



RESEARCH UPDATES

For the latest in worldwide integrated cancer care

July 2009



Breast

Michael, YL, N. E. Carlson, R. T. Chlebowski, et al. **Influence of Stressors on Breast Cancer Incidence in the Women's Health Initiative.** *Health Psychology.* 2009 March; 282:137-146.

Objective: To examine associations among life events stress, social support, and breast cancer incidence in a cohort of postmenopausal women. **Design and main outcome measure:** Women's Health Initiative observational study participants, breast cancer free at entry, who provided assessment of stressful life events, social support, and breast cancer risk factors, were prospectively followed for breast cancer incidence (n = 84,334). **Results:** During an average of 7.6 years of follow-up, 2,481 invasive breast cancers were diagnosed. In age-adjusted proportional hazards models, 1 stressful life event was associated with increased risk, but risk decreased with each additional stressful life event. After adjustment for confounders the decreasing risk was not significant. Stressful life events and social support appeared to interact in relation to breast cancer risk such that women who had greater number of stressful life events and low social support had a decreased risk of breast cancer. **Conclusions:** This study found no independent association between stressful life events and breast cancer risk. The results are compatible with a more complex model of psychosocial factors interacting in relation to breast cancer risk. copyright 2009 American Psychological Association

We systematically reviewed studies obtained through a thorough Medline literature search and identified 15 epidemiologic publications on soy consumption and 9 on isoflavones in association with prostate cancer risk. We extracted the most adjusted relative risks (RRs) and odds ratios (ORs) of the highest and the lowest reported categories of intake from each study and conducted this analysis using a random-effects model in which studies with smaller SEEs are given greater weight in the summary measure. **RESULTS:** Our analysis of studies on soy intake yielded a combined RR/OR of 0.74 (95% CI: 0.63, 0.89; P = 0.01). When separately analyzed, studies on nonfermented soy foods yielded a combined RR/OR of 0.70 (95% CI: 0.56, 0.88; P = 0.01) and those on fermented soy foods yielded a combined RR/OR of 1.02 (95% CI: 0.73, 1.42; P = 0.92). The analysis of studies on isoflavones yielded a combined RR/OR of 0.88 (95% CI: 0.76, 1.02; P = 0.09). Further separate analyses showed a combined RR/OR of 0.52 (95% CI: 0.34, 0.81; P = 0.01) from studies with Asian populations and 0.99 (95% CI: 0.85, 1.16; P = 0.91) from studies with Western populations. **CONCLUSIONS:** The results of this analysis suggest that consumption of soy foods is associated with a reduction in prostate cancer risk in men. This protection may be associated with the type and quantity of soy foods consumed.

Mori, M, N. Masumori, F. Fukuta, et al. **Traditional Japanese Diet and Prostate Cancer** *Molecular Nutrition & Food Research.* 2009 Feb; 532: 191-200.

Prostate

Yan, L and E. L. Spitznagel. **Soy Consumption and Prostate Cancer Risk in Men: A Revisit of a Meta-Analysis.** *Am J Clin Nutr.* 2009Apr;894:1155-1163. **BACKGROUND:** Epidemiologic studies have shown that the consumption of soy foods may be associated with a reduction in cancer risk in humans. **OBJECTIVE:** The purpose of this study was to conduct a meta-analysis on the association between soy consumption and prostate cancer risk in men. **DESIGN:**

The traditional Japanese diet has been suggested by some researchers to be associated with a decreased risk of prostate cancer (PCa). In this paper, we assumed the following three characteristics of the traditional Japanese diet high in soybean products, high in fish, and low in red meat. Isoflavones, polyunsaturated long chain (n - 3) fatty acids, and saturated fatty acids were thought to be micronutrients in biological etiology relevant to soybean products, fish, and red meat, respectively. Analytical epidemiological studies on the risk of PCa were identified using the MEDLINE database

In this issue

Cancer	
Breast	1
Prostate	1
Colorectal	2
Therapies	
Nutrition	2
Supplements & Botanicals	2
Exercise	3
Lifestyle	3
Accupuncture	3
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.

