



# RESEARCH UPDATES

For the latest in worldwide integrated cancer care

October 2007



**InspireHealth**  
INTEGRATED CANCER CARE

## In this issue

### Cancer

Breast	1
Prostate	1
Esophagus/Stomach	2
Pancreas	3

### Therapies

Hormones	3
Nutrition	3
Supplements	3
Exercise	4

### CAM of the Month

4

*Research Updates* is produced once a month by InspireHealth to inform those interested of newly published articles in integrative cancer care. Authoritative articles are selected based on their evidence and their relevance to this area of medicine.

Thank you to The  
Canadian Breast Cancer  
Foundation  
BC/Yukon Chapter for  
their generous support.



[www.CBFC.org](http://www.CBFC.org)

## Breast

Palesh O, Butler LD, Koopman C, et al. **Stress history and breast cancer recurrence.** *J Psychosom Res.* 2007 Sep;63(3):233-239.

**BACKGROUND:** There is mixed evidence regarding the possible association between a history of stressful or traumatic life events and more rapid breast cancer progression. **METHOD:** Retrospective reports of past experiences of traumatic life events were assessed among 94 women with metastatic or recurrent breast cancer. A traumatic event assessment was conducted using the event-screening question from the posttraumatic stress disorder (PTSD) module of the Structured Clinical Interview for the DSM-IV-TR (SCID; 2002). Each reported event was judged by two independent raters to determine whether it met DSM-IV-TR PTSD A1 criteria for a traumatic event. Those events that did not meet such criteria were designated "stressful events." **RESULTS:** Nearly 42% of the women in the sample were judged to have experienced one or more traumatic events; 28.7% reported only stressful events. A Kruskal-Wallis test found significant differences in disease-free interval among the three groups [ $\chi^2(2, N=94)=6.09, P<.05$ ]. Planned comparisons revealed a significantly longer disease-free interval among women who had reported no traumatic or stressful life events (median=62 months) compared to those who had experienced one or more stressful or traumatic life events (combined median=31 months). **CONCLUSIONS:** A history of stressful or traumatic life events may reduce host resistance to tumor growth. These findings are consistent with a possible long-lasting effect of previous life stress on stress response systems such as the hypothalamic-pituitary-adrenal (HPA) axis.

Schwartz AL, Winters-Stone K, Gallucci B. **Exercise effects on bone mineral density in women with breast cancer receiving adjuvant chemotherapy.** *Oncol Nurs Forum.* 2007;34(3):627-633.

**PURPOSE/OBJECTIVES:** To test the effects of aerobic and resistance exercise on changes

in bone mineral density (BMD) in women newly diagnosed with stage I-III breast cancer receiving chemotherapy. **DESIGN:** Randomized clinical trial. **SETTING:** Two National Cancer Institute-designated cancer centers in metropolitan areas. **SAMPLE:** 66 women with stage I-III breast cancer beginning adjuvant chemotherapy. **METHODS:** Participants were randomized to aerobic or resistance exercise and usual care. At the beginning of chemotherapy and at six months, patients completed exercise testing and BMD assessment of the lumbar spine by dual energy x-ray absorptiometry. **MAIN RESEARCH VARIABLES:** BMD, aerobic capacity, and muscle strength. **FINDINGS:** The average decline in BMD was -6.23% for usual care, -4.92% for resistance exercise, and -0.76% for aerobic exercise. Aerobic exercise preserved BMD significantly better compared to usual care. Premenopausal women demonstrated significantly greater declines in BMD than postmenopausal women. Aerobic capacity increased by almost 25% for women in the aerobic exercise group and 4% for resistance exercise. Participants in the usual care group showed a 10% decline in aerobic capacity. **CONCLUSIONS:** The data suggest that weight-bearing aerobic exercise attenuates declines in BMD and that aerobic and resistance exercise improve aerobic capacity and muscle strength at a time when women generally show marked declines in functional ability. **IMPLICATIONS FOR NURSING:** Exercise may prevent or at least minimize bone loss observed during chemotherapy and may prevent or delay the long-term effects of osteoporosis.

