The Role of Dietary Supplements during Cancer Therapy1

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This guide was compiled after recommendations by the American Institute for Cancer Research (AICR) Cancer Resource Advisory Council. It encompasses the AICR position on current issues in nutrition for cancer survivors during treatment and is intended to provide advice about dietary supplements for cancer survivors who are still being treated. Current scientific findings about the safety and effectiveness of some commonly used dietary antioxidants and nonantioxidant supplements during chemotherapy are presented and assessed. Use of dietary supplements during cancer treatment remains controversial. Patients are cautioned that vitamin and mineral supplements as therapies are not substitutes for established medicine. The current recommendation for cancer patients is to only take moderate doses of supplements because evidence from human clinical studies that confirm their safety and benefits is limited. A daily multivitamin containing supplements at the levels of the Dietary Reference Intakes can be used safely as part of a program of healthy nutrition. In addition, the AICR Cancer Resource Advisory Council concluded that further scientific research is needed to provide a set of firm guidelines for the use of vitamin and mineral supplements by cancer patients during treatment.

KEY WORDS: • dietary antioxidant • dietary supplement • micronutrients • chemotherapy

This guide is intended to provide advice about dietary supplements for cancer survivors who are still being treated, their families, their physicians, other health care providers (including dietitians), and the research community. It is concerned primarily with interactions among antioxidant supplements during chemotherapy rather than with their possible chemoprevention activities before treatment. The guide was compiled after recommendations by the American Institute for Cancer Research (AICR)3 Cancer Resource Advisory Council. It encompasses the AICR position on current issues in nutrition for cancer survivors during treatment.

AICR has always recommended a diet for cancer survivors that is low in fat; is high in fruits, vegetables, and whole-grain products; and has adequate levels of the major macronutrients as well as the various vitamins and minerals necessary to maintain good health (1). For cancer patients undergoing specific treatments, other nutritional regimens may be considered based on treatment status and disease stage.

Although nutrition has an important effect during treatment, oncologists often avoid giving advice, particularly about supplements. Individualized dietary advice during treatment is important so that undesirable weight loss or excessive weight gain can be avoided. During cancer treatments with either chemotherapy or radiation, patients often experience nausea, vomiting, diarrhea, and loss of appetite, leading to a lower intake of dietary constituents and weight loss. Supplemental intakes of essential vitamins and minerals may seem to be desirable but may not always be so. Before taking any supplements, patients should discuss the matter with their physicians because dietary interactions with the treatment may affect the outcome of therapy. Of special concern here are dietary supplements with antioxidant properties, but supplements without antioxidant properties may also influence the efficacy of cancer treatments.

Dietary supplements include macronutrients, vitamins, and minerals that are essential to human health as well as a wide variety of nonessential nutrients, such as certain phytochemicals, hormones, and herbs. The recommendation for cancer patients is to take only moderate doses of supplements because evidence from human clinical studies that confirm their safety and benefits is limited (2). Use of dietary supplements during cancer treatment remains controversial.

The source of a nutrient—that is, whether it is from a supplement or a natural food—influences the recommended level of intake. Fruits and vegetables eaten in the AICR recommended amounts of 5/d or more are safe for cancer patients during treatment except for patients with extreme sensitivity to potential infections, such as those undergoing bone marrow transplantation or aggressive chemotherapy while hospitalized under sterile conditions. Dietary Reference Intakes (DRI) established by the Institute of Medicine include the Recommended Dietary Allowance (RDA), Adequate Intake (AI), and Tolerable Upper Intake Level (UL) (2). The RDA is the average daily dietary intake sufficient to meet the nutrient requirement of nearly all healthy individuals. An AI is set when evidence is not sufficient to set an RDA. The UL is the highest level likely to pose no risk to nearly all individuals; it may be affected by cancer as well as cancer treatment.

This guide complements the AICR booklet "Nutrition of the Cancer Patient" (3). The term "dietary supplement" as used here is distinct from nutritional complementary or alternative (integrated) medicines, including specific botanicals. Current scientific findings about the safety and effectiveness of some commonly used dietary antioxidants and nonantioxidant supplements during chemotherapy are presented and assessed.