InspireHealth's 'Life Program', facilitated by our medical doctors, is an important opportunity to learn more about improving health and survival with a Cancer diagnosis. **Call today to register: 604 734 7125**

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



from 1998 to 2007. Some published studies showed a negative association of soybean products and isoflavones to PCa risk, an inverse association for fish or polyunsaturated long chain (n - 3) fatty acids such as eicosapentaenic acid (EPA) and docosahexaenoic acid (DHA) with PCa risk, and a positive association of red meat or saturated fatty acids with PCa risk, respectively. In conclusion, although it is possible that the traditional Japanese diet may reduce the risk of PCa through a combination of characteristics such as being high in soybean products, high in fish, and low in red meat, further well-designed epidemiological studies such as nested case-control studies with nutritional analyses of blood samples are needed to confirm this association. [References: 48]

 Thank you to the **BC Foundation for Prostate Disease** for their generous support.
www.BCPROSTATECANCER.org

Colorectal

Billson, HA, K. L. Harrison, N. P. Lees, C. N. Hall, G. P. Margison and A. C. Povey. **Dietary Variables Associated with DNA N7-Methylguanine Levels and O6-Alkylguanine DNA-Alkyltransferase Activity in Human Colorectal Mucosa.** *Carcinogenesis*. 2009 Apr; 30(4): 615-620.

Components of human diets may influence the incidence of colorectal adenomas, by modifying exposure or susceptibility to DNA-damaging alkylating agents. To examine this hypothesis, a food frequency questionnaire was used to assess the diet of patients recruited for a case-referent study where biopsies of normal colorectal mucosa were collected during colonoscopy and subsequently analysed for DNA N7-methylguanine (N7-MeG) levels, as an indicator of exposure, and activity of the DNA repair protein O6-alkylguanine DNA-alkyltransferase (MGMT), as an indicator of potential susceptibility. Cases with histologically proven colorectal adenomas (n = 38) were compared with referents (n = 35) free of gastrointestinal neoplasia. The case group consumed significantly more red meat (4.5 versus 3.4 servings/week, P < 0.05), processed meats, (4.7 versus 3.2 servings/week, P < 0.05) and % food energy as fat (34.9 versus 30.7%, P < 0.001). N7-MeG [mean: 95% confidence interval (CI)] levels were significantly lower in the group that consumed the highest proportion of dietary fibre/1000 kcal in comparison with the group with the lowest intake (0.61; 0.35-0.86 versus 1.88; 0.88-2.64 micromol/mol dG, P < 0.05). N7-MeG levels were also inversely associated with folate consumption (P < 0.05). MGMT activity (mean; 95% CI) was significantly higher in the group with the lowest consumption of vegetables than in the group with the greatest vegetable consumption (7.02; 5.70-8.33 versus 4.93; 3.95-5.91 fmol/microg DNA, P < 0.05). Our results are consistent with the hypothesis that dietary factors may modify exposure or susceptibility, respectively, to DNA damage by alkylating agents.

Nutrition

Hughes, MCB, G. M. Williams, A. Fourtanier and A. C. Green. **Food Intake, Dietary Patterns, and Actinic Keratoses of the Skin: A Longitudinal Study.** *Am J Clin Nutr*. 2009 01 Apr; 89(4): 1246-1255.

Background: Actinic keratoses (AKs) are premalignant actinic tumors of the skin. Evaluation of the role of diet in their

development is lacking. Objective: The objective was to determine whether intake of certain food groups or dietary patterns retard the occurrence of AKs over a 4.5-y period. Design: In a community-based study of skin cancer in Queensland, Australia, food intake of 1119 adults was assessed in 1992, 1994, and 1996 by using a validated food-frequency questionnaire. Dermatologists counted prevalent AKs during full-body skin examinations in 1992 and 1996. The relative ratio (RR) of AK counts in 1996 relative to 1992 was compared across increasing intakes of 26 food groups, and for 3 dietary patterns identified by principal components analysis, with the use of generalized linear models with negative binomial distribution, allowing for repeated measures. All analyses were adjusted for confounding factors, including skin color and sun exposure indexes. Results: AK acquisition decreased by 28% (RR: 0.72; 95% CI: 0.55, 0.95) among the highest consumers of oily fish (average of one serving every 5 d) compared with those with minimal intake. Similarly, the rate of acquisition of AKs was reduced by 27% (RR: 0.73; 95% CI: 0.54, 0.99) in those with the highest consumption of wine (average of half a glass a day in this study population). There was no consistent association of dietary pattern with AK acquisition. Conclusion: Moderate intake of oily fish and of wine may decrease the acquisition of AKs and thus complement sun protection measures in the control of actinic skin tumors. copyright 2009 American Society for Nutrition.

Supplements & Botanicals

Giovannucci, E **Vitamin D and Cancer Incidence in the Harvard Cohorts** *Ann Epidemiol*. 2009 Feb; 19(2): 84-88.