## Prostate

Gallus S, Foschi R, Negri E, et al. **Dietary zinc and prostate cancer risk: a case-control study from Italy.** *Eur Urol.* 2007 Oct;52(4):1052-1057.

**Objectives:** Zinc concentration is higher in the prostate than in most other tissues. Since information on the role of zinc on prostate carcinogenesis is controversial, we analysed the issue in a case-control study. **Methods:** Between 1991 and 2002, we conducted a multicentre hospital-based case-control study

on prostate cancer in Italy. Cases included 1294 men with incident, histologically confirmed prostate cancer. Controls included 1451 patients admitted to the same hospitals as cases for a wide spectrum of acute non-neoplastic, non-hormone-related diseases. Zinc intake was computed from a valid and reproducible food frequency questionnaire, with the use of an Italian food composition database. Odds ratios (OR) of dietary intake of zinc and the corresponding 95% confidence intervals (CI) were estimated by unconditional multiple logistic regression models, after allowance for several covariates, including total energy. Results: Compared with the lowest quintile, the OR for the highest quintile was 1.56 (95% CI, 1.07-2.26), with a significant trend in risk ( $p = 0.04$ ). The trend in risk was significant for advanced cancers only, the OR being 2.02 (95% CI, 1.14-3.59) for prostate cancers with a high Gleason score. Conclusions: In this large study we found a direct association between high zinc intake and prostate cancer risk, particularly for advanced cancers. Our findings allow one to exclude a favourable effect of zinc on prostate carcinogenesis. Copyright 2007 European Association of Urology.

Giovannucci E, Liu Y, Platz EA, et al. **Risk factors for prostate cancer incidence and progression in the health professionals follow-up study.** *Int J Cancer.* 2007 01 Oct;121(7):1571-1578.

Risk factors for prostate cancer could differ for various subgroups, such as for "aggressive" and "non-aggressive" cancers or by grade or stage. Determinants of mortality could differ from those for incidence. Using data from the Health Professionals Follow-Up Study, we re-examined 10 factors (cigarette smoking history, physical activity, BMI, family history of prostate cancer, race, height, total energy consumption, and intakes of calcium, tomato sauce and alpha-linolenic acid) using multivariable Cox regression in relation to multiple subcategories for prostate cancer risk. These were factors that we previously found to be predictors of prostate cancer incidence or advanced prostate cancer in this cohort, and that have some support in the literature. In this analysis, only 4 factors had a clear statistically significant association with overall incident prostate cancer: African-American race, positive family history, higher tomato sauce intake (inversely) and alpha-linolenic acid intake. In contrast, for fatal prostate cancer, recent smoking history, taller height, higher BMI, family history, and high intakes of total energy, calcium and alpha-linolenic acid were associated with a statistically significant increased risk. Higher vigorous physical activity level was associated with lower risk. In relation to these risk factors, advanced stage at diagnosis was a good surrogate for fatal prostate cancer, but high-grade (Gleason [greater-than or equal to] 7 or Gleason [greater-than or equal to] 8) was not. Only for high calcium intake was there a close correspondence for associations among high-grade cancer, advanced and fatal prostate cancer. Tomato sauce (inversely) and alpha-linolenic acid (positively) intakes were strong predictors of advanced cancer among those with low-grade cancers at diagnosis. Although the proportion of advanced stage cancers was much lower after PSA screening began, risk factors for advanced stage prostate cancers were similar in the pre-PSA and PSA era. The complexity of the clinical and pathologic manifestations of prostate cancer must be considered in the design and interpretation of studies. Copyright 2007 Wiley-Liss, Inc.

 Thank you to the **BC Foundation for Prostate Disease** for their generous support.  
[www.BCPROSTATECANCER.org](http://www.BCPROSTATECANCER.org)

## Esophageal/Gastric

Wu AH, Tseng CC, Hankin J, et al. **Fiber intake and risk of adenocarcinomas of the esophagus and stomach.** *Cancer Causes Control.* 2007 Sep;18(7):713-722.

