ANTIOXIDANT SUPPLEMENTS MAY REDUCE CANCER RISK: NEW FINDINGS FROM THE EPIC STUDY

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An important research article appeared in the European *Journal of Nutrition* in 2011 showing that individuals, who were taking antioxidant supplements at the start of the 11-year study period, had a 48% reduction in the risk of cancer mortality. In addition, the risk of dying from all-causes (all-cause mortality), was 42% lower in the antioxidant supplement users. Of interest is the fact that taking only a basic multiple vitamin and mineral supplement (i.e., not enriched with meaningful doses of antioxidants) did not confer any protection against cancer or all-cause mortality. These findings suggest that antioxidant supplements provide an important defence against cancer and death from other causes. (1)

Most enlightened health care professionals are familiar with the experimental and preclinical studies showing that antioxidants quench and neutralize free radicals. Free radicals are unstable compounds that have been shown to damage DNA and increase risk of genetic mutations that can lead to cancer. (2) Human clinical trials have also shown that antioxidant supplements can improve immune function in older individuals. Immune function is an important part of cancer prevention, as various immune cells either directly kill emerging cancer cells or modulate other immune cells that destroy cancer cells or prompt cancer cells to undergo apoptosis (programmed cell death).(3) In addition, certain antioxidant vitamins exhibit other important anti-cancer properties, such as preserving gap junctions, inhibiting peptides (Bcl-2) that block apoptosis in cancer cells, sensitizing cytokine and cell membrane death receptors, inhibiting nuclear factor-kappa beta, down-regulating epidermal growth factor receptors, IGF-1 receptors, tyrosine kinase and phosphatidylinositol-3 kinase, within cancer cells, as well as other anticancer mechanisms. (4,5,6,7,8,9,10)

Diet, Lifestyle and Cancer

There is a marked overall difference in the total cancer incidence between developed and developing countries. Cancer of the cervix, liver, stomach and mouth are the most common cancers in developing countries. In Iran, esophageal cancer is a major concern and in Southeast Asia, naspharyngeal cancer is disproportionately high. In developed countries, lung cancer, colon cancer, breast cancer, prostate cancer and bladder cancer are the leading cancers of clinical significance (skin cancer has the highest incidence of all cancers, but only melanomas present significant mortality risk). Worldwide, the incidence of colon cancer varies 20-fold (highest in the US, lowest in India), and breast cancer varies 7-fold (highest in US Hawaiians, lowest in Israeli, non-Jews). In Europe, total cancer rates are approximately 50% lower in Greece compared to Germany. (11)

Evidence that this variation in cancer incidence is primarily a result of environmental and lifestyle factors, rather than genetic factors, is derived from several lines of investigation. First, studies of migrants moving from low-to high-risk areas have shown that migrants acquire the cancer incidence rate of their new country, within a relatively short period of time. For example, colon cancer incidence can increase up to 20-fold within a single generation. As well, rising and declining incidence of tobacco-

associated lung cancer, has also been shown. Forty years ago the incidence of colon cancer in Japan was extremely low and rare. Today, Japanese men living in Japan have colon cancer rates twice as high as seen in the United Kingdom. Clearly, there has been too little time for the Japanese gene pool to change sufficiently to account for this sudden rise in colon cancer incidence. Whereas, the affluence witnessed in Japan after World War II has brought with it significant changes to their dietary patterns (e.g. more meat consumption, less fiber consumption etc.) that mirrors the dietary patterns of much of the Western world, where colon cancer is the second leading cause of cancer death, after lung cancer. A similar transformation has also occurred in Hong Kong, where rates of cancer of the colon, breast, prostate, endometrium and lung, have gone from being among the lowest in the world to incidence rates similar to that of the United States. Once again, recently acquired affluence has brought about a Westernized shift in dietary and lifestyle practices in this region. (11)

In regard to colon cancer in Japan, experts suggest that the Japanese likely had a susceptibility to colon cancer that has been unmasked in recent years by their rapidly changing dietary patterns. Additional evidence to validate the contention that diet and lifestyle factors influence cancer risk more than genetic inheritance, is highlighted by the finding that there is only a 10% cancer correlation among identical twins, even though both twin pairs stem from the same sperm and egg cell at conception. As such, in 90% of cases where one of the twin pairs develops a particular cancer, the other twin pair does not, even though they share the same genetic blueprint. As well, since the 1940's many studies have examined the association between diet and cancer, in various population studies. Taken together, the evidence suggests that 32-35% of cancers are attributed to nutrition, although the contribution of diet to specific types of cancer varies from as little as 10% for lung cancer, to 80-90% for colo-rectal cancers. These studies suggest that nutrition appears to account for approximately 50% of breast cancer, and 75% of prostate cancer. (11, 12)