Dietary antioxidants

AICR and the World Cancer Research Fund advise that five or more servings of fruits and vegetables be consumed daily to reduce the risk of certain cancers (1). The beneficial effects of fruits and vegetables for both healthy people and cancer survivors have sometimes been associated with the presence of various antioxidant micronutrients. It has been claimed that oxidative processes are involved in various stages of carcinogenesis, that excessive antioxidants interfere with the cytotoxic effects of antineoplastic agents on cancer cells, and that certain micronutrients affect cancer prevention and treatment through their antioxidant properties. These micronutrients include vitamin E, vitamin C, ß-carotene, and other carotenoids, which are available singly or combined. The trace element selenium has an important role in antioxidant defenses as a crucial component of selenoproteins, such as glutathione peroxidase. Phytochemicals with antioxidant properties also include some flavonoids, such as quercetin, and some polyphenols.

Overall, there is no convincing evidence that antioxidant nutrients in the amounts obtained from fruits and vegetables in the diet have any deleterious effects on human health (1). However, trials in which selected antioxidants are taken in amounts or combinations much higher than those normally found in foods have yielded conflicting data regarding cancer risk (4–6). Cancer patients should try to eat sufficient fruits and vegetables daily to provide adequate levels of

antioxidants, with the addition of a daily multivitamin-multimineral pill. The benefits of eating fruits and vegetables may be much greater than are the effects of any of the individual antioxidants they contain because the various vitamins, minerals, and phytochemicals in these whole foods may act synergistically (1,7).

Two opposing views exist about the use of antioxidants in cancer therapy. One working hypothesis recently proposed is a complementary approach in which multiple antioxidant supplements together with a low fat, high fiber diet and lifestyle modifications, including physical exercise, may markedly improve the efficacy of standard and experimental cancer therapies (8). Dietary supplementation with antioxidants may provide a safe and effective means of enhancing the response to chemotherapy and improving quality of life by reducing or preventing side effects (8–10). On the other hand, an argument against using supplemental antioxidants during chemotherapy is that they may interfere with the oxidative breakdown of cellular DNA and cell membranes necessary for the agents to work (11,12). A further argument for avoiding the addition of large doses of antioxidants during cancer treatment comes from evidence that the apoptotic breakdown of tumor cells is selectively increased by the presence of reactive oxygen species within the tissue and that this process will be slowed down by an antioxidant-replete diet (13).

Because of the widespread use of antioxidants by cancer patients, further research is needed to establish the clinical implications of various doses. Effects may vary depending on the amount available to normal and tumor cells. Tumor cells are hypothesized to have impaired homeostatic control mechanisms, which would allow excess uptake of vitamins and minerals. This uptake could subsequently shut down oxidative reactions required for vital cellular functions and lead to cell death, reduced cell proliferation rate, or induction of differentiation that would override any protective effect of antioxidants (8). Theoretically, these effects overall would be advantageous in the treatment of tumors, but the results must be carefully examined, not only during and immediately after cessation of chemotherapy, but over the long term (12,14). It should be remembered that so-called antioxidant nutrients under certain circumstances may act as prooxidants.

A large percentage of cancer patients undergoing active treatment take supplemental antioxidants in addition to a daily multivitamin-multimineral preparation probably with the belief that, at the very worst, they can do no harm. However, more research is needed before definitive positive or negative advice can be given about the use of antioxidant dietary supplements as adjuncts to cancer chemotherapy or radiotherapy. It is recommended that a daily multivitamin-multimineral supplement containing quantities at the levels of the DRI can be used safely as part of a program of healthy nutrition. Taking dietary supplements containing levels of nutrients with antioxidant properties much greater than the DRI is not recommended during chemotherapy because higher levels may have adverse effects and interfere with efficacy of treatment. Patients should not be discouraged from taking folic acid at the level of the RDA because this has many other benefits for health.

No good advice for cancer patients currently exists; a greater understanding of processes involved in the regulation of tumor growth is needed. After reviewing the available scientific literature, AICR has concluded that supplementation of the diets of cancer patients undergoing active treatments with individual or combined antioxidants above their DRI cannot be recommended as safe or effective. A second overall conclusion from the available data is that use of high levels of antioxidants as the sole treatment protocols is not advisable because they may be deleterious to normal cells via a prooxidant effect or may confer an advantage to cancer cells. A recent comprehensive guide providing nutritional advice for patients at different stages of cancer survivorship concluded that patients undergoing chemotherapy or radiotherapy should be advised not to exceed the UL for vitamin and mineral supplements and to avoid other nutritional supplements that contain large doses of antioxidants (7). Specific recommendations for a particular antioxidant remain controversial.