**BACKGROUND:** Since the 1970s, incidence rates for esophageal and gastric cardia adenocarcinomas have risen substantially for reasons that are not well understood. We sought to determine the role of dietary factors in these tumor types. **METHODS:** This analysis on dietary factors included 206 esophageal adenocarcinoma, 257 gastric cardia, 366 distal gastric adenocarcinoma patients and, 1,308 control subjects from a population-based, case-control study conducted in Los Angeles County. Polytomous logistic regression was used to calculate odds ratios (ORs), as an estimate of the relative risk, and corresponding 95% confidence intervals (CIs) for the three tumor types. **RESULTS:** Intake of fiber had a significant impact on risk of esophageal and gastric cardia adenocarcinoma after adjustment for age, gender, race, birthplace, education, cigarette smoking, body size, history of reflux, and vitamin use. Compared to subjects in the lowest quartile of fiber intake, subjects in the highest quartile of intake showed odd ratios of 0.44 (95% CI = 0.26-0.76) for esophageal adenocarcinoma ( $P$  trend = 0.004) and 0.58 (95% CI = 0.38-0.88) for gastric cardia adenocarcinoma ( $P$  trend = 0.016); these inverse associations remained after further adjustment for intake of fat. Positive associations between dietary fat and the three tumor types weakened after adjustment for fiber intake and were no longer statistically significant. For distal gastric cancer, a significant inverse association with fiber was observed only after adjustment for fat intake. The significant inverse associations with fiber remained after further adjustment for *H. pylori* infection for all three tumor types. **CONCLUSIONS:** High intake of fiber was associated with significant reduced risks of esophageal and gastric cardia adenocarcinoma even after adjustment for dietary fat, *H. pylori* infection and other covariates.

## Pancreas

Larsson SC, Bergkvist L, Wolk A. **Consumption of sugar and sugar-sweetened foods and the risk of pancreatic cancer in a prospective study.** *Am J Clin Nutr.* 2006 01 Nov;84(5):1171-1176.

**Background:** Emerging evidence indicates that hyperglycemia and hyperinsulinemia may be implicated in the development of pancreatic cancer. Frequent consumption of sugar and high-sugar foods may increase the risk of pancreatic cancer by inducing frequent postprandial hyperglycemia, increasing insulin demand, and decreasing insulin sensitivity. **Objective:** The objective of the study was to examine prospectively the association of the consumption of added sugar (i.e., sugar added to coffee, tea, cereals, etc) and of high-sugar foods with the risk of pancreatic cancer in a population-based cohort study of Swedish women and men. **Design:** A food-frequency questionnaire was completed in 1997 by 77 797 women and men aged 45-83 y who had no previous diagnosis of cancer or history of diabetes. The participants were followed through June 2005. **Results:** During a mean follow-up of 7.2 y, we identified 131 incident cases of pancreatic cancer. The consumption of added sugar, soft drinks, and sweetened fruit soups or stewed fruit was positively associated with the risk of pancreatic cancer. The multivariate hazard ratios for the highest compared with the lowest consumption categories were 1.69 (95% CI: 0.99, 2.89;  $P$  for trend = 0.06) for sugar, 1.93 (1.18, 3.14;  $P$  for trend = 0.02) for soft drinks, and 1.51 (0.97, 2.36;  $P$  for trend = 0.05) for sweetened fruit soups or stewed fruit. **Conclusion:** High

consumption of sugar and high-sugar foods may be associated with a greater risk of pancreatic cancer. Copyright 2006 American Society for Nutrition.

## Hormones

Lissoni P. **Biochemotherapy with standard chemotherapies plus the pineal hormone melatonin in the treatment of advanced solid neoplasms.** *Pathol Biol (Paris)*. 2007 Apr-May;55(3-4):201-204.

