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**GUIDE TO
COMPREHENSIVE
CANCER CARE**

**PATIENT / FAMILY
RESOURCE CENTER**

SELF CARE GUIDES

TESTS & PROCEDURES

**COMPLEMENTARY /
ALTERNATIVE CARE**

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August 2003

from

The Duke Patient/Family Resource Center

The Duke Patient/Family Resource Center is:

- A lending library offering books, audio and video tapes, magazines and free brochures dealing with cancer and certain blood disorders and with issues of coping, survivorship, caregiving, and grieving
- Open 8:30 to 5:00 every day the Morris Clinics are open
- Located in the White Zone, first floor, of the Morris Cancer Clinic, Room 15123.
- Our phone number is 919-684-6955. Our email address is FamilyLibrary@mc.duke.edu

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Nutritional and Herbal Supplements

In our July issue of the newsletter devoted to cancer and nutrition, we promised you a follow-up dealing with "all those pills" - the substances extracted from normal food or from roots and herbs and sold as health enhancers of one sort or another. Genistein, from soy; Vitamins A,C, and E from plant foods; ginkgo biloba, from the leaves of the ginkgo tree; quercetin, from various plant pigments - all are examples of what we will, for present purposes, call simply "supplements." All are purported to have some medicinal or beneficial properties. Some are promoted for preventing cancer; others for fighting cancer. Even more are promoted as helping to ameliorate the side effects of chemotherapy and radiation. Recent studies have raised red flags about some, and all cost money that your insurance company will not reimburse. It is estimated that up to 25% of cancer patients experiment with supplements. But how promising is this path?

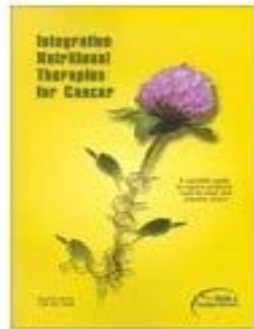
I will begin by giving two items of personal experience. An acquaintance of mine, in whose care I participated, had metastatic breast cancer. After learning that her cancer had spread, she decided to give up any further "western medicine" in favor of natural and herbal supplements. I don't know what she took but it was a huge inventory running to hundreds of dollars. She died of her illness in about four months from the diagnosis of the metastasis, with no great quality of life. By contrast, my own father, who was diagnosed with metastatic prostate cancer at an advanced age enjoyed good quality of life for about a year on a Chinese herbal concoction dubbed PC-SPES. It was recommended to him by his oncologist. Unfortunately PC-SPES is not currently on the market because the herbal product was found to be contaminated with various prescription drugs over the past few years, including diethylstilbestrol (a hormone), indomethacin (an anti-inflammatory), and warfarin (a blood-thinner). Hmmm. Was it the herbs or the contaminants that were fighting my father's cancer? Clinical studies are continuing, but the company that manufactured PC-SPES has ceased operations and it is not clear when or if another company will be able to produce an herb-only product. These

two examples are just a taste of the ups and downs of finding a good "supplement." In theory, there are things out there that, if not cancer cures exactly, can be helpful. In practice, even ones with a quite promising buzz can crash and burn a year or so later once a new study comes out. Sounds a bit like "western medicine", doesn't it?

The fact is, many of the current exciting supplements have not yet been subject to adequate testing, while many exciting ones of the past, once tested, were found not to live up to their early promise. Because of this, we at the Patient/Family Resource Center have to take a very conservative approach in our guidance. We will not be recommending any particular supplement for any particular condition. Instead, we will try to give you the tools to do your own research if you should choose to pursue this option. What follows will be a book review, some website reviews, and discussions both of antioxidants and of supplements that interact with tamoxifen. These should help get you launched on your explorations.

If you should decide to add supplements to your treatment plan, here is an important piece of advice: clear your list of supplements with *all* your medical teams. You may be seeing doctors for other conditions besides cancer and will have a list of pharmaceuticals for these other conditions, as well as from your oncologist. Any of these lists may contain substances that interact harmfully with a certain supplement. Or there may be bothersome interactions between any two supplements.

Book Review



Integrative Nutritional Therapies for Cancer by Nagi B. Kumar, Susan Moyers, Kathy Allen, Karen Besterman-Dahan, and Diane Riccardi.