Since the hypothesis that vitamin D reduces the risk of some cancers was initiated in 1980, this hypothesis has been studied in the Harvard cohort studies, including the Nurses' Health Study (NHS), the Health Professionals Follow-Up Study (HPFS), and the Physicians' Health Study (PHS). Three approaches have been used, the study of circulating 25(OH)vitamin D (25(OH)D) level, of dietary and supplementary intake, and of predicted 25(OH)D. These cohorts strongly support an inverse association with colorectal cancer, because this association has been viewed in both the NHS and HPFS cohorts, for cancers and adenomas, and for plasma, diet, and predicted 25(OH)D analyses. In the NHS, about a 30% reduction in risk was observed for breast cancer comparing the highest with lowest quintiles of 25(OH)D levels. Vitamin D intake also was associated with a lower risk of pancreatic cancer in both men and women, but studies of plasma or predicted 25(OH)D level or dietary intake have generally not been supportive of a major role of vitamin D status in middle-age or elderly men on prostate cancer risk. Results from the HPFS also suggest that the poor vitamin D status generally in African-Americans contributes to their higher incidence and mortality from various malignancies. [References: 42]

Lissoni, P, F. Rovelli, F. Brivio, et al. **A Randomized Study of Chemotherapy Versus Biochemotherapy with Chemotherapy Plus Aloe Arborescens in Patients with Metastatic Cancer.** *In Vivo*. 2009 Jan-Feb; 23(1): 171-175.

BACKGROUND: The recent advances in the analysis of tumor immunobiology suggest the possibility of biologically manipulating the efficacy and toxicity of cancer chemotherapy by endogenous or exogenous immunomodulating substances. Aloe is one of the of the most important plants exhibiting anticancer activity and its antineoplastic property is due to at

least three different mechanisms, based on antiproliferative, immunostimulatory and antioxidant effects. The antiproliferative action is determined by anthracenic and antraquinonic molecules, while the immunostimulating activity is mainly due to acemannan. **PATIENTS AND METHODS:** A study was planned to include 240 patients with metastatic solid tumor who were randomized to receive chemotherapy with or without Aloe. According to tumor histotype and clinical status, lung cancer patients were treated with cisplatin and etoposide or weekly vinorelbine, colorectal cancer patients received oxaliplatin plus 5-fluorouracil (5-FU), gastric cancer patients were treated with weekly 5-FU and pancreatic cancer patients received weekly gemcitabine. Aloe was given orally at 10 ml thrice/daily. **RESULTS:** The percentage of both objective tumor regressions and disease control was significantly higher in patients concomitantly treated with Aloe than with chemotherapy alone, as well as the percent of 3-year survival patients. **CONCLUSION:** This study seems to suggest that Aloe may be successfully associated with chemotherapy to increase its efficacy in terms of both tumor regression rate and survival time.

Mohr, SB **A Brief History of Vitamin d and Cancer Prevention** *Ann Epidemiol.* 2009 Feb; 192: 79-83.

PURPOSE: To review the history of vitamin D and its use in cancer prevention. **METHODS:** The literature on published studies of vitamin D and its role in human health was reviewed and summarized. **RESULTS:** The modern history of vitamin D began in the mid-1800s, when it was noticed that city children were more likely to have rickets than rural children. Half a century later, Palm reported that children raised in sunny climates virtually never developed rickets. McCollum isolated vitamin D, and Windaus its precursors, receiving the Nobel Prize. Other scientists later observed that people with skin cancer had lower prevalence of nonskin cancers, and that lower overall mortality rates from all internal cancers combined existed in sunnier areas. These observations went largely unnoticed, and the field stagnated until 1970, when maps were created of cancer mortality rates. Through study of these maps, Cedric and Frank Garland of Johns Hopkins University reported a strong latitudinal gradient for colon cancer mortality rates in 1980, and hypothesized that higher levels of vitamin D compounds in the serum of people in the south were responsible, and that calcium intake also would reduce incidence. Edward Gorham and colleagues carried out cohort and nested studies, including the first study that found an association of a serum vitamin D compound with reduced cancer risk. William B. Grant then carried out numerous ecologic studies that extended the vitamin D-cancer theory to other cancers. **CONCLUSIONS:** The history of the role of vitamin D in human health is rich and much of that history is yet to be written not only by scientists, but by policy makers with the vision and leadership necessary to bridge the gap between research and policy. [References: 45]