It is known since many years that the pineal hormone melatonin (MLT) may play anticancer activity through several mechanisms, including antiproliferative and immunostimulating effects. Moreover, it exerts an important antioxidant action. Therefore, MLT could be useful in the treatment of human neoplasms, either alone or in association with chemotherapy. The present study was performed to evaluate the influence of a concomitant MLT administration on efficacy and toxicity of several chemotherapeutic combinations in metastatic solid tumor patients, suffering from non-small cell lung cancer (NSCLC) or gastrointestinal tumors. The study included 370 patients who were randomized to receive chemotherapy alone or chemotherapy plus MLT (20 mg/day orally in the evening every day). NSCLC patients received cisplatin (CDDP) plus etoposide or CDDP plus gemcitabine. Colorectal cancer patients were treated with oxaliplatin plus 5-fluorouracil (5-FU), or weekly CPT-11 or 5-FU and folates (FA). Finally, gastric cancer patients received CDDP, epirubicin, 5-FU and FA or weekly 5-FU plus FA. The overall tumor regression rate achieved in patients concomitantly treated with MLT was significantly higher than that found in those treated with chemotherapy alone. Moreover, the 2-year survival rate was significantly higher in patients concomitantly treated with MLT. These results confirm in human the anticancer therapeutic properties of the pineal hormone MLT, which may enhance the efficacy of the standard anticancer chemotherapies.

## Nutrition

Ngo ST, Williams D, Cobiac L, et al. **Does garlic reduce risk of colorectal cancer? A systematic review.** *J Nutr*. 2007 October 1;137(10):2264-2269.

Colorectal cancer (CRC) is the 3rd leading cause of cancer death in the United States and the 2nd leading cause of cancer death in Australia. Environmental factors play important roles in the multiple-stage process of CRC and nutritional intervention has been identified as playing a major role in its prevention. The aim of this study was to review systematically the scientific evidence from all studies conducted over the last decade that examined effects of garlic on CRC. Levels of evidence were ranked from level I to level V according to study designs and the quality of each study was assessed against a set of quality criteria based on those used by the National Health and Medical Research Council in Australia. One randomized controlled trial (RCT, level II) reported a statistically significant 29% reduction in both size and number of colon adenomas in CRC patients taking aged garlic extract. Five of 8 case control/cohort studies (level III) suggested a protective effect of high intake of raw/cooked garlic and 2 of 8 of these studies suggested a protective effect for distal colon. A published meta-analysis (level III) of 7 of these studies confirmed this inverse association, with a 30% reduction in relative risk. Eleven animal studies (level V) demonstrated a significant anticarcinogenic effect of garlic and/or its active constituents. On balance, there is consistent scientific evidence derived from RCT of animal studies reporting protective effects of garlic on CRC despite great heterogeneity of measures of intakes among human epidemiological studies.

Doughman SD, Krupanidhi S, Sanjeevi CB. **Omega-3 fatty acids for nutrition and medicine: considering microalgae oil as a vegetarian source of EPA and DHA.** *Curr Diab Rev*. 2007 Aug;3(3):198-203.

Long-chain EPA/DHA omega-3 fatty acid supplementation can be co-preventative and co-therapeutic. Current research suggests increasing accumulated long chain omega-3s for health benefits and as natural medicine in several major diseases. But many believe plant omega-3 sources are nutritionally and therapeutically equivalent to the EPA/DHA omega-3 in fish-oil. Although healthy, precursor ALA bio-conversion to EPA is inefficient and production of DHA is nearly absent, limiting the protective value of ALA supplementation from flax-oil, for example. Along with pollutants certain fish acquire high levels of EPA/DHA as predatory species. However, the origin of EPA/DHA in aquatic ecosystems is algae. Certain microalgae produce high levels of EPA or DHA. Now, organically produced DHA-rich microalgae oil is available. Clinical trials with DHA-rich oil indicate comparable efficacies to fish oil for protection from cardiovascular risk factors by lowering plasma triglycerides and oxidative stress. This review discusses 1) omega-3 fatty acids in nutrition and medicine; 2) omega-3s in physiology and gene regulation; 3) possible protective mechanisms of EPA/DHA in major diseases such as coronary heart disease, atherosclerosis, cancer and type 2 diabetes; 4) EPA and DHA requirements considering fish oil safety; and 5) microalgae EPA and DHA-rich oils and recent clinical results. Copyright 2007 Bentham Science Publishers Ltd.

