Oncology Nutrition Connection

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Message from the Executive Committee:

In this age of nutrition informatics, evidence-based practice and outcomes research, how can the Oncology DPG best support your professional needs and help you advance your career in oncology nutrition? We are now nearly 1900 members strong, with greater than 560 registered members on our electronic mailing list (EML). As of September 2010 there are 370 Board Certified Specialists in Oncology Nutrition. Members are involved in inpatient and outpatient clinical care, management, education, private practice, and oncology outreach initiatives. We are a diverse group, yet united by the understanding that nutrition is essential to quality oncology care and improved treatment outcomes.

The newsletter, our EML, and certainly our website provide both accurate and current information and resources for our members. We have also begun to provide outstanding webinars for our entire membership, while supporting members providing webinars within their own state membership or through special interest groups (SIGs). Our current goal is to provide at least three webinars a year, and we have actually supported four webinars just within the 2010/2011 year thanks to the guidance and expertise of ON DPG past chair Maureen Huhmann, DCN, RD, CSO. Our PowerPoint slide library, which is located on our website underneath the *Member Benefits* tab, provides PowerPoint slides which you can modify to make your own. Thank you to Wesley L. Fankhauser, MS, RD, LD, for his generous contribution of slides on prostate cancer as well as a professional handout *Reduce Risk of Prostate Cancer Recurrence*. The ON DPG Executive Committee (EC) overwhelmingly favored an increase in funding for members to attend professional conferences by providing two education awards; they can be found at our website under *Awards* (entitled *Professional Development Awards)*. The ON DPG is also committed to fostering your growth in oncology nutrition by way of outreach through both Area and State Representatives. These efforts are led by a dynamic group of members that include Colleen Gill, MS, RD, CSO, Katie Harper, MS, RD, CSO, Nancy Joliffe, RD, CSO, LD, and

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Bethany Smith RD, LD. Maureen Gardner, MA, RD, CSO, LDN, is our new Social Media Chair. Maureen plans to jump start initiatives to reach out to our members by way of Facebook, YouTube, and Twitter. These initiatives demonstrate efforts of the EC to support your advancement in oncology nutrition and improve communication among members. Let us know if they are meeting your professional needs!

This issue of *Oncology Nutrition Connection* (*ONC*) begins with an interview with Mark Messina, PhD, an international soyfoods expert. It addresses many questions about soy and breast cancer that oncology RDs are frequently asked. We all know that technological innovations are transforming life almost daily, and Lindsey Hoggle, MS, RD, PMP, has provided a primer on nutrition informatics. Lindsey discusses a wide range of ideas to help oncology RDs integrate new technologies into their practice. The winter issue also challenges clinicians to review their neutropenic diet and, thanks to the work of Debra DeMille, MS, RD, CSO, redefine it based on current evidence. Eating right is an important component of a healthy lifestyle, and a new feature reviews a cancer fighting food. Finally, we also share a list of several oncology conferences scheduled in 2011, an update of the table on Pancreatic Enzyme Replacement Therapy (PERT) first published in the fall 2010 issue of *ONC*, and a notice from ADA about navigation changes to the *Journal of the American Dietetic Association*. We hope you enjoy the news brought to you in the winter 2011 issue of *Oncology Nutrition Connection*!

Jeannine Mills, MS, RD, CSO, LD
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EXPERT INTERVIEW with Mark Messina, PhD: Soyfood and Breast Cancer

Background

Soybeans are the second largest crop in the U.S., and worth $31.8 billion yearly to our economy (1). But soy is in the news most often because of its valued, though sometimes controversial, health benefits. Evidence suggests that soyfoods reduce the risk of coronary heart disease and help strengthen bones. However, soy's role in cancer prevention, and in particular its potential to decrease the risk of breast cancer, has been debated for years (2). This review brings you an update on soy and breast cancer, including an interview with international soy expert Mark Messina, PhD.

Soyfood provides complete protein, a number of vitamins and minerals, fiber, and a plant-based source of omega-3 fat. In addition, soy is a unique dietary source of isoflavones, which are responsible for many of the proposed health benefits of soy, including the potential to reduce the risk of breast cancer. Isoflavones are a category of flavonoids, which are plant compounds responsible for the array of colors in plant foods. They also influence multiple biological processes (2). Evidence suggests flavonoids can inhibit blood clotting and promote vasodilation, and also exert anti-oxidant, anti-inflammatory, hypoglycemic, immune-enhancing, and anti-neoplastic effects (2–4).

Dietary isoflavone intake in Shanghai is approximately 25-50 mg per day (5). Intake in other parts of Asia may be somewhat lower, but is certainly greater than amounts consumed in many Western countries, which average less than 3 mg/day (2). Asians consume natural food sources of isoflavones such as tofu, tempeh, and miso in their daily diets. Westerners consume edamame, soy milk, and soy yogurt, but also more highly processed forms of soy such soy-based meat substitutes and soy bars.

Genistein, daidzein, and glycitein are the three isoflavones in soy, with relative content of each distributed in foods in a 50/40/10% ratio (2). Table 1 summarizes total isoflavone content as well as daidzein and genistein content of soyfoods, in milligrams (mg) per stated serving size (5).

Protein isolated from soybeans is used in a variety of processed food products. However, the isoflavone content of these soy protein products, such as soy protein isolate (which is >90% protein) and soy protein concentrate isolates (which are ~70% protein), varies according to the processing method. When prepared using an ethanol wash, much of the isoflavone content is lost, whereas when prepared via an aqueous wash, most is retained. Each gram of soy protein in whole or minimally processed soy foods provides approximately 3.5 mg isoflavones (5).

Soy and Breast Cancer

There is consensus about an association between estrogen and breast cancer. Greater lifetime estrogen exposure increases the risk of breast cancer. The chemical structure of isoflavones is similar to estrogen, so they are able to bind to estrogen receptors (ER). For this reason they are classified as phytoestrogens, plant-derived compounds with estrogenic activity. However, isoflavones preferentially bind to and transactivate ER, in comparison to ER· (2, 7) whereas estrogen has equal affinity for each. Importantly, these

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Table 1. Total Isoflavone, Genistein, and Daidzein Content of Select Soy Foods in milligrams (mg) per serving

Food	Serving Size	Total Isoflavone Content (mg)	Genistein (mg)	Daidzein (mg)
Soy protein concentrate, aqueous washed	3.5 oz	102	56	43
Soy protein concentrate, alcohol washed	3.5 oz	12	5	7
Miso	1/2 cup	59	34	22
Soybeans	1/2 cup	47	24	23
Tempeh	3 oz	37	21	15
Soybeans, dry roasted	1 ounce	37	19	15
Soy milk	1 cup	30	17	12
Tofu yogurt	1/2 cup	21	12	7
Tofu	3 oz	20	12	8
Soybeans green boiled (Edamame)	1/2 cup	12	6	6
Meatless (soy) hot dog	1	11	6	3
Soy cheese, mozzarella	1 oz	2	1	0.3

receptors have different functions and tissue distributions within the body. For example, in the breast, activation of ER, inhibits the proliferative effects of ER· activation.

Interest in the relationship between soy food intake and breast cancer began with the observation that women in Asian countries, who typically consume soy from an early age, are significantly less likely to develop breast cancer than women living in Western countries. Epidemiological studies have confirmed this association, but animal studies have yielded mixed results, with some even indicating an increased risk. Consequently, many women are left with serious questions about soy, including whether the protective effects of soy are limited to those who consumed it as a youth; whether the type of soy consumed makes a difference; whether soy's biological effects are influenced by menopausal status, estrogen status, and stage of cancer; and whether soy supports the role of drugs such as tamoxifen in preventing recurrence of breast cancer (7).

These and other questions were posed to Mark Messina, PhD, an adjunct associate professor at Loma Linda University and an internationally recognized expert on soy and chronic disease. Dr. Messina is a consultant for numerous health professional organizations and for the soy industry.

Q: Upon what are the concerns about soy and breast cancer based?

A: ***Isoflavones have estrogen-like properties. The primary isoflavone genistein stimulates the growth of MCF-7 cells (an estrogen receptor positive human breast cancer cell line) in vitro and stimulates the growth of existing mammary tumors in ovariectomized athymic mice implanted with these same cells.***

Q: Do cell studies and animal studies, combined with knowledge of the biological activity of isoflavones, provide adequate evidence for making recommendations about soy intake and breast cancer?