Vitamin E. Vitamin E is a lipid-soluble antioxidant. It is naturally synthesized only by plants, and its various forms occur in different proportions. The main sources of vitamin E are edible polyunsaturated vegetable oils. Vitamin E is the most important nutrient for preventing polyunsaturated fatty acid peroxidation. -Tocopherol is the form of the vitamin most commonly used as a supplement, but vitamin E succinate is also used. The RDA for vitamin E is 15 mg/d; the UL is 1000 mg/d (15).

Vitamin E may prove to be an important nutrient for enhancing antineoplastic activity because of its role in preventing the peroxidation of lipids. This property maintains the rapid proliferation of cancer cells, which is essential to chemotherapy, while preventing damage to normal cells and having beneficial effects on immune function. Some evidence shows that in cancer cells vitamin E has a synergistic effect with chemotherapy and radiation (10). In animal studies, combinations of high doses of vitamin E and chemotherapy have had beneficial effects, detrimental effects, and no effect (10).

Vitamin E may be useful in the management of treatment for some cancer patients because it has been shown to reduce pain (16), prolong survival in conjunction with (n-3) polyunsaturated fatty acids (17), reduce fibrosis from radiation treatment (18), and decrease oral mucositis associated with chemotherapy (19). Vitamin E, although reported to reduce somewhat the cardiotoxicity of doxorubicin, had no striking effect otherwise (20,21). Treatment of oral leukoplakia with vitamin E was successful and well tolerated (22). Intensive topical treatment with vitamin E may facilitate the healing of chemotherapy-induced stomatitis (23).

In considering the possible use of supplementary vitamin E, it is essential to remember that vitamin E may act as a prooxidant in cigarette smokers, particularly if they are following a diet with high amounts of (n-6) fatty acids (24). In addition, vitamin E acting as a prooxidant in high concentrations was shown to directly inhibit human prostate tumor growth via induction of tumor cell apoptosis without affecting surrounding tissues (25). 5-Fluorouracil is possibly the single most effective treatment for advanced colorectal cancer; vitamin E was shown to induce cell death in colorectal cancer cells and to enhance growth inhibition of these cells by 5-fluorouracil (26), suggesting an adjuvant therapy for colorectal cancer.

Although vitamin E appears to be beneficial in some cases, and some animal experiments have suggested that high doses of vitamin E may enhance the efficacy of chemotherapeutic drugs, AICR has concluded that the evidence is not sufficiently strong to warrant its routine use by patients receiving chemotherapy or radiation therapy. Oversupplementation with vitamin E is not recommended during traditional therapies. The UL of vitamin E should not be exceeded in supplements given to cancer patients. The RDA may safely be provided for cancer patients to prevent deficiency. If there is serious malabsorption, the amount of vitamin E has to be increased.

Vitamin C. Vitamin C is a water-soluble nutrient that has antioxidant properties. It is common in a variety of fresh fruits and vegetables. It is widely used by cancer patients but its effect on conventional treatment is not known. Limited preclinical data suggest that vitamin C may either stimulate or inhibit tumor growth depending on the form, dose, and timing of supplementation, cancer site, and type of chemotherapy (9). The interactions of vitamin C with chemotherapy and radiotherapy remain unclear in the absence of rigorous, comprehensive preclinical and clinical research, although vitamin C in high concentrations increased the toxicity of some chemotherapeutic drugs in animals (10).

The RDAs for vitamin C are 90 mg/d for men and 75 mg/d for women; the UL is 2000 mg/d (15). Some evidence shows that the recommendations for vitamin C intake should be several times higher to achieve tissue saturation in normal people (27). Adverse effects of vitamin C (diarrhea, gastrointestinal disturbances, abdominal bloating) are rare and are associated with an intake of several grams daily. A recent review of studies pointing to the dangers of consuming excessive amounts of vitamin C noted that in large amounts, vitamin C changes from a protective

antioxidant agent to a harmful prooxidant that may interfere with standard therapies (28). Vitamin C can induce the decomposition of lipid hydroperoxides in vitro, which theoretically could give rise to DNA damage in vivo (29). The investigators used concentrations of vitamin C comparable with what they thought would be found in the human body with an intake of 200 mg/d. Whether these same conditions actually prevail in the human body remains uncertain (30). Many studies have shown that the amount of vitamin C that the body can store is limited, so a question remains about what beneficial effect is possible with large doses. Data are sufficient for people to be wary of taking megadoses (600 mg/d).

One clinical study suggested protection against chemotherapy-induced mutagenesis after daily supplementation with 1 g vitamin C (31); supplementation with 100 mg vitamin C had no significant effect. In another study vitamin C was believed to enhance immune function by increasing natural killer cells and the function of T- and B-cell lymphocytes (32).