Here is an herb-and-supplements book that will take you right to the cancer-relevant items, while providing information on the other diseases or conditions that a supplement is also used for. After all, some people are already taking a certain substance for their heart, or their eyes, or their short-term memory. They will want to know how well this old standby integrates with the new medicines they will be facing or with the new supplements they wish to try. The book covers most of the well-known and a few of the obscure herbal/nutritional supplements in alphabetical order. Each one is given its own monograph citing relevant research and findings. To make things easy, you can cut to the chase and read just the "Recommendations" that come at the end of each monograph. Be prepared to find that many of the recommendations read: "Because of the lack of conclusive evidence on the efficacy in cancer treatment and prevention, [this supplement] is not recommended..."

This is not an adventurous book. But it can save you some time and grief. There are appendices in the back that warn you of harmful herbs and other supplements associated with harm and injury, of drug-supplement

interactions, and of things considered unwise during pregnancy.

Website Reviews

■ *M.D. Anderson's Complementary/Integrative Medicine Website*

M.D. Anderson is Houston's world-renowned comprehensive cancer center. It's main website, www.mdanderson.org, is vast and excellent. We plan to review it at greater length in a future newsletter. For now, we will confine ourselves to that one branch that leads you to supplementals. This is:

<http://www.mdanderson.org/departments/cimer/>

Once you arrive at the Complementary/Integrative page, click on "Review of therapies" (on the left), then "Herbal/Plant Therapies." The various herbals will be highlighted and available for clicking. While M.D. Anderson's recommendations are, for the most part, conservative, you will be intrigued to find that certain media-hyped items, like shark cartilage, are still under serious investigation. This is also a good place to read about the fate of the prostate cancer formula, PC-SPES. While you're at the CIMER site, you may also want to explore "Biological/organic/pharmacological therapies." Check out the ongoing promising trials of a cancer-fighting virus labeled MTH-68, for instance.



■ *Memorial Sloan-Kettering's Herbal Website*

We also urge you to visit the herbal page for Memorial Sloan-Kettering, the world renowned cancer center of New York City. It is:

<http://www.mskcc.org/mskcc/html/11571.cfm>

While the reviews here are also conservative in their recommendations, the list of supplements is longer, there is more information given on each and often you get to see what a plant looks like. Other substances besides herbals also appear on the list, such as cartilage, chitin, calcium, inositol hexophosphate, etc. All in all, a nice chewy information source.



The Antioxidant Controversy

Perhaps the best-known supplements relevant to cancer are the "antioxidants." Several vitamins and minerals have antioxidant properties.

These include C, E, A (including beta carotene), and selenium. Numerous other substances also have antioxidant properties, including coenzyme Q10, melatonin, N-acetylcysteine, glutathione, lycopene, green tea, and pycnogenol. The theory behind the beneficial effects of antioxidants is as follows. Harmful "free radicals" are produced in the body during normal metabolism and in response to UV light, chemicals, radiation, and infectious agents. These free radicals play a role in the most common health problems, including cancer and heart disease, as well as degenerative problems associated with aging. Antioxidants act in numerous ways to block or repair the damage done by free radicals. In the past, numerous studies suggested that supplemental levels of antioxidant vitamins (E, C, beta carotene) would reduce an individual's risk for certain cancers and cardiovascular disease. This is how antioxidants made their way into the cancer world. People with diagnosed cancer began gulping antioxidants even while undergoing standard treatment. Then controversy erupted!

Notice how the theory above is addressed only to the prevention of cancer. Cell damage can lead to cell mutation and cell mutation can lead to cancer. If you can reduce the number of cells damaged by free radicals, in theory you have reduced the number of mutated/damaged cells that might go on to become the mother cell of a budding malignant tumor. But suppose a cell has already gone on to become a cancer mother cell? It is too late to prevent it, or its offspring, from being mutants. Rather, wouldn't one want to damage these cancer cells even further so that they die off? This is, roughly, the theory behind chemotherapy and radiation. Many cancer doctors have long believed that chemotherapy and radiation work to destroy cancer cells by first *oxidizing* them and that, therefore, one doesn't want any *anti-oxidant* substances circulating in the body during the time of treatment. Accordingly, many doctors still urge their patients to stay away from antioxidant supplements while undergoing chemo or radiation.

