Cancer Prevention Laboratory

BreastWatch Times

Colorado State University
Knowledge to Go Places

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A Word From Henry

Greetings and salutations. Winter weather is upon us, but that bodes well for all since Spring must be just around the corner! Your Cancer Prevention Laboratory (CPL) research team has been hard at work since you received your Fall Newsletter. I thought that you might appreciate a quick summary of what we have been doing.

We are keeping busy with our Enrich Project, enrolling participants, and collecting and evaluating samples. We are growing a little concerned about the rate at which participants are being accrued and encourage folks to consider joining the study! This is further discussed in this newsletter.

A lot of time is being invested in statistical evaluation, interpretation, and publication of the results of the series of Cuisine studies that were conducted (Original, Nouveau, and Challenge). We will be sharing our findings in this and subsequent newsletters.

In order to bring you new programs, we are constantly writing grant applications because it is only through grant support that we can offer you high quality projects in which to participate. We are seeking funding in the following areas:

Weight Control and Cancer Prevention. Many, many of you have informed us of your interest in a weight control program. We also have intense interest in this area. The trick is for us to not only offer you a program that will help you lose and maintain a lower body weight, but to do this while addressing critical questions about the effects of weight lose and weight maintenance on the risk for either the initial occurrence or the recurrence of breast cancer. Individuals at risk for cancer and cancer survivors will be eligible to participate. We are seeking funding from NIH.

Tailored Antioxidant Supplementation Data emerging from the Cuisine Projects have indicated that it may be possible to identify individuals who will benefit most from interventions designed to increase the ingestion of antioxidant phytochemicals or antioxidant supplements. It is possible that there may be an inherited basis for an individual's need for antioxidants and that different antioxidants are needed by different folks...but we need to study this idea very specifically. Therefore, we are seeking funds for this from NIH.

Supplements and Chemotherapy There are many unanswered questions about the potential effects of various dietary supplements on the outcome of chemotherapy. We think that these questions should be addressed and have been seeking funding for this work from the Department of Defense.

Special points of interest:

- Research Update
- Selenium Study still open!
- Vitamin E and disease prevention

Inside this issue:

Please Consider Joining Our Enrich Project

As I mentioned in my comments, enrollment in our Enrich Project is rather slow. If you are eligible to participate and have not yet inquired about the project, we would appreciate your help, even if you decide not to volunteer for the study. First, I would like to give you a few facts about the project, and then explain how you can help us, even if you decide not to participate.

- Currently, there is a very large study on selenium supplementation to prevent prostate cancer. This study has rapidly enrolled eligible men; overall 20,000 men are currently participating.
- Similar studies are not being done in women because available evidence, which is quite limited, is not considered strong enough to merit clinical studies of selenium for cancer prevention in women.
- Our study was funded to address this deficiency in information. Is there a gender difference in the response to selenium supplementation for cancer prevention such that only men will benefit, or has there been insufficient work with women such that the potential benefit to them has not yet been identified? You could help us resolve this issue.

Inquiring About the Project Can Help Us Even If You Decide Not To Participate

As I mentioned above, we are currently seeking funding for other supplement projects. We understand from participants that have completed Enrich that it was an easy study in which to participate. So, we need to better understand why potential participants decide not to volunteer for the study, and we want to get a better handle on those reasons. If you can, we'd appreciate your assistance!

Research News

New Findings From the Challenge Cuisine for Cancer Prevention Project

Presented at the Second Annual Frontiers In Cancer Prevention Research Meeting
American Association for Cancer Research, Phoenix, AZ, October 2003

For those of you who enjoy reading the nitty gritty science, here is the abstract of the work that was presented at the meeting:

A total of 267 women were enrolled in an 8-week dietary intervention to reduce oxidative stress, measured as the urinary excretion of 8-isoprostane F-2α (8-EPG), an index of whole-body lipid peroxidation; 208 women (78%) completed the study. The diets evaluated had comparable levels of all macronutrients and met national dietary guidelines but varied in their content of vegetables (V), fruits (F), and whole grains (WG). Study participants were given a cookbook containing menus and recipes that prescribed all the foods that were to be consumed during the study. Food records were maintained to document what was eaten. Following a 2-week run-in diet that was low in V, F, and WG, subjects were randomized to diets either high in VF (>10 servings per day) and low in WG or low in VF (<5 servings/day) and high in WG. At the initiation of the study and at 2-week intervals thereafter, samples of blood and 3 consecutive day first void urine specimens were obtained. The run-in diet reduced mean 8-EPG by 33%, and after 2 weeks on the two intervention diets, mean levels were further reduced by VF, but the difference between the two diet groups was not statistically significant. Further analysis revealed that the response to the dietary intervention was dependent on the baseline level of oxidative stress. Baseline levels of 8-EPG ranged from 160 to 7670 pg/ mg creatinine. The population was divided into quartiles (EPG<450, 450≤EPG<640, 640≤ EPG<940, and EPG>940 pg/mg creatinine) and the response of women in each quartile to the dietary interventions was assessed.

A dramatic difference in response was observed depending on baseline level of 8-EPG. The greatest reductions in urinary 8-EPG were observed among individuals with the highest baseline levels of this analyte. After two weeks on the run-in diet, the mean 8-EPG in the highest quartile was reduced 47% ($p<0.001$), and in the lowest three quartiles, only 18% ($p<=0.001$). After 2 weeks on the study diets, the difference in mean 8-EPG between diet groups in the highest quartile was 205 pg, $p=0.03$. P-values are based on contrasts estimated in a repeated measures mixed model using the log transform of 8-EPG. No significant change in urinary excretion of 8-EPG was observed in individuals in the lowest quartile of baseline 8-EPG (4.5 and 8.0 % respectively in the low versus high VF intervention groups). The beneficial effect of the high VF diet seen after two weeks was maintained at the same levels thereafter. Interestingly, individuals in the highest baseline quartile of 8-EPG, despite experiencing dramatic reductions in the urinary excretion of this analyte, still remained higher in 8-EPG excretion than individuals in the lower three quartiles irrespective of the diets to which they were assigned throughout the 8-week intervention. The factors that account for differences observed in urinary excretion of 8-EPG are under investigation.

For folks who like to read a slightly lighter version of the same material:

Approximately 200 women participated in an 8-week dietary study to determine how diets rich in fruits and vegetables or grains affected oxidative damage to cellular molecules that may be involved in the development of cancer. Oxidative damage is the result of the same chemical processes that cause cars to rust or apples to turn brown when they are cut. Oxidation occurs continuously in the body when food is processed (metabolized) to make energy available to our cells.

We have thus far made several surprising observations. First, oxidative damage was markedly reduced by our very nutritious run-in diet that was low in fruits and vegetables and in whole grain products. Second, the high fruit and vegetable diet further decreased oxidative damage in comparison to the high whole grain diet, but the effects was not as great as the initial effect observed when participants ate the run-in diet. Third, and newly found, those who experienced the largest reductions in levels of one measure of oxidative damage, were participants who were excreting high levels of oxidation products when they entered the study. Big effects were limited to those folks in the highest 25% of oxidation product excretion. The remaining 75% of participants benefited much less or not at all. If we can confirm this observation via additional work, it could have a profound impact on determining who is likely to benefit from phytochemical and perhaps supplement based interventions intended to reduce oxidative damage to cellular molecules.

Research Opportunities

ENRICH Selenium and Breast Cancer Prevention

The purpose of this study is to determine whether selenium, taken as a tablet, causes changes in early indicators of breast cancer risk. The study is being conducted in a group of women at increased risk for breast cancer. Past research indicates that the amount and type of selenium can reduce deaths due to cancer of the lung, prostate, and colon. However, the effects of selenium on breast cancer have not been studied. That is the purpose of this project.