A: ***No, but sometimes that might be all you have. The cautionary stance against soyfood use by estrogen-sensitive breast cancer patients was more appropriate 10 years ago because there were no epidemiologic and clinical data upon which to evaluate this issue. However, with the epidemiologic data suggesting possible benefit and the clinical data suggesting soyfoods are not harmful, recommendations aimed at breast cancer patients need to be revised. Pre-clinical data are often the basis for hypothesis generation, but for the hypothesis to be accepted epidemiologic and more importantly, clinical data are needed. Generating clinical data in the cancer field is difficult. Ideally, tumor development would be the primary study outcome. However, for practical reasons, more often, the outcomes are markers of tumor risk.***

Q: Do you think that soy isoflavone may be most protective when consumed during childhood and adolescence?

A: ***If you are referring to consuming soy isoflavones for the prevention of breast cancer — absolutely.***

Q: How does soy interact with aromatase inhibitors and selective estrogen receptor modifiers (SERMs)?

A: ***Aromatase inhibitors block production of estrogen while SERMs like tamoxifen prevent estrogen from exerting effects on cells. A recently published Chinese epidemiologic study by Kang et al. found that soy intake enhanced the efficacy of anostrozole, although there was no interaction with tamoxifen. The latter finding agrees with a larger Chinese study published one year earlier. That study found that soy enhanced the prognosis of both estrogen receptor positive and negative breast cancer patients. The findings from both of these studies directly contradict the animal data upon which concern about soy is based.***

A study published in November 2010 found that whole soy inhibited the growth of chemically induced based tumors and enhanced the effects of tamoxifen. This is not the first animal study to show soy enhances the effects of tamoxifen. However, the animal and epidemiologic data may not be a sufficient basis for making clinical recommendations, especially when there are conflicting data. Furthermore, it is important to recognize that rodents metabolize isoflavones much differently than humans, so any extrapolation of the results in rodents to humans should be done very cautiously if at all.

Q: The U.S. Study — Life After Cancer Epidemiology Study — noted a trend towards an improved prognosis in those consuming soy. How can we translate results from research on breast cancer risk conducted on Chinese women to the general U.S. population, given that overall incidence of breast cancer is significantly different in Chinese women vs U.S. women and average BMI is also significantly different in these populations?

A: ***The vast majority of women in this study were Caucasian. Not unexpectedly, Asian women were more apt to consume larger amounts of soy than women of other ethnicities. However, the ethnic composition of the women in the 95th percentile genistein intake was not indicated. There are always reservations about extrapolating research results from one ethnic group to another, which is why researchers try to repeat findings in different ethnicities. In addition to the ethnicity issue, there is the issue of whether tumors in women who consumed isoflavones early in life respond differently to isoflavones than tumors in women who have not previously consumed soy.***

Q: Is there enough evidence to advise all breast cancer survivors to follow the same phyto-estrogen/isoflavone recommendations — regardless of ER status?

A: ***Based upon the in vitro and animal work, there is in theory no concern that soy or isoflavones would stimulate the growth of ER– tumors. However, although breast tumors are classified as ER- or ER+ and treated accordingly, there is some overlap between the two types. In any event,***

because of the recent data supportive of safety, I think recommendations for breast cancer patients will not differ according to tumor type. It is also worth noting that although greater lifetime estrogen exposure is thought to increase breast cancer risk, the evidence that oral estrogen therapy increases breast cancer risk or recurrence in breast cancer patients is unimpressive. For example, in the Women's Health Initiative trial, although estrogen plus progestin use increased breast cancer risk, estrogen only use decreased it.

Q: How do you assess relative soy intake (i.e., what intake reflects "less/low" and "more/high")?

A: ***In general, soy protein provides 3.5 mg isoflavones per gram protein in whole soy foods. Average intake in Japan and in cities such as Shanghai is 25 to 50 mg/day. Relatively few Asians consume more than 100 mg/day. One serving of a traditional soyfood provides about 25 mg isoflavones. My adult soy intake recommendation is two to four servings per day, based on Asian intake and the amounts in clinical and epidemiologic studies associated with benefits. The upper intake of 4 servings is not based on concern that exceeding this amount poses health risks. In fact, clinical studies have used amounts much higher than this and not observed any adverse effects. Rather, the upper limit is set at four servings simply because it is inappropriate to place too much emphasis on any single food, regardless of how healthy it may be.***

Q: Some research suggests that biological effects of soy isoflavones are influenced by their metabolism, and in particular the milieu of bacteria colonizing the intestine. For example, daidzein may be metabolized to equol in about one-third of Westerners, a conversion with clinical significance because equol has greater estrogenic activity than daidzein, and may have anticarcinogenic potential. How important do you think the metabolism of isoflavones is to their overall biological activity?

A: ***It is true that approximately 25 to 30% of Westerners (and approximately 50% of Asians) convert daidzein into equol, and that conversion rates are determined by differences in intestinal bacteria. The ability to make equol can be temporarily lost after antibiotic treatment, but in general someone is an equol producer — or not.***

Nearly 10 years ago, one of the true pioneering researchers in the isoflavone field proposed that equol-producers are more likely to benefit from soyfood consumption than non-producers. Since then, this hypothesis has been very actively investigated. However, only within the past several years has sufficient material become available to conduct clinical trials. Preliminary data indicate that equol alleviates hot flashes and perhaps inhibits bone loss. On the other hand, we know for certain that isoflavones, unrelated to equol production, alleviate hot flashes and improve endothelial function. So I think that both isoflavones and equol are likely to exert benefits. There is also the issue of interindividual differences in isoflavone metabolism independent of equol production. In response to the ingestion of the same amount of isoflavones, differences in serum levels of parent isoflavones and metabolites can vary hundreds fold. It stands to reason that for at least those health outcomes affected by isoflavones, differences in metabolism can affect efficacy.

Q: Soy protein is added to many food products, including Kashi cereals and nutrition bars. Does the type of soyfood consumed influence potential benefits? Are there any products that should be avoided?

A: ***The short answer to that question is yes. Most of the proposed benefits of soyfoods are attributed to either the protein or isoflavones. There is convincing evidence for example, that isoflavones alleviate hot flashes and improve endothelial function. There is more speculative evidence that soyfoods reduce risk of breast and prostate cancer. If they do, it is almost certainly because they provide isoflavones. On the other hand, soy protein lowers blood cholesterol levels and may help to prevent renal disease relative to animal proteins. Plus, some products contain fiber and omega-3 fatty acids and some don't.***

What is important is not so much the type of product but its chemical composition. In my view, hot flashes will be alleviated whether a women obtains 50 mg isoflavones from tofu or 50 mg from a nutrition bar containing isolated soy protein. Of course, isoflavones in pill form will alleviate hot flashes but not reduce cholesterol levels because of the absence of protein.

There is no reason to avoid certain soy products, but some are preferable to others. As is the case for all foods, nutritionists recommend consuming whole over more processed foods. This same principle applies to soyfoods. On the other hand, I eat soy burgers instead of hamburgers even though the former is a more processed soy product and are not good sources of isoflavones. They are however, good sources of protein that are low in saturated fat.

Q: What is your recommendation to breast cancer patients?

A: ***In an editorial I recently co-authored along with Donald Abrams, an oncologist at the University of California at San Francisco and Mary Hardy, the head of the integrative oncology program at the University of California at Los Angeles, we reached the following conclusions. First, the current default position of most oncologists to advise their breast cancer patients against using soy is no longer justified. Second, there is insufficient evidence to actively recommend soyfoods solely for the purpose of improving prognosis. Third, oncologists should allow women who consume soyfoods and develop breast cancer to continue consuming soy and should allow their patients who want to begin consuming soy, for whatever reason, to do so.***

Q: Would you mind commenting on the following statements about soy and breast cancer?

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To decrease the risk of developing breast cancer (i.e. for prevention), it is most important to consume soy early in life (i.e. childhood and adolescence).

The lack of clinical data precludes reaching a definitive conclusion about this hypothesis, but the epidemiologic and animal data are quite encouraging. Because there is no downside to a young girl consuming one or two servings of soy per day, I see no reason not to recommend that girls consume at least one serving of soy daily. If the breast cancer hypothesis is not confirmed by future research, the addition of soyfoods to the diet would still have been nutritionally advantageous.

Consuming soy as an adult does not decrease the risk of developing breast cancer.

I agree with this statement although I am hopeful research will prove me wrong. But the clinical studies showing adult soy intake does not affect breast tissue density or breast cell proliferation argue against soyfoods being protective. It is conceivable however, that soy is still exerting a benefit not identified by these types of clinical studies, such as inhibiting metastasis. There is intriguing human work in this area for prostate cancer.

Isoflavones may decrease metastases of breast cancer — even when first consumed as an adult.

No idea. There is simply insufficient data upon which to reach a conclusion about this statement.