LaVecchia C, Bosetti C. **Diet and cancer risk in Mediterranean countries: open issues.** *Public Health Nutr*. 2006 Dec;9(8A):1077-1082.

**OBJECTIVE:** To analyse various aspects of the Mediterranean diet in relation to the risk of several common cancers in Italy. **DESIGN:** Data from a series of case-control studies conducted in northern Italy between 1983 and 2004 on over 20,000 cases of several major cancers and 18,000 controls. **RESULTS:** For most digestive tract cancers, the risk decreased with increasing vegetable and fruit consumption, with relative risks between 0.3 and 0.7 for the highest level of intake, and the population-attributable risks for low intake of vegetables and fruit ranged between 15 and 40%. Less strong inverse relations were observed for other (epithelial) cancers, too. A number of micronutrients contained in vegetables and fruit showed an inverse relation with cancer risk. In particular, flavones, flavonols and resveratrol were inversely related to breast cancer risk. Olive oil, which is a typical aspect of the Mediterranean diet, has also been inversely related to cancers of the colorectum and breast, and mainly of the upper digestive and respiratory tract. Consumption of pizza, one of the most typical Italian foods, was related to a reduced risk of digestive tract cancers, although pizza may simply be an aspecific indicator of the Italian diet. **CONCLUSIONS:** Adherence to the Mediterranean diet is a favourable indicator of the risk of several common epithelial cancers in Italy. A score summarising the major characteristics of the Mediterranean diet was related to a priori defined reduced risks of several digestive tract neoplasms by over 50%.

## Supplements

Moss RW. **Do antioxidants interfere with radiation therapy for cancer?** *Integr Cancer Ther*. 2007 Sep;6(3):281-292.

Despite recent comprehensive review articles concluding that supplemental antioxidants do not undermine the effectiveness of cytotoxic therapies, the use of antioxidants during cancer

treatment remains controversial. Many oncologists take the position that antioxidants by their nature undermine the free radical mechanism of chemotherapy and radiotherapy and should therefore generally be avoided during treatment. For their part, many integrative practitioners believe that antioxidants taken during cancer treatment not only alleviate some of the adverse effects of that treatment but also enhance the efficacy of cancer therapy. Until recently, research attention has focused primarily on the interaction of antioxidants with chemotherapy; relatively little attention has been paid to the interaction of antioxidants with radiotherapy. This article reviews the clinical literature that has addressed whether antioxidants do in fact interfere with radiation therapy. Studies have variously investigated the use of alpha-tocopherol for the amelioration of radiation-induced mucositis; pentoxifylline and vitamin E to correct the adverse effects of radiotherapy; melatonin alongside radiotherapy in the treatment of brain cancer; retinol palmitate as a treatment for radiation-induced proctopathy; a combination of antioxidants (and other naturopathic treatments) and external beam radiation therapy as definitive treatment for prostate cancer; and the use of synthetic antioxidants, amifostine, dexrazoxane, and mesna as radioprotectants. With few exceptions, most of the studies draw positive conclusions about the interaction of antioxidants and radiotherapy. Although further studies are needed, the preponderance of evidence supports a provisional conclusion that dietary antioxidants do not conflict with the use of radiotherapy in the treatment of a wide variety of cancers and may significantly mitigate the adverse effects of that treatment.

### Exercise

Schneider CM, Hsieh CC, Sprod LK, et al. **Exercise training manages cardiopulmonary function and fatigue during and following cancer treatment in male cancer survivors.**

*Integr Cancer Ther.* 2007 Sep;6(3):235-241.