Lifestyle

Chen, L, L. Gallicchio, K. Boyd-Lindsley, et al. **Alcohol Consumption and the Risk of Nasopharyngeal Carcinoma: A Systematic Review** *Nutrition & Cancer.* 2009 611: 1-15. The evidence concerning the influence of alcohol drinking on the risk of nasopharyngeal carcinoma (NPC) has yielded intriguing findings but has lacked a clear-cut interpretation due to inconsistencies. To unify this body of evidence, we performed a systematic review. With funding and using a

protocol developed by the World Cancer Research Fund (WCRF), 15 bibliographic databases were searched for epidemiological studies that reported a measure of association between alcoholic beverage consumption and NPC. Pooled odds ratios (ORs) for highest-vs.-lowest categories of total alcohol intake was obtained by using an inverse-variance weighted random-effects model. A dose-response trend was examined in models using generalized least square estimation. The search identified 14 case-control studies from 5 countries. For total alcohol intake, the pooled ORs in a comparison of the highest to the lowest category was 1.33 (95% CI: = 1.09-1.62) in 11 studies. Data from 6 studies indicated a J-shape dose-response trend, with NPC risk decreasing with up to 15 drinks/wk and increasing with higher intake. Fewer data were available to assess the associations between NPC and intake of beer, wine, and spirits. The potential J-shaped dose-response trend suggests a reduced risk of NPC related to the light alcohol drinking, an observation that warrants further study. Considered in total, the quantitative summaries of the case-control evidence suggest that heavy alcohol consumption is associated with an increased risk of NPC. [References: 68]

Accupuncture

Ye, F, D. Liu, S. Wang and L. Xu. **Effects of Electro-Acupuncture on T Cell Subpopulations, NK Activity, Humoral Immunity and Leukocyte Count in Patients Undergoing Chemotherapy.** *Journal of Traditional Chinese Medicine.* 2007 Mar; 271: 19-21.

OBJECTIVE: To observe the effects of electro-acupuncture on T cell subpopulations, natural killer cell (NK) activity, humoral immunity and leukocyte count in patients undergoing chemotherapy. **METHODS:** Electro-acupuncture was added for patients undergoing chemotherapy. Tests were done on T cell subpopulations, NK activity, humoral immunity and leukocyte count before treatment and after 4 courses of treatment. **RESULTS:** After 4 courses of treatment with chemotherapy and electro-acupuncture, no obvious changes were found in T cell subpopulations, NK activity, humoral immunity and leukocyte count ($P > 0.05$) as compared with those before treatment. Patients undergoing chemotherapy combined with electro-acupuncture showed obviously higher leukocyte count than that of the control group given no leukogenic drugs ($P < 0.01$). **CONCLUSION:** Electro-acupuncture may reduce immunologic damage caused by chemotherapy, thus it can be used as the auxiliary therapy for patients undergoing chemotherapy.

Exercise

Newton, RU and D. A. Galvao. **Exercise in Prevention and Management of Cancer** *Current Treatment Options in Oncology.* 2008 Jun; 92-3: 135-146.

OPINION STATEMENT: Regular and vigorous physical exercise has been scientifically established as providing strong preventative medicine against cancer with the potential to reduce incidence by 40%. The effect is strongest for breast and colorectal cancer; however, evidence is accumulating for the protective influence on prostate cancer, although predominantly for more advanced disease and in older men. Following cancer diagnosis, exercise prescription can have very positive benefits for improving surgical outcomes, reducing symptom experience, managing side effects of radiation and chemotherapy, improving psychological health, maintaining physical function, and reducing fat gain and muscle and bone loss. There is now

irrefutable evidence from large prospective studies that regular exercise postdiagnosis will actually increase survivorship by 50%-60% with the strongest evidence currently for breast and colorectal cancers. In our work with prostate cancer patients, we have found that exercise can limit or even reverse some of the androgen deprivation therapy (ADT) adverse effects by increasing muscle mass, functional performance, and cardiorespiratory fitness without elevating testosterone levels. Hormone therapies for breast and prostate cancer can result in alarmingly increased risk of cardiovascular disease, obesity, type 2 diabetes, osteoporosis, and sarcopenia. Increasingly, patients are questioning the benefit of some cancer treatments as the risk of morbidity and mortality from other chronic diseases begins to outweigh the initial cancer diagnosis. Over three decades of research in exercise science and many hundreds of RCTs demonstrate the efficacy of appropriate physical activity for preventing and managing these secondary diseases. Based on this evidence it is now clear to us that exercise is a critical adjuvant therapy in the management of many cancers and will greatly enhance the therapeutic effects of traditional radiation and pharmaceutical treatments by increasing tolerance, reducing side effects, and lowering risk of chronic diseases, even those not aggravated by cancer treatment. While patients and their clinicians deal with their cancer, other chronic disease mechanisms continue unabated. Anxiety, depression, poor nutritional choices, and a counterproductive rest strategy will accelerate these processes, while a well-designed exercise program adhered to by the patient and supported by the medical and exercise professionals will effectively control and even reverse these diseases and disabilities. In the wide range of cancer populations that we work with, both young and old and with curative and palliative intent, our overwhelming experience is that exercise is first well tolerated, and benefits the patient psychologically and physically. While some of our patients are on individual, home-based programs, we find that small group exercise sessions with close supervision by Exercise Physiologists (EP) provides a more motivating setting and the social interaction is critical for adherence and retention as well as greater psychological benefits such as reduced anxiety and depression and enhanced social connectedness. While managing many hundreds of cancer patients over the last 6 years, our clinic has not experienced any instances of the exercise hindering patient recovery or treatment purpose, nor have any significant injuries occurred. However, it is critical that the exercise prescription and management be tailored to the individual patient and that they are monitored by appropriately trained and professionally accredited exercise specialists. For those patients at low exercise risk and without significant musculoskeletal issues, community-based physical activity is of excellent benefit where the emphasis should be on adherence, affordability, convenience, and enjoyment. [References: 45]