The change from a normal breast cell into breast cancer cells takes many years and occurs in many stages. It is thought that breast cells destined to become cancer display changes that can be identified by laboratory tests long before breast cancer occurs. Reversal of these changes by an agent such as selenium would suggest that we might be able to stop the cancer process. Due to selenium's antioxidant characteristics it may be possible to interrupt the chain of events that lead to breast cancer. The goal of this study is to determine whether taking selenium will decrease these cellular changes in the blood, urine, and breast which may then help to decrease the risk of breast cancer.

Role of Participants:

- You will be asked to schedule three clinic visits; baseline, 6 months and 12 months. At each visit you are asked to give a sample of blood and to provide three first void urine specimens. At the first and last clinic visit, a sample of nipple aspirate fluid will also be obtained (optional).
- You will be asked to take a selenium or placebo supplement along with a vitamin-mineral supplement on a daily basis for one year, at no charge to you.
- You will be asked to fill out a new BreastWatch questionnaire upon enrollment in the study, and fill out an update questionnaire at the end of the study.
- You will be asked to discuss any questions or concerns with the Clinical Coordinator at any time. Also, will also be asked to update your health and pregnancy (if applicable) status at the monthly follow-up calls.

Eligibility Criteria:

- Participant must be female
- Must not have been diagnosed with any type of cancer in the past (except basal or squamous cell skin cancer)
- Must be at least 21 years old
- Must be willing to limit alcohol consumption to 1 or less serving of alcohol per day (on average)
- Must refrain from using tobacco products
- Must not take a specific selenium supplement
- Must be willing to discontinue taking other vitamin-mineral supplements and take the vitamin-mineral supplement provided free of charge for everyone in the study. It is okay to continue Calcium supplements
- Must not be pregnant or lactating
- Must not intend to become pregnant during the study
- Must be a patient of Rocky Mountain Cancer Centers - Rose Office

*There are no costs to participate in this study apart from the costs associated with your regular clinic visit, and your annual mammography.

If you are interested in or have questions about the ENRICH study, please call Becky Meinecke at 303-370-7924 or email at becky.meinecke@colostate.edu

Vitamin E and Chronic Disease Prevention

by Pat Kendall, Ph.D., R.D.
Food Science and Human Nutrition Specialist
Colorado State University
Cooperative Extension

E. While it's just one letter, it's the most frequently used letter in the English language. If you want to communicate, you've got to have "E". Likewise, vitamin E is indispensable for good health. Every cell in the body needs some, but it's especially important in protecting red blood cells, the nervous system, skeletal muscle and the retinas of your eyes from free-radical damage.

Vitamin E works with other antioxidants, such as vitamin C and selenium, to help protect the body from damage caused by free radicals. In the case of heart disease, it's thought to reduce the risk of heart attack by helping to protect low-density-lipoprotein (LDL) cholesterol from becoming oxidized. As LDL cholesterol becomes oxidized (a process similar to that by which butter becomes rancid), it's more likely to promote the buildup of fatty plaque in coronary artery walls, leading to atherosclerosis. Vitamin E may also help protect against heart disease by reducing the blood's ability to clot and by helping to reduce inflammatory processes.

Unfortunately, most clinical trials have not found vitamin E supplementation, even in high doses and among high-risk patients, to actually protect against coronary heart disease (CHD). According to a recent review article in the Journal of the American Medical Association, three of 4 large clinical trials examining the effect of vitamin E supplementation in patients with CHD or at high risk of heart disease failed to show a benefit. Those studies that have reported a protective effect have all been observational studies, not clinical trials, and with lower-risk populations.

Vitamin E has also been studied for its role in helping prevent or reduce the effects of a wide range of other diseases, including certain cancers, arthritis, cataracts, Parkinson's, diabetes, and Alzheimer's disease. So far, however, the evidence regarding the effects of vitamin E supplementation on these diseases remains inconsistent or preliminary. The best evidence so far suggests that alpha tocopherol, one form of vitamin E, may have a role in helping reduce the risk of prostate cancer in smokers.