But how valid are either of these theories - the prevention one and the destruction one? Controversy leads to research and there has been considerable research on the role of antioxidants in cancer prevention and cancer treatment. The results of this research so far have been... well, puzzling. Here are some highlights.

- *The cancer prevention role of antioxidants has been called into question*

This July, 2003, the U.S. Preventive Services Task Force came out with a comprehensive report entitled, "Routine Vitamin Supplementation to Prevent Cancer and Cardiovascular Disease." A summary of their recommendations reads as follows:

The U.S. Preventive Services Task Force (USPSTF) concludes that the evidence is insufficient to recommend for or against the use of supplements of vitamins A, C, or E; multivitamins with folic acid; or antioxidant combinations for

the prevention of cancer or cardiovascular disease.

The USPSTF found poor evidence to determine whether supplementation with these vitamins reduces the risk for cardiovascular disease or cancer. The available evidence from randomized trials is either inadequate or conflicting, and the influence of confounding variables on observed outcomes in observational studies cannot be determined. As a result, the USPSTF could not determine the balance of benefits and harms of routine use of supplements of vitamins A, C or E; multivitamins with folic acid; or antioxidant combinations for the prevention of cancer or cardiovascular disease.

The USPSTF recommends against the use of beta-carotene supplements, either alone or in combination, for the prevention of cancer or cardiovascular disease.

The USPSTF found good evidence that beta-carotene supplementation provides no benefit in the prevention of cancer or cardiovascular disease in middle-aged and older adults. In 2 trials restricted to heavy smokers, beta-carotene supplementation was associated with higher incidence of lung cancer and higher all-cause mortality. The USPSTF concludes that beta-carotene supplements are unlikely to provide important benefits and might cause harm in some groups.

You may read the details of this report at greater length by going to <http://www.ahrq.gov/clinic/3rduspstf/vitamins/vitaminsrr.htm#summary>

- *Some antioxidants seem to support some chemotherapies and radiation for certain cancers*



Oddly, while the prevention theory is not holding up very well, a different avenue of research has been giving credence to the idea that certain antioxidants may act as good supportive drugs to complement one's chemotherapy or radiation treatments. These supplements may ameliorate side effects without diminishing the efficacy of the treatment; or, in certain limited cases, they may actually increase the efficacy. What a reversal of thinking!

The widely noted article that set this thinking off, entitled "Antioxidants in Cancer Therapy: Their Actions and Interactions with Oncological Therapies," was produced by two research nutritionists, Davis W. Lamson and Mathew S. Brignall who pulled together the findings of numerous

small studies, some on humans, more on animals, quite a few in the test-tube. In 1999, their essay appeared in *Alternative Medicine Review* (4) 303-328. The next year a follow-up article by these two men, entitled "Antioxidants and Cancer Therapy II: Quick Reference Guide," appeared in the same journal (*AMR 2000 5 (2)152-163*). This second article reduces the previous findings to a guide that allows you to quickly determine whether the standard treatment you're taking for the cancer you have might be enhanced or supported in some way by a particular supplement.

One is advised to consult both of these articles with fine attention to detail, however, because the testing that our two authors cite often involved dose levels well beyond what you could administer to yourself using store-bought pills. Furthermore, some of the studies of test-tube interactions showed a positive benefit, while the same drugs and supplements in animal or human trials showed a negative effect. (Funny contradictions seem to abound in this area of research!) Remember too that cancers vary by type. An effective medicine for endometrial cancer, for instance, may be entirely useless for lung or kidney cancer. This point holds for helpful supplements as well. None of the human trials of supplements that these authors cite covers a wide range of different types of cancer; most refer to only one type. If that isn't the type you have, the supplement may be of little interest to you.

If you'd like to review these articles in detail, the Duke University Medical Center Library subscribes to *Alternative Medicine Review* and either they or we here at the Resource Center will be happy to help patients obtain a copy through the usual library methods.

Alert to Tamoxifen Users!

Tamoxifen is an antiestrogen commonly used in the treatment (and prevention) of breast cancer. Women may stay on tamoxifen for up to five years. During this entire period, tamoxifen users need to be aware of supplements that could potentially interact with tamoxifen. Some of these create positive interactions, others negative. They are:

Negative effect: Genistein, daidzein (found in soy products or as isoflavone supplements)

Negative effect: Tangeretin (found in citrus fruit peel and some 'natural' menopausal medications)

Positive effect: Gamma-linolenic acid (GLA) (found in evening primrose and borage oils)

Positive effect: Melatonin (natural hormone)

Let's look at each of these separately.