Consuming 50 mg isoflavones per day can help alleviate hot flashes.

Absolutely, as long as the isoflavones consumed represent the relative concentrations found in soybeans and soyfoods. Obviously, if one consumes 50 mg from foods this is not a concern. If however, the isoflavones are coming from supplements, it is important to make sure the major isoflavone is genistein.

If soy foods are part of your diet, continue to consume them if you develop breast cancer.

One can have a happy life without eating soyfoods. But the evidence suggests there is no reason to stop consuming soy if one develops breast cancer.

Consuming up to 4 servings per day of soy food is safe and acceptable. Consuming four servings of soy food per day is supported by a long history of safety.

This statement needs a bit of nuance. I do not think it is appropriate to consume four servings of soy meat substitutes per day because doing so could mean consuming as much as 60 grams of soy protein per day. That is too much because soyfoods would in all likelihood represent too large of a proportion of the total protein consumed. Plus, it is important to make sure to consume at least some whole soyfoods. On the other hand, consuming a serving of edamame, two of soymilk and one of tofu may only provide about 25 grams of protein, which is reasonable, although still at the very high end of Asian intake. So the issue isn't so much how much is safe, because for healthy individuals four servings is certainly safe, but rather, the issue is making sure not to place too much emphasis on one food.

Mark Messina, PhD, is an adjunct associate professor at Loma Linda University and an internationally recognized expert on soy and chronic disease. ON DPG sincerely thanks Dr. Messina for sharing his expertise with our members.

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Have You Reviewed Your Neutropenic Diet Lately?

Debra DeMille, MS, RD, CSO

Abstract

In the inpatient setting, the neutropenic diet has long been utilized as a standard of care for the treatment of neutropenia and immunocompromised patients. However, the lack of consistency of this diet among nutrition departments, as well as a dearth of evidence regarding its benefit, has led to confusion among health care professionals, and certainly among our patients. In 2002, Elena Ladas wrote an excellent review entitled "The neutropenic diet: an examination of the evidence" (1). Nine years later, it is time to examine the research again. Small studies have been conducted on the neutropenic diet, but the impact of this diet on clinical practice and outcomes still remains unclear. This article will review available studies and nutrition department practices related to the neutropenic diet, and outline steps to consider when evaluating the neutropenic precaution policy within one's institution.

Background

Patients undergoing cancer treatment are at risk for side effects, which must be monitored and managed in order to complete treatment safely and effectively. Neutropenia, the lowering of white blood cell count as a result of damage to the bone marrow, is a side effect of many chemotherapy regimens. To assess the significance of a patient's bone marrow status, clinicians monitor the number of bacteria-fighting blood cells (i.e., neutrophils), referred to as the absolute neutrophil count (ANC). ANC values higher than 1,000/mm^3 significantly reduce the risk of developing an infection (2), and most patients with an ANC higher than 500 per cubic millimeter (mm^3) of blood do not develop major infections. Once the ANC drops below 500/mm^3, the chance of developing an infection increases significantly (3). However, actual incidence varies considerably. Some patients with ANCs far above 500/mm^3 will develop infections, while others with ANCs below 500/mm^3 will remain infection-free. A significant factor related to the risk of infection is the severity and duration of neutropenia. White blood cell count is at its lowest point (i.e., nadir) within 10 to 14 days of beginning chemotherapy. At that point, patients are most susceptible to infection, and prevention is of greatest importance.

For many years the neutropenic diet has been an important component of a comprehensive plan to limit or prevent infections in myelosuppressed and immunosuppressed populations. Food normally contains sizable bacterial counts, and the theory behind the neutropenic diet is to prevent patients from consuming potentially pathogenic organisms in food, thus preventing infections resulting from ingesting these organisms. Studies have identified gram-negative organisms such as Pseudomonas aeruginosa, Escherichia coli, Klebsiella, and Proteus in a variety of foods (4–6). A complete summary of types of potentially harmful organisms found in food is included in the fact sheet *Food Safety for People with Cancer* published by the United States Department of Agriculture (USDA) (7).

Most organisms pass through the normal gastrointestinal (GI) tract without adhering to the mucosal surface, are destroyed by stomach acid, or are controlled by endogenous flora. However, anti-cancer therapy, the tumor itself, and antibiotic therapy can alter the balance that enables endogenous flora within the alimentary tract to control bacterial counts, thus enabling pathogens to colonize, seed the blood, and initiate infection. If pathogens do pass through the gastrointestinal tract into the blood stream, lymph nodes, or other organs, there is a potential for serious infection (8). Additionally, nutrition-related side-effects from therapy, such as mucositis and diarrhea, may further increase a patient's risk for infection. The neutropenic diet was developed as an attempt to minimize a patient's exposure to foreign bacteria from food-borne sources during such high-risk settings.

In the early 1970's a total protective environment was provided in the hospital setting for the treatment of some cancers, primarily of leukemia (9–11). By limiting exposure to endogenous and exogenous sources of bacteria, this environment was a means to attempt to avoid infections and allow for administration of the full, intended dose of chemotherapy. The neutropenic diet, most often called the sterile diet at that time, was just one component of the protective environment, which also included isolation rooms, laminar airflow units, and gut sterilization by antimicrobial suppressive agents. Original versions of this diet omitted foods with high gram (–) bacilli (>500 ml of Bacillus spp), allowed only very well-cooked, commercially canned, packaged, or autoclaved foods, and required specialized aseptic food preparation and service (historical report from the National Institutes of Health (NIH) Clinical Research Center). These diets were labor intensive and expensive to prepare, while being restrictive and unpalatable, and ultimately less acceptable for patients.

As oncology practice evolved, new treatment regimens and techniques for managing infection risk were developed. In addition, the impact of the neutropenic diet on intake became a greater concern as the role of nutrition in oncology care gained

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importance. These changes called into question the benefit of the neutropenic diet, and the need to investigate its effectiveness.

Antibiotics, Colony-Stimulating Factors, and Neutropenic Infection Rate

The use of antibiotics in the total protective environment has been studied extensively. In all cases, a sterile diet or foods known to have low bacterial counts were included as a control factor in the study (12–14). These studies showed that patients in protective isolation who were administered non-absorbable antibiotics had fewer infections than anticipated. The contribution of the neutropenic diet to this outcome was not evaluated. Nevertheless, use of the neutropenic diet in a total protective environment has since been applied to all neutropenic settings based on logic, prudent practice, and reasonable theoretical rationale (15–16). Moody et al. (17) pointed out that various components of a total protective environment have been abandoned in medical practice because they are labor intensive and expensive, and may raise quality-of-life issues for patients. The only exception has been the neutropenic diet, despite the fact that the concept has the least amount of evidence supporting its usefulness. With the advent of colony-stimulating factors, fewer neutropenic patients are being admitted to the hospital, further calling into question the benefit of a neutropenic diet.

The neutropenic diet is often referred to in the literature as the low-bacterial diet and the low microbial diet. In addition, inpatient nutrition departments in most hospitals and medical centers refer to the neutropenic diet in unique ways, such as a "regular diet for decreased immune system," "regular diet without fresh fruits and vegetables," and "diet for immunocompromised patients." A "sterile" diet that uses autoclaved food served to patients in laminar flow units is now rarely, if ever, used.

Inconsistencies in the Neutropenic Diet

While most healthcare facilities have institutional policies regarding dietary restrictions for neutropenic patients, no standard definition of the neutropenic diet exists. Surveys have been conducted using a number of definitions for the neutropenic diet (18). A 1987 survey of 35 bone marrow transplant programs found that a variety of diets were used, most often a completely sterile diet (i.e., foods that have been rendered sterile by canning, prolonged baking, autoclaving, or irradiation), a low-bacteria diet (i.e., well-cooked foods or foods with a minimum of potential pathogen-forming units), or a modified house diet (i.e., a regular diet without fresh fruits or vegetables) (19). In a small and more recent (2001) survey of hospitals performing pediatric bone marrow transplantation, French et al. found that the majority provided patients with a low microbial diet to reduce the potential risk of infections resulting from food-borne pathogens (18). The definition of low microbial diet was interpreted widely, from total avoidance of raw dairy products, herbs, honey, fresh fruits and vegetables, deli meats and cheeses, and well water to the exclusion of fresh fruits and vegetables only or the inclusion of only well-cooked foods. The surveys concentrated on inpatient bone marrow transplant units; outpatients receiving chemotherapy and outpatients following post-hospital diet restrictions were not included. Because studies supporting the efficacy of sterile and low microbial diets in preventing infections have not been conducted, there has been a trend toward less restrictive diets which patients can follow at home and find more palatable.