AICR recommends that cancer patients should follow a reasonable diet sufficient in the fruits and vegetables that provide vitamin C at least at the RDA level but that they should not take more supplemental vitamin C than the amount obtained in a reliable daily vitamin-mineral pill containing vitamin C at the level comparable with RDAs.

ß-Carotene. ß-Carotene is one of 600 plant compounds classified as carotenoids. ß-Carotene is the most abundant carotenoid and is found in orange vegetables and fruits and in dark-green leafy vegetables. It is widely used as a supplement but its only defined role in nutrition is as a precursor for vitamin A. Although ß-carotene is an antioxidant, its importance to health in this role is not established. No DRI is proposed for ß-carotene or other carotenoids (15) but existing recommendations (1) for increased consumption of carotenoid-containing fruits and vegetables are supported.

Because of evidence that ß-carotene supplements have not been shown to confer any benefit for the prevention of cancer and may actually cause harm in certain subgroups, ß-carotene supplements are not advised routinely for cancer patients. Four large studies involving ß-carotene supplementation have provided no evidence of a protective effect against cancer and two studies showed an increased risk of lung cancer and overall mortality (1).

Some data from studies in animal and human cancer cells in culture suggest that ß-carotene may increase the efficacy of chemotherapy and radiation (10). Most studies have been done with a combination of ß-carotene and other antioxidants. Studies in patients, however, are too few and too fragmentary to enable conclusions to be drawn about efficacy or to make definite recommendations or guidelines for patients and for health professionals.

It has also been suggested that ß-carotene is not an antioxidant exclusively and that its observed effects are related to other biological properties (33). AICR therefore recommends that patients not take ß-carotene in quantities unattainable from a normal diet and that it is more beneficial to eat carotenoid-rich fruits and vegetables.

Selenium. The trace mineral selenium is not itself an antioxidant but within cells it is incorporated into selenoproteins, some of which have antioxidant functions. The best characterized antioxidant selenoprotein is glutathione peroxidase. Selenium occurs naturally in cereal products, a wide variety of vegetables, and seafood. The richest source of selenium in a supplement is a selenium-enriched brewer's yeast. The RDA for selenium is 55 µg/d; the UL is 400 µg/d (15).

Recent studies with animals indicate that selenium supplementation may enhance the effectiveness of various chemotherapeutic agents (10,34,35). Thus, there is great interest in selenium as a preventative agent for cancer at a variety of sites. The suggested mechanism is that selenium (through glutathione peroxidase activity) acts as a scavenger for products of oxidation

reactions induced by standard therapies. In addition, selenium supplementation may directly cause tumor cell apoptosis.

The development of drug resistance is a major cause for the failure of chemotherapy, particularly in ovarian cancer. Research has focused on reversing drug resistance and the alternative approach of preventing the development of resistance. Selenium compounds were found to prevent the induction of drug resistance by cisplatin in human ovarian tumor xenografts (35).

Few studies in cancer patients have examined the extent to which selenium supplementation protects patients during chemotherapy and radiation. Oversupplementation is contraindicated because selenium is toxic at higher levels. Among dietary nutrients, selenium has a particularly narrower dose range between efficacy and toxicity. Evidence is not sufficient for either broad or precise recommendations to the public for cancer patients during treatment.

Combinations of antioxidants during cancer treatment

More research is needed on the effects of different combinations of antioxidant supplements on cancer patients during treatment. Because of extensive interactions—both synergistic and antagonistic—that occur in vivo, the outcome of their total action cannot be assumed to be equal to the sum of the individual antioxidant actions. The lack of information on such interactions raises concern about making recommendations for the indiscriminate use of these supplements. Therefore, the AICR recommendation of fruits and vegetables in the diet rather than relying on large amounts of a multivitamin-multimineral supplement is a sound strategy. In addition to consuming fruits and vegetables during the treatment of cancer, patients should only take a daily multivitamin-multimineral pill containing antioxidants below the UL.

Dietary supplements without antioxidant properties

Many nonantioxidant supplements are widely taken by cancer patients although their effects on the efficacy of chemotherapy treatments are controversial. Among these are soy foods and soy products, (n-3) fatty acids, and vitamin D.

Soy protein and isoflavones. Soy protein is the highest quality protein found in the plant kingdom and is eaten as a staple by two-thirds of the world's population. On the basis of numerous studies demonstrating that soy protein reduces serum cholesterol levels, the U.S. Food and Drug Administration approved the health claim that eating 25 g/d of soy protein reduces the risk of heart disease (36).