Because of insufficient evidence regarding its value in supplemental form, no national scientific bodies have recommended vitamin E supplements, except for certain medical conditions such as malabsorption. If you do decide to take a vitamin E supplement, be sure to let your primary care provider know because of possible interactions with drugs. Because daily doses greater than 1000 milligrams (the upper tolerable level set by the Institute of Medicine) may cause bleeding disorders in persons taking anticoagulant drugs to thin their blood, those on blood-thinning medication or taking high doses of pain relievers are advised to take vitamin E supplements only under their doctor's supervision. For others, while research on the effects of taking high doses of vitamin E is intriguing, it's still not clear if high doses are effective or safe for the general population.

The best bet is to make sure you're getting enough vitamin E in your diet. For adults, the current recommended dietary allowance (RDA) for vitamin E is 15 milligrams (22.5 International Units). On average, American adults consume about 8 to 12 milligrams per day of vitamin E in their diets. Vitamin E is found in small amounts in a variety of foods. The best sources are salad oils, such as sunflower, safflower, canola, corn, soybean and olive oil, and foods containing these oils. Nuts (especially almonds, filberts, Brazil nuts, walnuts, peanuts and pistachios), sunflower seeds and wheat germ are also good sources. Other important sources of vitamin E include whole grains, enriched or fortified cereals, fish and seafood, liver, peanut butter, eggs, legumes such as soybeans and pinto beans, tomato paste and sauce and green, leafy vegetables.

Food Sources of Vitamin E
Recommended Dietary Intake = 15mg

Using the chart below, choose a combination of foods to achieve the Recommended Dietary Intake for vitamin E (15 mg)

Natural Food Source	Amount Consumed	Total Vitamin E
Sunflower Seeds	¼ cup	16.09 mg
Almonds (dried)	¼ cup	8.52 mg
Hazelnuts (dried)	¼ cup	8.07 mg
Sunflower Oil	1 T	7.0 mg
Tomato puree, canned	1cup	6.30 mg
Tomato Soup	1 can	6.16 mg
Safflower Oil	1 T	6.03 mg
Almond Paste	1 oz.	5.74 mg
Tomato Paste	½ cup	5.63 mg
Almond Oil	1 T	5.5 mg
Cottonseed oil	1 T	5.36 mg
Wheat Germ	¼ cup	5.26 mg
Spaghetti Sauce	1 cup	5.25 mg
Soybeans (boiled)	1 cup	3.35 mg
Peanut Butter	1 T	3.2 mg
Palm Oil	1 T	3.05 mg
Corn Oil	1 T	2.96 mg
Canola Oil	1 T	2.93 mg
Peanuts (unroasted)	¼ cup	2.59 mg
Hummus	1 cup	2.46 mg
Avocado	1 medium	2.32 mg
Mango	1 medium	2.32 mg
Pinto beans (canned)	1 cup	2.26 mg
Broccoli	½ cup	1.32 mg

Source: Bowes & Church's Food Values of Portions Commonly Used, 17th ed., revised by Jean A.T. Pennington, 1998. Lippincott-Raven Publishers, Philadelphia PA.

BREASTWATCH

A COOPERATIVE CLINICAL RESEARCH PROGRAM

4500 E. 9th Ave.
Suite 600
Denver, CO 80220

Questions, Comments, Suggestions. . . .

If you have any questions, comments or suggestions regarding this publication, please contact Becky Meinecke at 303-370-7924 or by email at becky.meinecke@colostate.edu

Website: http://breastwatch.colostate.edu

If you are interested in supporting Breast Cancer Prevention research...

Donations towards our research activities would be welcome.
Please send a check made payable to:
BreastWatch
Attn: Becky Meinecke
4500 E. 9th Ave. Suite 600
Denver, CO 80220

This newsletter is brought to you by:

Henry Thompson, Ph.D.
Scot M. Sedlacek, M.D.
Dev Paul, D.O., Ph.D.
Ruth Oratz, M.D.
Kelly Mack, RN, MSN, AOCN, NP-C
Becky Meinecke, BS