When surveying the institutional practices of 400 members of the Association of Community Cancer Centers (ACCC) regarding diet restrictions for patients with neutropenia, Smith and Besser (20) found that although 78% of responding institutions placed patients on dietary restrictions during neutropenia, the definition of the neutropenic diet varied widely by institution. The most commonly prohibited food items were fresh vegetables (98%), fresh fruits (93%), fresh juices (93%), and raw eggs (76%). Food preparation and storage were not addressed. Seventy percent of institutions advised patients to continue the neutropenic diet, as it was defined, until they were no longer neutropenic. Other cancer centers, such as the National Institutes of Health (NIH) Clinical Research Center, incorporate both food safety guidelines and avoidance of a few high risk foods (e.g. unpasteurized foods) in their neutropenic diet recommendations, but allow well washed fresh fruits and vegetables, with the exception of fruit such as blackberries and raspberries, whose surfaces are difficult to thoroughly wash.

A Review of the Evidence

At the Joan Karnell Cancer Center (JKCC), we conducted a pilot study to determine the effect of the neutropenic diet in the outpatient setting (21). Twenty-three patients completed the 12-week study, which included instruction on neutropenic precautions including diet restrictions (developed from most frequently used restrictions in the above mentioned survey) as well as evidence-based food safety standards. Seventy percent of the patients were compliant with the diet. There was no difference in admission rate for neutropenia between the compliant and non-compliant group.

In a pediatric cancer setting, a pilot study was conducted to determine the incidence of infection in children undergoing chemotherapy treatment (22). Pediatric oncology patients were randomized to the neutropenic diet or to FDA's food safety guidelines for one cycle of chemotherapy. Of the 19 patients in the study, febrile neutropenia did not vary per group and adherence rate was 94% for the neutropenic diet arm and 100% for the food safety arm.

At MD Anderson Cancer Center, a study was conducted in 153 patients undergoing remission induction therapy for acute myeloid leukemia. Patients admitted to air-

filtered rooms were randomized to a diet containing no raw fruits and vegetables (cooked diet) or to a diet containing well-washed fresh fruits and vegetables (raw diet). Fever of unknown origin occurred in 51% of those randomized to the cooked diet arm and 36% of those randomized to raw diet arm (23). Major infection was experienced by 29% of the patients in the cooked diet arm compared to 35% of the patients in the raw diet group. There was no difference in the time to infection and survival. In addition, 20 adult patients were randomized to a normal hospital diet or a low bacteria diet and monitored for infection rate. Results revealed no difference in gut colonization for gram-negative rods or infection rate, suggesting that the normal hospital diet was safe and that no added benefit was observed from the low bacteria diet (24). Because hospitals do not include high risk foods such as unpasteurized foods and unwashed fruits and vegetables, these studies do not suggest that such foods are safe; indeed they are important components of food safety guidelines for neutropenia.

Quality-of-life issues related to the neutropenic diet also must be considered. Patients receiving chemotherapy must cope with many stressful issues related to physical symptoms, body image changes, an unsure future, and navigating the healthcare system. Often, patients and families emphasize appetite and food intake as variables that are within their control. Food is frequently seen as a nurturing entity. The side effects of chemotherapy and the disease itself can make nutritional intake difficult. Adherence to the restrictions of the neutropenic diet has long been identified in the literature as an area of concern (25–27). Pizzo (28) found implementation of the neutropenic diet, as a part of a total protective environment, to be cumbersome and expensive. The institutional expense also must be taken into consideration in terms of preparation, transportation and staffing to clarify the neutropenic diet versus standard food safety principles. Many questions remain as to the practice that will result in the best outcome for immunosuppressed patients undergoing chemotherapy.

Importance of Food Safety

A report on food safety published by the Centers for Disease Prevention and Control (CDC) in 2011 states that there are 47.8 million food borne illnesses resulting in 127,839 hospitalizations, and 3,037 deaths per year in the United States (29). These estimates are based on modeling statistics using case reports from five pathogen-specific surveillance systems and a mathematical formula estimating cases of acute gastroenteritis caused by domestic food consumption. Citing data from food surveillance systems, the CDC report states "We estimate that foods consumed in the United States that were contaminated with 31 known agents of food borne disease caused 9.4 million illnesses, 55,961 hospitalizations, and 1,351 deaths each year" (30). They also acknowledge effects of pre-existing conditions, stating "Particularly in vulnerable populations, dehydration or electrolyte imbalance from a gastrointestinal illness may exacerbate a chronic illness, resulting in hospitalization or death well after resolution of the gastrointestinal illness..." (30). These papers highlight the need for all consumers to "FIGHT BAC" and the need for vulnerable populations to be particularly vigilant about adhering to evidence-based food safety standards.

The USDA, Food and Drug Administration (FDA), CDC, and the World Health Organization (WHO) have each developed public health initiatives aimed at promoting food safety. It is the responsibility of RDs to ensure that food safety guidelines are being implemented and followed within the inpatient setting and that at risk inpatients and outpatients are educated on appropriate food safety standards. These guidelines address major factors related to food safety, including personal hygiene, adequate cooking, avoiding cross-contamination, keeping food at safe temperatures, and avoiding foods from unsafe sources (31).

An Institution's Approach

Though not conclusive, evidence suggests that the use of stringent food safety guidelines may be as acceptable as neutropenic diet restrictions in the setting of neutropenia or immunosuppression, and are preferred by patients undergoing treatment. There is insufficient research pointing to a specific benefit of the neutropenic diet in these populations, and the practice may be over-restrictive at a time when nutritional needs are high and patients have difficulty eating. In addition, different treatment settings may require different strategies; allogeneic stem cell transplant versus autologous stem cell transplant, inpatient admission for neutropenic fever, and chemotherapy in the outpatient setting may each respond to different food-based regimens for helping to prevent neutropenic infection. At this institution, in order to update current practice and bring it in-line with current evidence, a series of meetings were conducted with Infectious Disease, Food and Nutrition Services and the Medical Oncologist who is the Director of the Autologous Stem Cell Transplant program. With the evidence at hand, it was decided that the normal hospital diet, which includes strict food safety guidelines and is closely monitored by Food and Nutrition Services, would be appropriate for patients with neutropenic fever. Patients receive trays consistent with the rest of the hospital, served on china, appropriately garnished, with foods selected on an "as tolerated" basis. Neutropenic precautions continue to discourage plants and flowers in the room; however, raw fruits and vegetables are allowed as they are washed in the Food and Nutrition services department prior to service. Food brought in from outside vendors is also discouraged as close monitoring of these foods cannot be assured. No other changes are made in the trays for patients on neutropenic precautions. To date, no complications or complaints have been identified. Patient education emphasizes the importance of following food safety guidelines.

ADA's Nutrition Care Manual provides comprehensive instructional materials appropriate for the inpatient and clinic setting. *Low-Microbial Nutrition Therapy* (32) *and Food Safety Guidelines for Neutropenia* (33), based on the U.S. Food and Drug

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Administration Food Safety Guidelines, may be utilized for patients upon discharge (30). The USDA published a document in 2006: *Food Safety for People with Cancer*, that also outlines important food safety guidelines for this population (2). Additional food safety resources are listed below.

RD Practice Points:

1. Food safety is a concern for all consumers, and it is important for RDs to ensure that evidence-based food safety guidelines developed by the USDA, FDA, and similar public health organizations are followed by inpatient facilities. For inpatients, meal trays and foods requiring refrigeration should not sit at the bedside for more than one hour, and each facility's food service department must maintain the strictest food safety standards recommended.
2. Guidelines for neutropenic and immunocompromised patients should minimize the introduction of pathogenic organisms through evidence-based food safety guidelines while maximizing healthy food options and intake. RDs need to educate patients about safe handling, storage, and preparation of foods in the home, and food purchased in restaurants.
3. Dehydration or electrolyte imbalance from a gastrointestinal illness (including those from food-borne illnesses) may exacerbate chronic illness in vulnerable populations, making it essential for neutropenic and immunocompromised populations to be vigilant about safe food handling, food preparation, and food consumption.
4. Inpatient nutrition department policies for neutropenic and immunocompromised populations should address the need to restrict (or not): raw foods; unpasteurized dairy, juices, beer, and honey; raw, uncooked brewer's yeast; well water; cheese-based salad dressings that are not shelf-stable and require refrigeration; and luncheon meats.