A lot of evidence suggests that soy consumption may decrease breast cancer risk. This decrease has been largely attributed to isoflavones in the soy protein, primarily the phytoestrogens genistein and daidzein. Soy isoflavones inhibit the growth of both estrogen receptor–positive and receptor–negative breast cancer cells in vitro (37). In a review of 26 studies of the effects of soy or soy isoflavones on eight cancer sites in animals, soy had positive (inhibitory) effects in most cases (38). None of these studies indicated that soy increases tumor development. However, as recently reviewed, the overall epidemiologic evidence relating soy and breast cancer risk remains controversial (39).

Isoflavones may exert antiestrogenic effects on breast tissue and for this reason soy products and isoflavone supplements are widely taken by breast cancer patients. However, recent concerns over the possible detrimental effects of soy isoflavones on breast cancer patients because of their estrogen-like properties demonstrated in some experimental systems has led to considerable controversy as to whether they should be taken by these patients (39). Genistein, for example, inhibits the growth of both hormone-dependent and -independent breast cancer cells in vitro, but at low concentrations proliferation of at least one breast cancer cell line is stimulated by genistein (39).

A recent review of the available data addressed two extreme and opposing claims: soy is effective against breast cancer and because of this should be recommended for consumption by healthy women and breast cancer patients, and soy is harmful for women with a history of breast cancer or who are at high risk and therefore should be avoided by such women (39). The authors concluded that the data are not convincing enough to support either claim and that strong conflicting data exist regarding both.

AICR concludes that at this time information is not sufficient to make a recommendation about soy foods or soy products. Supplements containing isoflavones are not recommended because the levels of the isoflavones contained are in most cases much higher than what can be obtained in the diet.

Polyunsaturated fatty acids. Two families of polyunsaturated fatty acids are essential: the (n-6) and the (n-3) families, which are grouped according to their chemical structures. Although plants can synthesize both the basic (n-6) and (n-3) structures, animals (including humans) cannot and must obtain them from dietary sources. Linoleic acid is the parent fatty acid of the (n-6) family and -linolenic acid is the parent of the (n-3) family. The Western diet is rich in (n-6) fatty acids and poor in (n-3) fatty acids because of the large amounts of vegetable oils and meats and relatively low amounts of fish in the diet. Both (n-6) and (n-3) polyunsaturated fatty acids are important components of animal and plant cell membranes.

-Linolenic acid comes from green leafy vegetables, flaxseed, rapeseed, and walnuts. Humans can form eicosapentaenoic acid and docosahexaenoic acid from -linolenic acid or get them from eating fish. Most liquid vegetable oils, including corn, are rich in linoleic acid. Humans can form arachidonic acid from linoleic acid or get it from eating meat. Eicosapentaenoic acid and arachidonic acid are precursors of prostaglandins and leukotrienes.

Indications are that dietary (n-3) fatty acids can significantly retard the growth of tumors whereas (n-6) fatty acids potentially can increase tumor development (40). However, the data are largely derived from animal experiments (41), and regulation of the growth of human cancers is still a controversial issue. Mechanisms of fatty acid effects on tumorigenesis and tumor growth are not well defined, but evidence exists that high levels of prostaglandin E2, derived from (n-6) fatty acids, promote tumor growth. Fish oil–enriched diets containing eicosapentaenoic acid and docosahexaenoic acid decrease the formation of prostaglandin E2, which coincides with retarded growth of tumor cells. An alternative mechanism proposed is that oxidative damage of the polyunsaturated fatty acids in fish oil enhances lipid peroxidation in the tumor to toxic levels.

Fish oil supplementation enhanced the efficacy of the cancer chemotherapeutic agent CPT-11 (irinotecan) against MCF7 breast carcinoma xenografts and ameliorated intestinal side effects in MCF-7–bearing mice (42). The explanation given is that the combination of fish oil and CPT-11 leads to the selective accumulation of lipid peroxidation products to cytotoxic levels in the MCF7 xenografts.

