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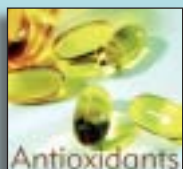
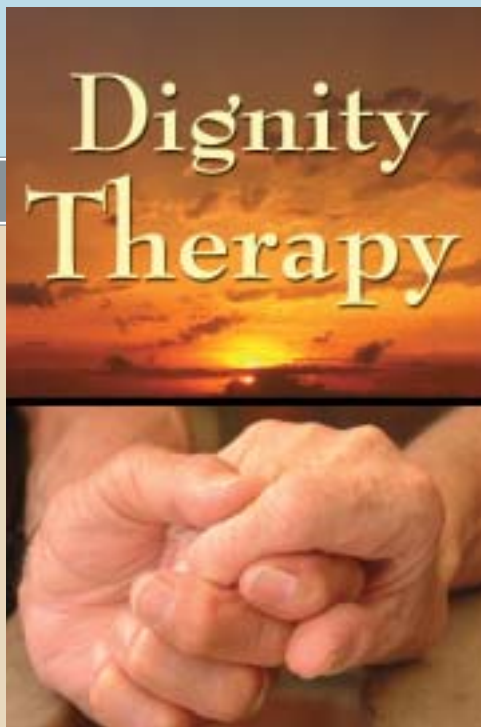
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THE **NEWS CENTER** FOR THE CANCER CARE TEAM

'Dignity Therapy' Innovators Aiming to Make Dying a More Positive, Fulfilling Experience

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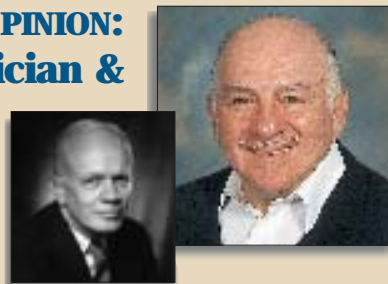
Antioxidants, New Research: (1) In Head & Neck Cancer, Supplements

Reduce RT Side Effects but Boost Recurrences; and (2) Data at American Chemical Society Meeting Finds Surprising Role for Coffee

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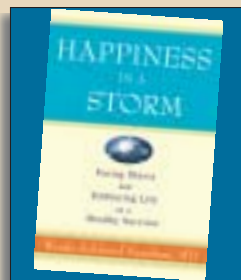
Participants in the Walk must promise to raise a minimum of \$2,100.

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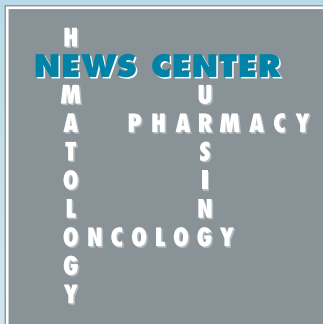
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Head & Neck Cancer: Antioxidant Supplements Reduce RT Side Effects But Boost Recurrences

By Devon Schuyler

Many patients undergoing radiation therapy for cancer take antioxidant vitamin supplements in an effort to reduce side effects and improve treatment effectiveness. According to a new study of people with head and neck cancer, however, although this approach does appear to reduce side effects, it may also increase the risk of recurrence.

"This study is a warning that there could be adverse effects of antioxidant supplementation on radiation therapy," said François Meyer, MD, Professor of Epidemiology at Laval University in Quebec, one of the study's investigators. He hypothesized that the supplements might interfere with radiation's ability to destroy cancerous cells.

The study, published in the August 20 issue of the *Journal of Clinical Oncology* (2005;24:5805-5813)—the lead investigator was Professor Isabelle Bairati, MD, PhD—is one of just a handful to examine the link between radiation and antioxidants; most studies of antioxidants and cancer treatment have looked at chemotherapy only.

The study included 535 Stage 1 or 2 head and neck cancer patients who were scheduled for treatment with radiation therapy. They had to be at least 18 years old and take no more than 50 IU of vitamin E and 6 mg of beta-carotene supplements a day in order to partici-

sonnel were blinded to the patients' group assignments throughout the study.