There are a variety of excellent booklets, fact sheets, and guidelines on the topic of food safety developed by authoritative organizations such as the USDA and the FDA. For example, in 2008 the USDA published *Kitchen Companion: Your Safe Food Handbook* that provides a comprehensive review of "all the basic information you need to know about food safety . . .". It is accessible via the USDA website,and is one of many fact sheets located at http://www.fsis.usda.gov/Fact_Sheets/index.asp. *Food Safety for People with Cancer* is also available at this website. *The Dangers of Raw Milk: Unpasteurized milk can pose a serious health risk* is available through the FDA at http://www.fda.gov/Food/ResourcesForYou/Consumers/ucm079516.htm and *Playing it Safe With Eggs: What consumers need to know* is available at http://www.fda.gov/Food/ResourcesForYou/Consumers/ucm077342.htm

Additional food safety resources include:
http://www.fightbac.org/
http://www.fightbac.org/fightbac-downloads/spanish-resources?start=5
http://www.foodsafety.gov/
http://www.fda.gov/food/foodsafety/default.htm
http://www.cdc.gov/foodsafety/
http://www.fsis.usda.gov/Fact_Sheets/index.asp.
http://cfsan.fda.gov
http://www.cdc.gov/travel/index.htm
http://cdc.gov/ncidod/diseases/water/index.htm

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Nutrition Informatics for the Oncology RD

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Introduction

As the U.S. moves towards an electronic delivery and management system of health care, nutrition professionals as well as other health care providers are adjusting to efficient electronic processes and technologies. This article identifies resources, tools, and strategies for transitioning to technology-based care, defines "nutrition informatics" for the oncology dietitian, and suggests strategies for identifying effective informatics processes. Throughout this transition it is important to focus on informatics processes that optimize patient care, provide access to evidence-based information, foster health care team collaboration, and result in desired nutrition outcomes.

Background

Use and application of the term "nutrition informatics" was first introduced in 2006 (1). A year later (2007), the American Dietetic Association (ADA) sanctioned a Nutrition Informatics Work Group that defined nutrition informatics as:

> "The effective retrieval, organization, storage and optimum use of information, data, and knowledge for food and nutrition related problem solving and decision making. Informatics is supported by the use of information standards, information processes and information technology." (2)

This definition was adapted from a well established general definition for *biomedical informatics*, taking into consideration the unique applicability of nutrition (3). Realizing the need to communicate a simple message on what nutrition informatics entails, the ADA Nutrition Informatics Committee in 2010 translated this definition into one simple line:

> "Nutrition informatics is the intersection of information, nutrition and technology." (4)

Knowledge and work in the field of biomedical and health informatics is not new. The first nutrition article documenting the work of nutrition and computers was published in 1952 (5). Recognizing the success of the nursing profession in incorporating informatics processes into their practice, leaders in nutrition informatics have collaborated with the nursing profession to advance this specialty in the field of nutrition. Indeed, the original work of the Technology Informatics Guiding Educational Reform (TIGER) (6), a successful nursing educational collaborative, may soon play a role in the development of a robust strategy for nutrition informatics competencies. ADA continues to promote the integration of nutrition informatics throughout the profession (7), and some online resources made available by ADA include a blog (8), a webpage with key information, and an exhaustive reference list of over 800 nutrition informatics citations.

Impact on the Profession

Perhaps the informatics format most familiar to RDs is the electronic health record (EHR). The national focus on EHRs began in 2004, when then President George W. Bush issued an Executive Order stating that all Americans should have access to an EHR by the year 2014 (9). While this order increased awareness of the critical need to digitize health care, nationwide adoption rates by health care facilities and providers inched forward at a sluggish pace; only about 4 to 16 percent of health care facilities had transitioned to EHRs by 2008 (10).

In February 2009, the federal government passed the Health Information Technology

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for Economic and Clinical Health (HITECH) Act (11). HITECH is a component of the American Recovery and Reinvestment Act (ARRA) (12), which was established to provide financial incentives to specific eligible providers (EP) of Medicare/Medicaid and also to create a nationwide infrastructure to support EHR adoption. The HITECH Act provided much needed financial support to the Office of the National Coordinator of Health Information Technology (ONC), which was also charged with promoting individual health data exchange and improving the quality and efficiency of healthcare. It puts in place training programs in informatics which will increase the workforce necessary to support nationwide adoption of EHRs. ADA has allocated resources to advocate for nutrition inclusion in EHRs and across the continuity of care. It is critical that all healthcare providers stay abreast of the rapid developments of Health Information Technology (HIT) driven by the HITECH Act to assure nutrition care is included during all three stages of the program, which is scheduled to be completed in 2021. Further details of this program and related ADA activities are available in other recent publications (13).

Many dietetic professionals have participated in EHR Planning Teams, and some have moved into leadership and/or more technology specific areas. All EHR Planning Committees should have at least an RD and/or dietetic technician, registered working collaboratively with other health team members to assure nutrition care is prevalent in EHRs. Regardless of the venue or specialty area, all RDs should begin planning for the use of HIT in completing their daily tasks. Realizing that the health care industry is one of the last to move towards electronic operations, there will eventually become a day when paper charts are no longer viable alternatives.

Perhaps the best pathway for integrating informatics into your practice or place of work is to divide the process into three categories: those which are of professional nature, those which are more directly related to the care of your patients/clients, and those with shared benefits. By starting with professional informatics, it helps to take a close look at the activities of your day. Many RDs already record workplace activity by documenting the number of patients assessed for their nutritional needs, numbers of nutrition care plans implemented, numbers of patients educated on modified diets, and the amount of time spent in committee work, patient rounds, etc. By examining daily workload and comparing notes with peers inside and outside the profession, RDs can streamline work processes.

Several questions you should ask:

1. What data do you use longitudinally, over time, for comparison of trends or outcomes? If you are transcribing data by hand, determine whether you can export it from another source or record and update it in spreadsheets, a database or other software, and/or graph/display results over time.
2. What activities, if processed electronically, could save staff time and/or improve accuracy by reducing human error? Contrary to early concerns, increased use of technology has not caused job losses, but rather increased the need for higher level tasks by position/job.
3. What tools and techniques work best for you? Consider additional training or instruction prior to making your decision about what is most helpful.

Professional areas where informatics is beneficial to the oncology dietitian:

1. Electronic nutrient databases
   A review of supplemental dietary resources was published in late 2010 (14). Fortunately, government agencies provide robust access to nutrient data in the public domain. Most have a mobile version which can be used on a smart phone or tablet. Proprietary databases are also available with paid nutrition software license fees.
   Examples:
   - The National Nutrient Database for Standard Reference (NNDSR) (15) is maintained by the United States Department of Agriculture (USDA). In its 23rd Release, it provides nutrient content for over 7,500 foods.
   - The Food and Nutrient Database for Dietary Studies (FNDDS) (16) is used primarily for dietary studies including *What We Eat in America* and the *National Health and Nutrition Examination Survey* (NHANES) (17).
   - The Dietary Supplement Ingredient Database (DSID) (18) is managed by the Office of Dietary Supplements at the National Institutes of Health (NIH). While it is intended primarily for research use, over half of the American population, and an even greater percentage of cancer survivors, take dietary supplements.
   - The National Medicines Comprehensive Database (19) is a credible reference and consumer database which provides monographs on evidence based research, natural medicine interactions, and safety ratings of many dietary supplement products.
   - Oncology Statistics Databases include the Surveillance Epidemiology and End Results (SEER) (20).

2. Tools to monitor weight, lab values, or other clinical parameters (e.g. BMI, weight changes and metabolic parameters)
   - RDs monitor and graph inpatient /outpatient weight and weight trends.
   - RDs graph nutrition screening and assessment criteria and use screening/ evaluation tools available from groups such as the National Comprehensive Cancer Network (21).
   - RDs encourage patients to participate in nutrition care through self-monitoring tools.
   - Via ongoing monitoring of intake and other assessment/reassessment data and tracking data on informatics tools, RDs can efficiently develop, monitor, and revise nutrition care recommendations.

3. Enteral or parenteral nutrition (EN or PN) software
   - Software allows RDs to streamline calculations, monitor outcomes, and potentially limit human error.

4. Nutrition Information Systems at the departmental or facility level
   - By maintaining an individual's longitudinal history related to food and nutrition, clinicians can better assess outcomes of Medical Nutrition Therapy (MNT).

5. ADA online resources such as the Evidence Analysis Library (EAL) (22), EHR Toolkit (23), Nutrition Care Manual (24), Nutrition Care Process and Model (NCPM) and International Dietetics and Nutrition Terminology (IDNT) (25)
   - These resources facilitate up-to-date, evidence-based nutrition care.

6. Online Medline (26)
   - Medline provides a tool to search research and professional publications, including the *Journal of the American Dietetic Association* (27).