This investigation determined the cardiopulmonary function and fatigue alterations in male cancer survivors during treatment as well as following treatment utilizing similar exercise assessment protocols and individualized, prescriptive exercise interventions. The study included 45 male cancer survivors that were referred by local oncologists. Following a comprehensive screening and physical examination, cardiovascular endurance, pulmonary function, and fatigue were assessed leading to the development of 12-week individualized exercise prescriptions and exercise interventions. The cancer survivors were divided into during treatment (DTm) and following treatment (FTm) groups. Repeated-measures analysis of variance and analyses of covariance were used to compare pre- versus postintervention and between groups. Cardiopulmonary function was maintained in the DTm, whereas the FTm showed significant reductions in resting heart rate ( $P < .05$ ) with concurrent increases in predicted  $VO_{2max}$  and time on treadmill ( $P < .05$ ) postexercise intervention. Fatigue levels did not increase in the DTm group, whereas the FTm group showed significant reductions in behavioral fatigue, affective fatigue, sensory fatigue, cognitive/mood fatigue, and total fatigue ( $P < .05$ ) after the exercise intervention. The results of the current study suggest that moderate intensity, individualized, prescriptive exercise intervention maintains or improves cardiovascular and pulmonary function with concomitant reductions in fatigue in cancer survivors during and following cancer treatment. Exercise appears to be a safe, efficacious strategy for improving physical fitness in cancer survivors during and following treatment.

### CAM of the Month

Fonfa AE. **Patient perspectives: barriers to complementary and alternative medicine therapies create problems for patients and survivors.** *Integr Cancer Ther.* 2007 Sep;6(3):297-300.

There are multiple barriers to better understanding of complementary and alternative medicine (CAM) approaches and the use of natural substances to reduce cancer risk. CAM approaches are not patentable, and the pharmaceutical industry has no interest in the area. Research generally approaches concepts from the deconstructionist side: there may be interest in herbal mixtures but its "active" constituents are explored one at a time, missing any synergistic or even additive effects. Little attention has been paid to environmental pollutants and exposures. Most patients believe these are active causes of their disease, but researchers are still exposing animals to one chemical one time, which fails to duplicate human exposures. Attention to lifestyle issues is presented almost solely in terms of obesity—a concept that is a barrier to change by itself. Research animals rarely if ever are fed dietary components that humans normally eat, such as soda or diet soda, potato chips, and high-fructose corn syrup, artificial colors, artificial flavors, other additives, or combinations of bad fats with too much sugar, too much salt, and artificial ingredients. Long-term treatment effects on survivors may not necessarily require a solely pharmaceutical approach. Drugs to treat each condition separately may require even more drugs to offset the unwanted effects of each. Whole systems approaches to research are urgently needed. A final barrier is that once a treatment is accepted in mainstream, it ceases to be considered "alternative." The genesis is soon forgotten and the remaining alternative modalities continue to be viewed with suspicion, doubt, and misunderstanding, to the detriment of both patients in treatment and cancer survivors.

InspireHealth provides an integrated whole person approach to health for individuals living with cancer. Our medical doctors guide patients to explore and learn about a variety of wellness approaches to health and healing in addition to conventional cancer treatment. This integrated medical model, which engages people in their own care, improves quality of life and reduces the likelihood of cancer recurrence. The editorial board includes: Dr. Hal Gunn, CEO and Co-founder, Dr. Janice Wright, Dr. Teresa Clarke and Dr. Ron Puhky.

Robert Stibravy, Clinical Librarian, compiles Research Updates under the supervision of the editorial board. He has a Master's degree in Library and Information Studies from the University of British Columbia, a Bachelor's degree in Biology from UC Berkeley, and has worked in a variety of medical library settings. Rob can be contacted at [rstibravy@inspirehealth.ca](mailto:rstibravy@inspirehealth.ca) or 604-734-7125, ext 228.