutritional direction at the time of their sessions. Findings will need to be blended with the complexities of genetic predisposition risk, environmental risk factors, infection, pollution,

occupational risk factors, and other lifestyle risk factors for individualized diet plans to reduce cancer risk. Research estimates that two-thirds of cancer deaths in the United States can be linked to poor diet, obesity, lack of exercise, and tobacco use, all of which can be changed at an individual level.

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