Experimental studies indicate that very-long-chain polyunsaturated fatty acids, in particular docosahexaenoic acid, may increase the sensitivity of mammary tumors to several cytotoxic drugs, including doxorubicin (43). Omega-3 (n-3) fatty acid supplementation for breast cancer chemoprevention is strongly supported by epidemiologic and experimental studies. Experimental data and data from a case-control study conducted on a homogeneous population in France suggest that -linolenic acid may have a protective effect in breast cancer (44). The association between levels of fatty acids stored in breast adipose tissue and the response of the tumor to chemotherapy in patients with an initially localized carcinoma was studied (45); primary chemotherapy combined mitoxantrone, vindesine, cyclophosphamide, and 5-fluorouracil. The results suggested that docosahexaenoic acid could increase the response of the tumor to the cytotoxic agents used. Dietary supplementation with (n-3) fatty acids was evaluated in several clinical trials, and the results suggest some benefits to cancer patients (17,46).

Recommendations made by AICR and other official organizations are that energy from dietary fat should be 30% of the total energy intake. Research indicates that the type of dietary fat is also important for normal growth and development and for treatment of cancer and other diseases. The ratio of (n-6) to (n-3) fatty acids seems to be critical in some cases. It is recommended that cancer patients and healthy people should consume the recommended AI for polyunsaturated fatty acids (47).

Vitamin D-3. Biological modifiers of cancer cells that are designed to retard proliferation; induce differentiation of these cells to a quiescent, nondividing stage; and promote cell death have been intensively studied in recent years. Several research studies have used a combination of vitamin D-3 (cholecalciferol) analogs with radiation.

Vitamin D-3 is a hormone produced in the skin by the action of sunlight. Supplements of vitamin D contain vitamins D-2 (calciferol; of plant origin) and D-3 (animal origin), both of which are biologically relatively inert and first have to be metabolized to the active form 1,25-dihydroxyvitamin D. Vitamin D-3 is biologically largely inactive until it is converted to 1,25-dihydroxyvitamin D-3. This active form not only plays a central role in bone and calcium metabolism but also has been shown to suppress the growth of tumors of different origins, including breast cancer cells (48). The AI for vitamin D are 5 μg/d for ages 19–50 y, 10 μg/d for 51–70 y, and 15 μg/d for 70 y. The UL is 50 μg/d (49).

A series of studies suggested a possible role for increased dietary calcium and vitamin D in the chemoprevention of colon and breast cancer (50,51). A major drawback to a clinical application in cancer therapy is that high doses of dihydroxyvitamin D-3 are needed; such high doses can lead to hypercalcemia and death (52). A major focus of chemoprevention research has been the synthesis of analogs of dihydroxyvitamin D-3 that have antiproliferative and prodifferentiation effects against cancer cells without resulting in hypercalcemia. The results are new synthetic vitamin D-3 analogs that are potent inhibitors of cancer cell growth (53,54). Their exact mode of action remains largely unknown.

The synergistic effects of dihydroxyvitamin D-3 analogs with retinoids, antiestrogens, and conventional chemotherapeutic drugs may result in enhanced response rates and reductions in the concentrations of conventional anticancer drugs, thereby reducing side effects (55,56). These analogs are still in an experimental stage. Definitive recommendations for vitamin D-3 and its analogs cannot be made for cancer patients at this time.

The benefits of ample consumption of fruits and vegetables in their entirety may be much greater than the positive effects of any of their micronutrient components because individual components may act in synergy during treatment. No evidence exists that fruits and vegetables are harmful to the cancer patient during treatment.

Patients are cautioned that vitamin and mineral supplements as therapies are not substitutes for either sound nutrition or established medicine. Taking a daily multivitamin-multimineral supplement containing essential nutrients at the levels of the DRI can be used safely as part of a program of healthy nutrition. Further scientific research is needed to provide a set of firm guidelines for use of additional vitamin and mineral supplements by the cancer patient during treatment. AICR presents specific recommendations in Table 1. Animal studies and cell culture studies often use relatively high levels of supplements to achieve a positive effect, but few clinical trials with high doses have been conducted. Without clinical trials, no firm basis exists for constructing guidelines.

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TABLE 1 Dietary supplements during cancer treatment: specific recommendations from the American Institute for Cancer Research

FOOTNOTES

1 This paper is included in the proceedings of the symposium "International Research Conference on Food, Nutrition, and Cancer" but was not presented at the symposium. It was compiled as a position paper by the American Institute for Cancer Research (AICR) Cancer Resource Advisory Committee. The content of this paper is germane to those presented at the symposium in the session on cancer survivorship issues. Authors not employed by the AICR received honoraria for serving on the Cancer Resource Advisory Committee.
3 Abbreviations used: AI, Adequate Intake; AICR, American Institute for Cancer Research; DRI, Dietary Reference Intakes; RDA, Recommended Dietary Allowance; UL, Tolerable Upper Intake Level.

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