After some of the patients were enrolled, the results of the Beta-Carotene and Retinol Efficacy Trial came out. Because this was the second study to find an increase in lung cancer with beta-carotene, the researchers halted the use of beta-carotene and continued the trial with vitamin E and placebo alone.

Radiation oncologists and nurses evaluated the patients' side effects using the first version of the Radiation Therapy Oncology Group Acute Morbidity Scoring Criteria.

Side effects were graded on a scale from 0 (no symptoms) to 4 (severe symptoms) for six sites: skin, mucosa, ear, salivary glands, pharynx and esophagus, and larynx. Participants also completed two quality-of-life questionnaires at baseline, at the end of radiation therapy, and one month after radiation therapy ended.

Study Results

People in the supplement group tended to be less likely than those in the placebo group to experience Grade 3 or 4 side effects in all six sites during radiation treatment (19.2% vs 24.8%), but the difference was not statistically significant.

Dr. Meyer explained that in order to maximize the statistical power of the study, he and his colleagues looked at the odds of having an adverse effect score one grade higher (i.e., 1 instead of 0, 2 instead of 1, etc.) in each group compared with the other.

The researchers found that for the larynx alone, the odds of having an adverse effect score one grade higher during radiation treatment was 62% lower for people who took both vitamin E and beta-carotene than for those who took a placebo.

When all six sites were combined, adverse effects during radiation treatment also were less severe for people who took both vitamin E and beta-carotene. When patients took vitamin E alone, there was no reduction in adverse effects from radiation therapy.

The study also found a trend toward a higher rate of local recurrence in the supplement arm compared with the placebo arm. "Although this find-



François Meyer, MD, and lead investigator Isabelle Bairati, MD, said that the study is a warning that there could be adverse effects of antioxidant supplementation on radiation therapy. One explanation is that the supplements might interfere with the ability of radiation to destroy cancerous cells.

study is, did recurrence rates go up because patients had beta-carotene, because they didn't have beta-carotene, or because they had vitamin E?"

He pointed out that beta-carotene might be a helpful supplement for people who don't smoke, "but now no new study will touch it with a 10-foot pole, at least for some time."

What to Tell Patients?

As for what to tell patients who ask about taking antioxidants during radiation treatment, Dr. Meyer said he

would advise patients that any reduction in side effects is outweighed by a higher recurrence rate.

Dr. Camphausen said he also tells patients that they're putting themselves at increased risk for a local recurrence if they insist on taking high-dose antioxidants. He recommends that patients eat a healthy diet and take a daily multivitamin that contains relatively low doses of antioxidants.

Dr. Meyer explained that most of these people received beta-carotene for at least the duration of the radiation therapy; the duration of supplementation ranged from 21 to 609 days.

There was a statistically significant reduction in the severity of radiation side effects, both during and at the end of radiation therapy. By contrast, the 380 patients who had received vitamin E alone did not experience any reduction in side effects.

Self-reported side effects from the supplements, such as yellowing of the skin, occurred in 42% of people in the supplement group and 16% of those in the placebo group.

Accompanying Editorial

In an accompanying editorial, Kevin Camphausen, MD, Deputy Chief of the Radiation Oncology Branch of the National Cancer Institute's Center for Cancer Research, said, "The authors should be commended for running such a study and asking these questions. He said that the primary strength of this study was its large size, and the major weakness was the need to change the protocol partway through.

Harold E. Seifried, PhD, Program Director of the NCI's Nutritional Sciences Research Group in the Division of Cancer Prevention, agreed that although the authors were right to change the study protocol, it was unfortunate that they needed to.

"Now the big question with this

After some of the patients were enrolled, the results of the Beta-Carotene and Retinol Efficacy Trial came out. Because this was the second study to find an increase in lung cancer with beta-carotene, the researchers halted the use of beta-carotene and continued the trial with vitamin E and placebo alone.