Soy products are very popular with breast cancer patients / survivors for several reasons. Breast cancer occurs less frequently in the Japanese population and it has been hypothesized that this may be due, in part, to high levels of soy products in the Japanese diet. The isoflavones in soy

products are considered 'phytoestrogens', that is plant estrogens, and have weak, estrogenic effects. Many women have used soy products or isoflavone supplements to reduce menopausal symptoms, although the research suggests that they are not particularly effective. The most prevalent isoflavones in soy, genistein and daidzein, have been shown in test tube and animal studies to interfere with the ability of tamoxifen to inhibit breast cancer cell growth. This happened even at low doses of the supplements. **Take home message: To get the maximum benefit from tamoxifen, don't use soy products or isoflavone supplements while taking tamoxifen.**

Tangeretin is a citrus flavonoid found in high concentrations in the peel of citrus fruits. It has been evaluated in several cancer cell lines (cancer cells growing in a test tube) and found to have weak activity in slowing cancer cell growth. Ongoing research will determine how this might be used to help cancer patients but studies also show that it interferes with the effects of tamoxifen. **Take home message: Don't use Tangeretin supplements while taking tamoxifen.**

Gamma-linolenic acid (GLA) is an essential fatty acid. It is commercially available in evening primrose and borage oils and naturally available in fruits such as currants and gooseberries. GLA is being evaluated for anti-tumor abilities and has been shown in cancer cell lines (cancer cells growing in a test tube) to increase the response of some cancer cells to some chemotherapy drugs. This includes breast cancer cell sensitivity to vinorelbine and paclitaxel. It has also been evaluated in a small clinical study of patients receiving tamoxifen. In this small study, GLA improved the clinical response to tamoxifen. **Take home message: GLA may interact with tamoxifen, as well as other chemotherapy agents, to enhance benefit. These preliminary results need to be investigated further. Talk with your doctor if you are considering using GLA.**

Reference: Kenny FS, Pinder SE, Ellis IO, et al. Gamma linolenic acid with tamoxifen as primary therapy for breast cancer. *International Journal of Cancer*: 85, 643-648, 2000.

Melatonin is a hormone produced by the pineal gland, located at the base of the brain. Melatonin affects the circadian rhythms of the body, that is the variations throughout the day and night in how body tissues and organs function. Melatonin supplements are most commonly used to treat sleep disorders or to modulate the body's rhythms when traveling. Studies in cancer cell lines (cancer cells growing in a test tube) show that melatonin may decrease estrogen receptor expression and inhibit breast cancer cell growth. When cells were exposed to melatonin before tamoxifen, the effects of tamoxifen were increased. This effect occurred at much higher doses than usually used for short term sleep problems. **Take home message: Very preliminary studies suggest melatonin may interact with tamoxifen to enhance benefit. These results need to be investigated further. Talk with your doctor if you are considering**

using melatonin.

References:

Lissoni P, Barni S, Meregalli S, et al. Modulation of cancer endocrine therapy by melatonin: a phase II study of tamoxifen plus melatonin in metastatic breast cancer patients progressing under tamoxifen alone. *British Journal of Cancer*: 71(4):854-856, 1995.

Wilson ST, Blask DE, Lemus-Wilson AM. Melatonin augments the sensitivity of MCG-7 human breast cancer cells to tamoxifen in vitro. *Journal of Endocrinology and Metabolism* 75(2): 669-70, 1992.

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Other Books in Our Collection:

The Physicians Desk Reference, *The Physician's Desk Reference for Herbal Medicines*, and *The Physician's Desk Reference for Nutritional Supplements* are all available on our reference shelf. They cannot be checked out but you are free to peruse them. These are the standard FDA approved encyclopedias on medicines. Inside, the monographs on the drug or supplement items are listed alphabetically and the book will include several indexes so you can find substances that are listed under several different names or that fall into a particular class.

The Complete German Commission E Monographs: Therapeutic Guide to Herbal Medicines by Mark Blumenthal and others. Another compendium of herbal monographs put out by the German Federal Institute for Drugs and Medical Devices. Also on our reference shelf.

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