7. Online instruction, continuing education, and health trend updates (including web demonstrations, e-learning courses, Slide Share, You Tube, etc.)
   - While any non-subscription type site will obviously have a mixture of credible and less-than credible sites, multiple professional organizations utilize these resources as an educational connection with the public.

8. Professional networking through social media sites such as LinkedIn, Twitter, Facebook, etc.
   - Social media provides a means to communicate with other health professionals. Such sites typically have topic or interest-specific virtual groups where you can learn about new advances, publications or work in your area of interest. Knowing your expectations allows you to determine which sites are most appropriate for your needs.

9. Clinical Decision Support (CDS)
   - Often referred to as "CDS", it is an area of future practice — or should be. While much work has been completed in this area, most CDS tools address medication selection and disease management based upon clinical findings. Little work has been undertaken in the area of nutrition — such as diet/ MNT recommendations based upon diagnosis and findings. CDS serves as a paper decision tree translated to an electronic algorithm.

10. Research is for everyone!
    - Electronic storage, retrieval, and analysis of patient data provides all practitioners with the opportunity to turn real world practices into research. RDs should define what practices they want to examine and structure technology to collect relevant data. One particular area with significant potential is outcomes analysis based upon nutrition care delivery — a strong asset when justifying staffing requests. Some institutions store data in a warehouse, and allow clinicians such as RDs to access data for research purposes.

Patient Use of Health Related Technology on Online Offerings

Patients utilize online resources for a variety of different actions related to their own health care. When the Internet first surfaced, patients could access health information of any kind - both credible and suspect in nature. As creative technologies have evolved, online health content has had to withstand the scrutiny of health experts and patients, who are now better informed of potential treatments and aware of credible and quack diets and nutritional recommendations promoted for a variety of health ailments.

Patient Tools and Sites include:

- **Personal Health Records (PHR)**
  While electronic records maintained by the individual patient (PHRs) have not yet received widespread adoption, there are many who are hopeful that patients will eventually be engaged in maintaining their own records. Microsoft Health Vault, Google Health and Dossia Consortium — to name a few, all have products that allow patients to access and manage their own health data. Recent studies have shown that patients like mobile access to health tools so they can manage and use them when and where they are needed. In particular, one free online tool would allow families to record their family health history for other family members (28).

- **Patient Portals and Access to Their Data**
  Due to the consumer focused agenda of the HITECH Act, many collaborative initiatives are underway which serve to place an individual's health data in their own hands. Understanding that there are significant privacy and security requirements to be followed, this is beyond the scope of this article. An example is a collaboration between the Markle Foundation, the Adobe Company, and Department of Veteran Affairs that created the "Blue Button" (29) whereby Medicare/Medicaid recipients or Veterans can easily download their own medical information.

- **Online Communities**
  While it may seem that the advent of online health communities has occurred only within the past decade, an online cancer community has been active for several decades. While some question the scientific merit of such patient experiences, patients who share diagnoses and experiences have found these sites valuable and credible. The Association of Online Cancer Resources (ACOR) (30), a nonprofit organization funded by Gilles Frydman, hosts 159 electronic mailing lists and a variety of unique cancer websites. The mailing lists provide information and community support to over 44,000 patients and caregivers. ACOR delivers over 1,800,000 individual messages around the world every week.

- **Prevention and Wellness**
  The American Cancer Society states that 1/3 of cancers could be prevented by a healthful diet and increased activity. Online resources can provide an alternative to traditional health education formats and be used to motivate consumers to adopt a healthy diet and lifestyle.

- **Education**
  Patients are no longer limited to traditional face-to-face and/or group instruction. Utilizing online tools for learning, coaching, and interaction adds new opportunities for intervention and has been used by some providers for many years (31).

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- **Meal Planning**
  With a multitude of creative menu planning tools available online, patients have many options for supporting their recovery. An example of this is TherapEase Cuisine (32), which provides nutrition and meal planning advice for patients undergoing cancer treatment.

- **Self Monitoring**
  A quickly expanding market for consumers is in the area of self monitoring. Online technologies allow for a variety of interactions. Dubbed "Health 2.0", these websites, tools and electronic processes add unique opportunities for patients to manage their health care. One new example is TheCarrot.com (33), an online site that allows individuals to monitor a variety of different behaviors and values. This resource serves as a spin-off from a Robert Wood Johnson Foundation project encouraging healthy lifestyles.

- **Shared Informatics Functions Between Patient and Dietitian**
  Dietitians can begin to consider ways to integrate informatics tools that provide patients and dietitians with new channels of communication. For example, RDs who review patients' online food diaries can use this technology to provide expert advice and coaching.

Summary

Currently there exists many opportunities for RDs to integrate informatics into practice. Just as each practice and/or facility is unique and utilizes different care strategies, the method by which dietitians integrate nutrition informatics into their practice is also unique. After analyzing workflow and workplace processes, an informatics plan incorporates tools that can be beneficial to the dietitian and the patient, resulting in provision of best practices and improved outcomes.

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Eat Right to Fight Cancer

Whole foods have many cancer-fighting properties. This article is the first in a series that will bring information to you on foods to include in a cancer prevention diet.

Onions in a Cancer Prevention Diet

Maureen Leser, MS, RD, CSO, LD and Kim Reddin of the National Onion Association

History

While there is no conclusive evidence regarding the exact location and time of their origin, research suggests that our predecessors discovered and started eating wild onions long before farming became an organized activity. Some archaeologists, botanists and food historians believe onions came from Central Asia, but other research suggests that onions were first grown in Iran and West Pakistan. Regardless of their exact geographic origin, this humble vegetable was a staple in prehistoric diets.

More recently, a significant body of scientific research, including clinical, animal, and epidemiological studies, suggests consuming onions may be protective against cardiovascular disease, many forms of cancer, diabetes, and osteoporosis. Emerging research supports anti-inflammatory, anti-bacterial, and anti-viral effects of onions as well as digestive benefits.

Cancer Prevention and Management

Good diet and nutrition is key to preventing and managing most chronic illness, including cancer. According to the 2007 report of the World Cancer Research Fund of the American Institute for Cancer Research (AICR), approximately 30% of all cancers are directly linked to a person's dietary habits and may be preventable by appropriate food and nutrition (1). As part of recommendation 4 of the report, which advises consumers to eat mostly foods of plant origin, AICR recommends an intake of at least five portions/servings (at least 400 grams or 14 ounces) of a variety of non-starchy vegetables and of fruits every day (1). The AICR report also states that evidence indicates that Allium vegetables probably protect against stomach cancer (1).

Onion Nutrition

Onions are a member of the Allium family of vegetables, which also includes garlic, leeks, scallions, shallots, and chives. Similar to other Allium vegetables, onions contain a variety of phytochemicals, plant based compounds involved in multiple biological pathways and systems. Flavonols and anthocyanins are the two categories of flavonoids found in onions; querectin, kaempferol, myricetin, and isorhamnetin are the primary flavonols in onions (2). Anthocyanins, which impart vivid red, blue, and purple colors to plant foods, are found in red onions (3).

Flavonol intake has been estimated at 20 to 60 mg per day in the United States; anthocyanin intake is estimated at 180 to 215 mg daily. Onions are among the best sources of quercetin and kaempferol, two flavonols thought to have chemopreventive potential (4).

In vitro and animal studies suggest that antioxidant activity of anthocyanins can limit damaging effects of reactive oxygen species (ROS), which otherwise may promote DNA damage contributing to carcinogenesis. They also may stimulate expression of Phase II detoxification enzymes, which can help destroy molecules that may damage DNA, and may even decrease risk of mutations caused by carcinogens (5).

(Continued on next page)

Table 1. Flavonols in Onions (9)

Food	Quercetin (mg/100 grams)	Kaempferol (mg/100 grams)	Myricetin (mg/100 grams)	Isorhamnetin (mg/100 grams)
Onions, spring, red, leaves	12.6	4.1	–	–
Onions, cooked, boiled, drained, without salt	24.36	12.6	–	–
Onions, raw	21.42	0.62	0.02	5.01
Onions, red, raw	33.43	1.1	27	4.25
Onions, spring or scallions, raw	18.33	1.16	0	–
Onions, sweet, raw	14.8	1.03	1.7	–
Onions, welsh, raw	–	24.95	–	–
Onions, white, raw	7.29	0	0	0
Onions, young green, tops only	0.01	2.4	0.03	–

Additional anti-cancer compounds in onions include organosulfur compounds such as dipropyl and dipropenyl sulfides. Chopping and chewing releases organosulfur compounds in onions, freeing them to help detoxify carcinogens, limit angiogenesis, and alter cell cycles (6). In addition, the antibacterial potential of allyl sulfides may protect against Helicobacter pylori (H. pylori) infection, which is associated with an increased risk of stomach cancer (7).