Rashad, UM, S. M. Al-Gezawy, E. El-Gezawy and A. N. Azzaz. **Honey as Topical Prophylaxis Against Radiochemotherapy-Induced Mucositis in Head and Neck Cancer.** *Journal of Laryngology & Otology.* 2009 Feb;1232:223-228.

AIM: To evaluate the efficacy of pure natural honey as prophylaxis against radiochemotherapy-induced mucositis, through clinical scoring of oral and

oropharyngeal mucositis, and culturing of pathogenic oral and oropharyngeal microbes. **PATIENTS AND METHODS:** The study was done in Assiut University Hospital, Egypt, between January 2005 and July 2006. Forty patients diagnosed with head and neck cancer were entered into the trial. Enrolled patients were randomised to either the treatment group, receiving concomitant chemotherapy and radiotherapy (with a significant area of directly visible oral and/or oropharyngeal mucosa included in the radiation fields) plus prior topical application of pure natural honey, or the control group, receiving concomitant chemotherapy and radiotherapy without honey. Patients were evaluated clinically every week to assess development of radiation mucositis. Aerobic cultures and candida colonisation assessment were undertaken, via oral and oropharyngeal swabs, prior to and at the completion of irradiation, and when infection was evident. **RESULTS:** In the treatment group, no patients developed grade four mucositis and only three patients (15 per cent) developed grade three mucositis. In the control group, 13 patients (65 per cent) developed grade three or four mucositis ($p < 0.05$). Candida colonisation was found in 15 per cent of the treatment group and 60 per cent of the control group, either during or after radiotherapy ($p = 0.003$). Positive cultures for aerobic pathogenic bacteria were observed in 15 per cent of the treatment group and 65 per cent of the control group, during or after radiotherapy ($p = 0.007$). **CONCLUSION:** This study shows that prophylactic use of pure natural honey was effective in reducing mucositis resulting from radiochemotherapy in patients with head and neck cancer.

CAM of the Month

Schwartz, GG **Vitamin D and Intervention Trials in Prostate Cancer: From Theory to Therapy** *Ann Epidemiol.* 2009 Feb; 192: 96-102.

Studies of vitamin D and prostate cancer have advanced rapidly from the hypothesis that vitamin D deficiency increases the risk of prostate cancer to intervention trials of vitamin D administration in clinical cancer. The hormonal form of vitamin D, 1,25(OH)(2)D, exerts prodifferentiating, antiproliferative, anti-invasive, and antimetastatic effects on prostate cells. Moreover, normal prostate cells synthesize 1,25(OH)(2)D from serum levels of the prohormone, 25-hydroxyvitamin D. The autocrine synthesis of 1,25(OH)(2)D by prostatic cells provides a biochemical mechanism whereby vitamin D may prevent prostate cancer. Many prostate cancer cells have lost the ability to synthesize 1,25(OH)(2)D but still possess 1,25(OH)(2)D receptors. This suggests that whereas vitamin D (e.g., cholecalciferol) might prevent prostate cancer, existing prostate tumors likely would require treatment with 1,25(OH)(2)D and/or its analogs. The major obstacle to the use of 1,25(OH)(2)D in patients therapeutically is the risk of hypercalcemia. Several maneuvers to reduce this risk, including pulse dosing and the use of less calcemic 1,25(OH)(2)D analogs, have been explored in Phase I-III clinical trials. Once merely a promise, vitamin D-based therapies for prostate cancer may soon be medical practice. [References: 69]

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, Dr. Ron Puhkv. and Dr. Walter Lemmo. ND.