Based on the potential risks of antioxidants, Dr. Meyer advised against further studies of their use during radiation treatment for head and neck cancer. Instead, he suggested that follow-up studies examine the use of antioxidants after radiation therapy.

But Dr. Camphausen said that further studies were warranted even if

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Harold E. Seifried, PhD: "The big question with this study is, did recurrence rates go up because patients had beta-carotene, because they didn't have beta-carotene, or because they had vitamin E?"

Patients were randomly assigned to either a supplement group (400 IU of vitamin E and 30 mg of beta-carotene a day) or a placebo group. Supplementation started at the same time as radiation therapy and continued for three years. The patients and all study per-

American Chemical Society Annual Meeting

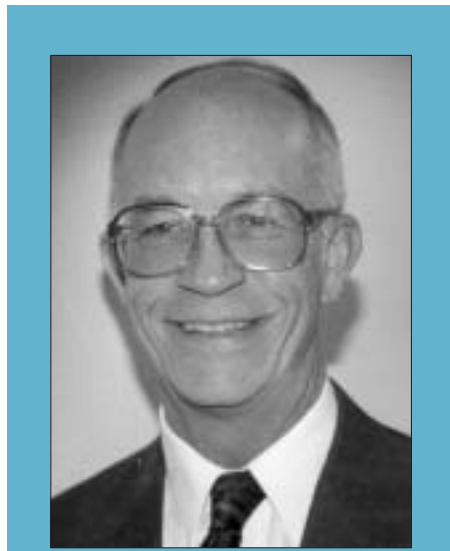
New Research on Antioxidants Shows Surprising Role for Coffee

By Peggy Eastman

WASHINGTON, DC—Recent studies from the American Institute for Cancer Research (AICR) and other groups have highlighted the importance of polyphenols, antioxidant compounds in fruits, vegetables, and tea, in reducing the risk of developing cancer. But, while groups such as the National Cancer Institute and the AICR have consistently advised Americans to eat more fruits and vegetables, Americans actually get most of their antioxidants from a surprising source: coffee.

That finding comes from research presented here at the American Chemical Society National Meeting by Joe A. Vinson, PhD, Professor of Chemistry at the University of Scranton (PA).

"I found out to my amazement that coffee was the number one source of antioxidants" in the US diet, he said, noting that both caffeinated and decaffeinated coffee brands seem to provide the same levels of antioxidants.



Joe A. Vinson, PhD: "I found to my amazement that coffee was the number one source of antioxidants in the US diet," and both caffeinated and decaffeinated coffee brands seem to provide the same levels of antioxidants.

On the basis of the amount of antioxidants per serving size, dates, cranberries, and red grapes are among the best fruits to eat.

Dr. Vinson measured in milligrams the top 10 sources of antioxidants consumed on average in the US diet. Coffee was far and away the number one source at 1,299 mg per day. Black tea, the second source, was not even close at 294 mg per day.

Trailing tea in order of the amount of antioxidants generally consumed daily were bananas (76 mg), dry beans

(72 mg), corn (48 mg), red wine (44 mg), lager beer (42 mg), apples (39 mg), tomatoes (32 mg), and potatoes (28 mg).

Dr. Vinson's study was an in vitro test, and he emphasized in an American Chemical Society news briefing that there are limitations to this kind of study, including not knowing how much of the antioxidant compounds are actually being absorbed by the body.

He also was quick to say that coffee-loving Americans should not overdo their coffee consumption in hopes of loading up on antioxidants. One or two cups of coffee a day are plenty, he said.

He also urged more consumption of tea for those who don't like coffee, along with a higher consumption of fruits and vegetables for the general population. Dr. Vinson noted that on the basis of the amount of antioxidants per serving size, dates, cranberries, and red grapes are among the best fruits to eat.