As a whole, phytochemicals in onions modulate phase I and II enzymes, induce DNA repair, induce apoptosis, enhance immunocompetence, and serve as antioxidants and anti-inflammatory agents, tempering an inflammatory environment associated with traditional western diets (8).

All allium vegetables store energy as inulin rather than starch, a unique physiologic event that imparts onions with prebiotic properties. Prebiotics help create a gastro-intestinal environment with a healthy mix of friendly bacteria that promotes regular bowel function, inhibits the growth of pathogenic bacteria, and even modulates inflammation. The National Cancer Institute's Drug Dictionary defines inulin as:

> "a naturally occurring, indigestible and non-absorbable oligosaccharide produced by certain plants with prebiotic and potential anticancer activity. Inulin stimulates the growth of beneficial bacteria in the colon, including Bifidobacteria and Lactobacilli, thereby modulating the composition of microflora. This creates an environment that protects against pathogens, toxins and carcinogens, which can cause inflammation and cancer. In addition, fermentation of inulin leads to an increase in short-chain fatty acids and lactic acid production, thereby reducing colonic pH, which may further control pathogenic bacteria growth and may contribute to inulin's cancer protective properties." (11)

Table 2. Nutrient Analysis of the Onion (10)

Nutrient	Nutrient Content per 1/2 medium onion (= 74 grams)	Percent Daily Value
Calories	23	n/a
Total Fat	0	0%
Cholesterol	0	0%
Sodium	2.5 milligrams	0%
Total Carbohydrate	5.5 grams	2%
Dietary Fiber	1.5 grams	6%
Sugars	4.5 grams	n/a
Protein	0.5 grams	n/a
Vitamin A	0	0%
Vitamin C	11.8 milligrams	10%
Vitamin B6	0.005 grams	2.50%
Calcium	18 milligrams	2%
Iron	0.3 milligrams	2%
Folic Acid	7.1 micrograms	2%
Potassium	95 milligrams	2.50%
Selenium	0.25 micrograms	0.50%
Zinc	0.1 milligrams	0.50%

The Evidence linking Onions to Cancer Prevention:

While a diet rich in plant-based foods is considered preventive medicine, not all fruits and vegetables have equal ability to potentially help prevent cancer occurrence and recurrence in all sites. According to AICR's second expert report, *Food, Nutrition, Physical Activity, and the Prevention of Cancer: A Global Perspective*, foods belonging to the Allium family of vegetables probably protect against stomach cancer (1). Epidemiological studies suggest an inverse relationship between intake of Allium vegetables such as onions and stomach, colorectal, and prostate cancers (12). Galeone and his team of Italian researchers reviewed case control studies of several cancers, examining the influence of a variety of factors, including diet, on cancer incidence (12). The food frequency (FFQ) form used in this study included specific questions on onion and garlic intake, asking, in the case of onions, whether subjects never consumed onions or whether intake was <1 to <7, and ≥7 portions/week. For each cancer site, cases consumed fewer vegetables and fewer onions than controls. Significant inverse associations were seen between onion intake > 7 portions per week and cancers of the oral cavity (OR 0.16), esophagus (0.12), colon (OR 0.44), larynx (OR 0.17), and ovary (0.27) (12).

An examination of the impact of several carotenoids and flavonoids on the risk of gastric cancer in Spain found a trend toward a lower risk of stomach cancer with higher intake of quercetin, which is found in onions and other Allium vegetables (13). The Netherlands Cohort Study also examined the relationship between diet and cancer in over 120,000 subjects. In 3.3 years of follow-up, the rate ratio for stomach cancer (non-cardia segment) in the highest onion intake group was 0.50 after controlling for other risk factors (14). The incidence of stomach cancer in Shanghai is second only to lung cancer. A case control examination in China, specifically in Shanghai (with 750 cases and 750 age- and gender-matched controls) and Qingdao (with 128 cases and 128 age- and gender-matched controls), examined epidemiological data for risk factors for stomach cancer. Researchers found a negative dose-response relationship between onion intake and distal stomach cancer risk in both Shanghai and Qingdao (8).

Studies examining the relationship between flavonoid intake and colon cancer have yielded inconsistent results. Using a more complete database of flavonoids in food that was developed by the U.S. Department of Agriculture (USDA), a case control study of data from the Polyp Prevention Trial (PPT) suggested an inverse association between high flavonoid intake, in particular flavonol intake, and colorectal cancer (CRC) risk. Authors observed a statistically significant decreased risk for the highest intake quartile of flavonols as compared with the lowest intake quartile (OR, 0.24; 95% CI, 0.11–0.53). Of specific flavonoids examined, there was a statistically significant decrease in risk for advanced adenoma recurrence as intakes of genistein, isorhamnetin, kaempferol, and formononetin increased (15). Onions were among several vegetables that provided 17.8% of the estimated flavonol intake, and are a primary source of kaempferol. A significant inverse association was only seen in the intervention group; few members of the control group consumed high intakes of flavonols. While the intervention diet provided a rich mix of phytonutrients, this study suggests that a flavonol-rich diet may help decrease the risk of advanced colorectal adenoma recurrence (15).

Men in China have the lowest rates of prostate cancer in the world, and onions may be an important dietary component of a prostate cancer-prevention diet. Results from an analysis of men's diets in China were published in 2002 in the *Journal of the National Cancer Institute*. The study investigated intake of 122 food items by 238 Chinese men with prostate cancer and 471 healthy case controls. Asking about dietary intake during the five year period prior to the interview, researchers wanted to determine whether foods or food groups were associated with prostate cancer risk. They found that men who consumed more than 10 grams per day of Allium vegetables had an almost 50% reduction in risk of developing prostate cancer as compared with those who consumed less than 2.2 grams per day (16), independent of intake of other food items investigated. Results showed a more pronounced cancer-reduction benefit from Allium vegetables than from fruits and vegetables overall, or even from cruciferous vegetables or food sources of lycopene (16).

Cell studies suggest that quercetin may inhibit growth of breast, ovarian, leukaemic, and colon cancer cells (17). MCF-7 is an estrogen-sensitive breast cancer cell line that has been used in many cell studies. A study examining the effects of genistein and quercetin on these cells found that quercetin significantly inhibited growth of MCF-7 cells in concentrations above 2.5uM (18). Results suggested it could counteract stimulatory effects of estradiol and growth factor TGF-a in MCF-7 cell lines. Quercetin did not compete with estrogen for estrogen receptors to the same degree as genistein, but was believed to exert anti-estrogenic effects by influencing estrogen-regulated genes (17).

Onions are a rich source of quercetin; Hung reported an average intake of quercetin and kaempferol of 20 mg/day. In addition, he reports an inverse association between intake of quercetin from onions (and apples) and lung cancer risk, and a role for quercetin in triggering apoptosis of cancer cells. His cell studies suggested that consumption of quercetin from onions and apples was inversely correlated with lung cancer risk (18).

Synergism Among Phytochemicals

Researchers are challenged to tease out unique chemo-preventive effects of individual nutrients, phytonutrients, and other dietary components within a single food. These healthful substances interact in a variety of ways, perhaps complementing each other's chemo-preventive effects, and potentially influencing multiple pathways involved in carcinogenesis. An emerging area of science is investigating the effects of food combinations on chronic disease (19). For example, research suggests that combining onion with foods high in lycopene, especially tomatoes, may provide even greater protection for the prostate than lycopene alone (20). Another recent study shows that certain vegetables, such as onions and broccoli, may together play a role in the prevention of skin cancer. The flavonoids kaempferol and quercetin seem to act synergistically in reducing cell proliferation of cancer cells, meaning that the combined effects of quercetin and kaempferol are more effective than the additive effects of each flavonoid (21).

Onions are sometimes overlooked for their health value because they are frequently used as a condiment rather than a true vegetable. But just like the vegetables promoted to add color to the dinner plate, yellow, red, and white onions contribute abundant and unique health-enhancing compounds such as flavonols, anthocyanins, organosulfur compounds, and inulin.

The body of scientific research on cancer supports a benefit for including onions in a plant based diet. In his book *Foods to Fight Cancer*, Dr. Richard Beliveau recommends a half-cup of onions daily as part of a cancer prevention diet (22). With the potential to incorporate them into every meal and many snacks, onions are one of the most versatile vegetables to prepare. They also add layers of flavor that compliment many other healthy foods.For additional information about onions, visit http://www.onions-usa.org/.