What is under intense investigation at this time are studies examining individual dietary nutrients, to help discern which dietary factors promote cancer and which ones may prevent cancer. There is broad consensus at this time that factors such as obesity and alcohol consumption increase cancer risk, and consuming fruits and vegetables reduces cancer risk. Experts also agree that cancer arises from a complex interaction between genetic factors, individual metabolic characteristics, and diet. By themselves, common gene polymorphisms (variation in gene coding from one individual to another) that regulate metabolism of food constituents and/or frequently encountered environment agents (tobacco smoke, air pollution, asbestos exposure etc), are unlikely to confer large cancer risks, but they might do so in individuals who smoke, drink alcohol regularly, have a particular dietary pattern, or are exposed to environmental agents to which they are susceptible. (11)

The EPIC Study

To help decipher the complex relationship between diet and cancer, The *European Prospective Investigation into Cancer and Nutrition* (The EPIC Study) was initiated in 1992. The EPIC Study has been following over 500,000 people, living in 10 European countries since (Denmark, France, Germany, Greece, Italy, Netherlands, Norway, Spain, Sweden, and the United Kingdom). A great deal of data including weight, height, lifestyle factors (including dietary behaviours) personal history, as well as

blood samples, were collected at the beginning of the study, with periodic follow-up of these parameters collected on an ongoing basis. (11)

In the 2011 EPIC Study update, published by K. Li et al, in the European Journal Of Nutrition, researchers showed impressive evidence for the use of antioxidant supplements in the prevention of cancer and all-cause mortality, as mentioned above. In the 2011 report, scientists based these findings on the analysis of 23,943 subjects, all free of cancer and heart disease at the start of the study. After 11 years of monitoring, there were 1,101 deaths, of which 513 were from cancer and 264 from cardiovascular conditions. After controlling for other confounding variables, researchers noted that individuals who voluntarily started taking antioxidant supplements prior to the beginning of the study showed a significantly reduced risk of both cancer and all-cause mortality. (1) Researchers affiliated with the EPIC Study indicate that studies such as this, which involve following large number of subjects for many years, are the only valid method to evaluate the influence of diet, lifestyle, and environmental factors on cancer risk. (11)

Application for Health Practitioners and Their Patients

The EPIC study suggests that antioxidant supplements have the potential to help reduce risk of cancer, heart disease, and all-cause mortality. Many experimental and preclinical studies have shown impressive anti-cancer and anti-heart disease mechanisms through which antioxidants may reduce risk of these and other diseases. In my teaching capacity as a faculty member of the Integrative Cancer Therapy Fellowship Program (a one-year program offered to medical doctors through the American Academy of Anti-aging Research-A4M), many integrative cancer doctors I have met in the program routinely incorporate the use of high doses of certain antioxidants into the treatment regime of their cancer patients. They do so in accordance with experimental evidence, which has demonstrated the multi-modal ways various antioxidants combat cancer (apoptosis, decreased proliferation, immune modulation, gap junction preservation etc). According to their experience, certain antioxidant supplements, along with other types of supplements and dietary practices, are an important aspect of cancer treatment for many patients. The first landmark clinical study of its kind to show the importance of supplementation with cancer patients was published in the Molecular Aspects of Medicine in 1994. These researchers showed that antioxidant supplements can play a key role in preventing the recurrence of breast cancer. (13) Over the years, other studies have shown important anti-cancer benefits of antioxidant supplements when administered to patients with prostate cancer, cervical dysplasia, oral leukoplakia, atrophic gastritis, and other cancerous and precancerous conditions. (7, 14,15,16,17,18)

In clinical practice it is common to encounter patients who take a standard multiple vitamin and mineral each day, for the purposes of increased well-being, energy, and to decrease risk of degenerative diseases. The EPIC Study suggests that unless a multiple vitamin supplement is enriched with meaningful doses of antioxidants, then it is unlikely to provide significant anti-cancer and anti-heart disease properties. (1) Accordingly, health practitioners should review the antioxidant dosages contained in the supplements their patients are taking and, where appropriate, direct them to supplements that contain meaningful concentrations of antioxidants (e.g. Vitamin E succinate - 400 IU, Vitamin C- 500-1000 mg,

Selenium 100-200 mcg etc). This one simple intervention may help reduce the patient`s risk of cancer by almost 50%, and all-cause mortality by 42%, over the ensuing decades, according to the finding of K Li et al.

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