In a world with some 8,000 polyphenols, it is impossible to know just what all of them do, Dr. Vinson said, noting that these compounds are designed to protect plants bombarded by ultraviolet radiation and other insults.

"There are thousands of polyphenols...we'll never know them all. We just don't know all the good things that come from these polyphenols yet. The proof is in vivo."

Other Research Highlights

Highlights of other cancer-related research presented at the meeting fol-

low.

■ A novel investigational compound that interferes with the production of gangliosides, molecules in the membranes of most cells, could potentially serve as an alternative to traditional cancer treatments such as chemotherapy and radiation or as a nontoxic addition to these standard treatments, reported Stephan Ladisch, MD, Director of the Center for Cancer and Immunology Research at the Children's Research Institute and Professor of Pediatrics and Biochemistry/Molecular Biology at George Washington University School of Medicine.

The synthesis and shedding of gangliosides by tumor cells (which produce gangliosides at a much more rapid rate than normal cells do) have been implicated in immune function, angiogenesis, and fibroblast proliferation. In work with an experimental mouse melanoma model, Dr. Ladisch administered a carbohydrate compound, OGT2378, which blocks the production of an enzyme cancer cells require to

make gangliosides.

The tumors in OGT2378-treated mice were one-tenth the size of tumors in untreated mice, said Dr. Ladisch, who noted that with this approach—unlike with toxic chemotherapy drugs—the tumor's own cellular mechanics are being manipulated and changed to stop its growth.

■ Benjamin Cravatt, PhD, Professor in the Department of Cell Biology and the Skaggs Institute for Chemical Biology at the Scripps Research Institute, reported on his work with activity-based protein profiling, an emerging proteomics technology that can detect the human proteins associated with breast cancer, including some not identified previously.

Dr. Cravatt combined activity-based protein profiling with the proteomics method multidimensional protein identification technology (MudPIT), which relies on mass spectrometry, to analyze protein pools in more detail. Dr. Cravatt said he hopes that using these two methods together could detect protein markers of disease that evade detection by other means.

■ Karen J. Brewer, PhD, Associate Professor of Inorganic Chemistry at Virginia Polytechnic Institute and State University, presented research on the assembly of manmade molecular complexes that can enter cancer cells, and when signaled to do so, can deliver anti-cancer drugs or cause the cancer cells to change.

These new manmade "supermole-

cules" have many units that will absorb light, and are used to deliver photodynamic therapy. To their cancer-fighting supermolecules Dr. Brewer and her team have added platinum, which has anti-cancer activity because it binds to DNA and inhibits cell replication.

The therapeutic supermolecule complexes activate only with visible light, so the researchers added a luminescent tag that glows in the presence of ultraviolet light. Dr. Brewer noted that since it is common practice in medicine to use luminescent dyes to study cells, pathology laboratories have the equipment needed to monitor cancer drug delivery via the supermolecules.

■ Researchers from Meiji Pharmaceutical University in Japan reported on their work testing some 50 Japanese mushrooms to find an inhibitor of tyrosine kinase, which plays a key role in intracellular signaling and cancer proliferation. The team has discovered that a methanol extract from the fruiting body of *Polyozellus multiplex*, the blue chanterelle mushroom, inhibited the activity of tyrosine kinase via the molecule polyozellin.



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In a separate study on mushrooms, Joy Dubost, a doctoral candidate in food science at Pennsylvania State University, found that cultivated mushrooms sold in US grocery stores are a good natural source of the antioxidant ergothioneine. She found that white button mushrooms, the kind most commonly eaten in the United States, have 12 times more of the antioxidant than wheat germ and four times more than

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Antioxidants

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there is a small increase in recurrence, because the side effects of radiation treatment for head and neck cancer are so dramatic.

"Being able to save normal tissues from horrible toxicity that makes someone unable to speak or swallow normally is paramount now that we're actually starting to cure patients," he said. "We may have to give up a couple of percentage points of cure to make life better for survivors." □