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2011 Oncology Events: Upcoming Conferences

March 14-18, 2011
Nutrition & Cancer Prevention Research Practicum
National Institutes of Health
National Cancer Institute
Division of Cancer Prevention
contact: Elaine Trujillo @ trujille@mail.nih.gov

March 15, 2011
Stars in Nutrition & Cancer Lecture: False Positives, False Negatives, and Small Effects: Genome, Exposome, and Nutrition
Dr. John Ioannidis
Stanford University
NIH Main Campus
Bethesda, MD
contact: Elaine Trujillo at trujille@mail.nih.gov

April 2-6, 2011
American Association for Cancer Research Annual Meeting
Orlando, Florida
www.aacr.org

May 5, 2011
Nutrition and Cancer Survivorship
Yale University
8:00 a.m.- 4:30 p.m.
Keynote Speaker: Suzanne Dixon, MPH, MS, RD
contact: maura.harrigan@yale.edu

May 9-11, 2011
Nutrition & Health Conference 2011
San Francisco, California
Hyatt Regency at Embarcadero Center
http://www.nutritionandhealthconf.org/forum/

June 3-7, 2011
American Society of Clinical Oncology (ASCO) Annual Meeting
Chicago, Illinois
http://chicago2011.asco.org/

CancerCare's is offering a FREE, four-part workshop series
These workshops are available via the telephone or live streaming through the internet. These workshops are free — no phone charges apply. However, pre-registration is required. To register, and for more information, go to the CancerCare website, www.cancercare.org/connect

April 12, 1:30-2:30 p.m. EST
Part 1: Chemobrain: The Impact of Cancer Treatments on Memory, Thinking and Attention

May 10, 1:30-2:30 p.m. EST
Part II, Weight Changes After Cancer Treatments: Why Is It Happening and What Can I Do About It?

June 14, 1:30-2:30 p.m. EST
Part III, Stress Management for Caregivers: Taking Care of Yourself Physically and Emotionally

July 12, 1:30-2:30 p.m. EST
Part IV, Fear of Recurrence and Late Effects: Living With Uncertainty

The table on pancreatic enzyme products (originally published in the fall 2010 issue of *Oncology Nutrition Connection*) has been revised.

Enzyme Name	Strength	Type	Dosing Instructions	
Creon® 6,000	6,000 USP units lipase/19,000 USP units protease/30,000 USP units amylase	E-C MS	Initial dose: 500 lipase USP units/kg PO w/meals & snacks; titrate to desired effect Alternative dosing: 500-4000 lipase USP units/g fat ingested PO; take w/meals & snacks; titrate to desired effect Snack dose usually one-half of meal dose; Use enzymes with oral supplement drinks Doses should be flexed with fat content in the meal. A high fat meal will need more capsules, while a predominantly carbohydrate meal will likely require the lowest enzyme dose.	Do not exceed a lipase dose >2500 USP units/kg/meal Or 10,000 lipase USP units/ kg/day Do not cut/crush/chew; may open caps and sprinkle on soft food w/pH less than 4, 4.5, and 4.5, for Creon®, Pancreaze® and Zenprep®, respectively
Creon® 12,000	12,000 USP units lipase/38,000 USP units protease/60,000 USP units amylase			
Creon® 24,000	24,000 USP units lipase/76,000 USP units protease/120,000 USP units amylase			
Pancreaze™ MT 4	4,200 USP units of lipase; 10,000 USP units of protease; 17,500 USP units of amylase	E-C MT		
Pancreaze™ MT 10	10,500 USP units of lipase; 25,000 USP units of protease; 43,750 USP units of amylase.			
Pancreaze™ MT 16	16,800 USP units of lipase; 40,000 USP units of protease; 70,000 USP units of amylase			
Pancreaze™ MT 20	21,000 USP units of lipase; 37,000 USP units of protease; 61,000 USP units of amylase.			
Zenpep®5	5,000 USP units lipase/17,000 USP units protease/27,000 USP units amylase	E-C MS		
Zenpep®10	10,000 USP units lipase/34,000 USP units protease/55,000 USP units amylase			
Zenpep®15	15,000 USP units lipase/51,000 USP units protease/82,000 USP units amylase			
Zenpep®20	20,000 USP units lipase/68,000 USP units protease/109,000 USP units amylase			

Oncology Nutrition News Brief

More About Soy and Cancer: Wishing You Were Young

Kimberlee Taylor, MS, RD, CSO, LD, CNSC

Stars in Nutrition is a series of biannual lectures sponsored by the Department of Cancer Prevention, National Cancer Institute (NCI)/National Institutes of Health (NIH). The aim of these lectures is to highlight the role of nutrition science in understanding biology and the way in which nutrition may modify cancer development. On October 4th, 2010 Stephen Barnes, PhD, Professor of Pharmacology & Toxicology at the University of Alabama at Birmingham presented a lecture on soy and breast cancer (1). Dr. Barnes has conducted numerous research studies and has extensively published in the area of polyphenols (genistein, resveratrol) on estrogen-dependent gene and protein networks in the breast.

Soyfoods contain a variety of chemical compounds. These include isoflavones such as genistein and resveratrol. In the soybean plant isoflavones are responsible for turning on ribosomal bacteria to form the root nodule, which allows for nitrogen fixation to a form that can be incorporated into proteins.

Soy is available in a variety of products; forms include tempeh, tofu, miso, textured vegetable protein, soy paste and soy sauce. The types and amounts of isoflavones in a soy product will vary based on processing and the source of the soybean. Another emerging source of isoflavones is the kudzu plant. While this is not eaten directly in the American diet, it is commonly found in processed soy products. On food packaging labels you may see "soy and other plant sources of natural estrogens"; "other plant sources" usually refers to kudzu plants.

Often RDs become aware of their patients' interests in soy intake after a diagnosis of breast cancer, especially in those that are estrogen positive. Some medications used in breast cancer treatment such as tamoxifen work by blocking the effects of estrogen. The research on soy and breast cancer after diagnosis is still forthcoming, and 2-3 servings of soy foods per day are generally thought to be safe (2).

After a discussion of the chemical composition of soy and the epigenetic effects caused by soy, Dr. Barnes focused on soy and breast cancer prevention. Interestingly, he highlighted how the incidence of both lung cancer and stomach cancer in the United States have dropped significantly over the last 70 years due to public health initiatives rather than research advances. The increase in "no smoking" policies may have helped to lower the lung cancer incidence, and increased refrigeration and decreased reliance on processed/cured foods may have helped to reduce incidence of stomach cancer. Perhaps preventive strategies such as an increase in soy intake beginning in childhood may also help reduce the incidence of breast cancer.

Studies in both animals and humans have looked at timing of exposure to isoflavones and the incidence of breast cancer. Xiao Ou Shu, MD, PhD, et al, using data from the Shanghi Breast Cancer Registry, looked at tofu intake in adolescence and breast cancer risk. He found that those with the highest intake had the lowest risk of breast cancer (2). Anna Wu, PhD, examined Asian-Americans females in California and their intake of tofu in adolescence and in adulthood and the risk of breast cancer. Her results are summarized below, and confirm Shu's study by showing that a higher intake of tofu in adolescence decreases the risk of breast cancer (3). High intakes of tofu throughout life appear to have the best preventive benefits.

Dr. Barnes concluded the lecture with the following points:

- Isoflavones given in the diet in animal models of breast cancer inhibit the appearance of carcinogen-induced mammary tumors, but only if given prior to puberty.
- Diet (and exercise) early in life may have an important role in determining the risk of adult breast cancer. Exercise helps to regulate mitochondria in tissues.
- Microarray analysis has identified the Krebs cycle, which occurs in the mitochondria, as the major pathway

(Continued on next page)

Tofu Intake and Risk of Breast Cancer

Adolescent	Adult	Risk
Low	Low	1
Low	High	0.93 (0.58-1.48)
High	Low	0.77 (0.51-1.16)
High	High	0.53 (0.36-0.78)

P=0.001

that is down-regulated at the time of maximum sensitivity to the carcinogen.

- Levels of a Krebs cycle intermediate may be the critical element explaining diet-regulated breast cancer susceptibility that begins in childhood and adolescence.

As the title of the lecture suggests, it's good to be wise when you are young and know the benefits of healthy eating and exercise. Instilling good diet and exercise habits from an early age may help promote cancer prevention.

Kimberlee Taylor, MS, RD, CSO, LD, CNSC, is a Supervisor, Clinical Nutrition with The University of Texas M.D. Anderson Cancer Center. Kimberlee A Taylor can be reached at KATaylor@mdanderson.org.

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