



RESEARCH UPDATES

For the latest in worldwide integrated cancer care

June 2009

Breast



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Yuvaraj, S, V. G. Premkumar, P. Shanthi, K. Vijayarathy, S. G. Gangadaran and P. Sachdanandam. **Effect of Coenzyme Q(10), Riboflavin and Niacin on Tamoxifen Treated Postmenopausal Breast Cancer Women with Special Reference to Blood Chemistry Profiles.** *Breast Cancer Research & Treatment.* 2009 Mar;1142:377-384. **BACKGROUND:** Tamoxifen (TAM) a non-steroidal antiestrogen, is widely used in adjuvant therapy for all stages of breast carcinomas and in chemoprevention of high-risk group. TAM also has estrogenic activity on liver and endometrium causing severe oxidative stress with various biochemical derangements. Coenzyme Q(10), Riboflavin and Niacin (CoRN) are well-known potent antioxidants and protective agents against many diseases including cancer. In this context, this study was undertaken to find if co-administration of TAM along with CoRN could alleviate the sole TAM-induced biochemical derangements in postmenopausal women with breast cancer. **METHOD:** The vitamin supplementation with TAM was given for a period of 90 days. Blood samples were collected at the base line, 45th and 90th day during the course of treatment. Various blood chemistry profiles were assessed in 78 untreated, sole TAM treated and combinatorial treated group along with 46 age- and sex-matched controls. **RESULTS:** A statistically significant alteration in various blood chemistry parameters, such as serum total bilirubin (S. BIL), serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), gamma glutamyl transpeptidase (gamma-GT), uric acid (UA), lipoprotein lipase (LPL), lecithin: cholesterol acyl transferases (LCAT), potassium, calcium and Na(+), K(+)-ATPase in sole TAM-treated group, was favorably reverted back to near normal levels on combinatorial therapy with CoRN. **CONCLUSION:** TAM on co-administration with CoRN has a favorable impact on various blood chemistry profiles. However, large scale randomized studies over a longer time span are required to ascertain the safety and efficacy of co-administrating antioxidants with conventional chemotherapy.

Forrest, G, C. Plumb, S. Ziebland and A. Stein. **Breast Cancer in Young Families: A Qualitative Interview Study of Fathers and their Role and Communication with their Children Following the Diagnosis of Maternal Breast Cancer.** *Psychooncology.* 2009 Jan;181:96-103. **OBJECTIVE:** To explore father-child communication following the diagnosis of maternal breast cancer, examine disparities in their understandings of the impact of the illness, and identify gaps in their need for support and information. **METHODS:** The design is the qualitative interview study with thematic analysis. The interviews were home-based with fathers and children in Oxfordshire, UK. The participants were 26 fathers whose partners had early breast cancer and 31 of their children aged between 6 and 18 years. **RESULTS:** Fathers described graphically their reaction to news of their partner's breast cancer and their attempts to provide support for their partners and maintain normal family life for their children. Fathers were keen to reassure and protect children but often said that they lacked sufficient information about breast cancer-especially side effects of treatments. Fathers sometimes did not recognise the extent of their children's distress and some interpreted their children's reactions as 'bad behaviour' or 'rudeness'. Children were often acutely aware of the father's emotional state, and expressed a wish to protect him. Some fathers would have liked an opportunity to talk to a clinician directly about the children but did not want to claim clinical time for themselves or their children. **CONCLUSION:** This study suggests that clinicians could improve their care of breast cancer patients by being more family-centred. Fathers routinely need more information and preparation about the likely impact of the illness and its treatment (especially side effects) on the mother, and how children of different ages may react to the emotional strain. Clinicians need to be prepared to offer to talk to teenagers. (c) 2008 John Wiley & Sons, Ltd. Zhang, M, J.

Huang, X. Xie and C. D. Holman. **Dietary Intakes of Mushrooms and Green Tea Combine to Reduce the Risk of Breast Cancer in Chinese Women.** *International*

Journal of Cancer. 2009 Mar 15; 1246: 1404-1408. To investigate effects of dietary mushrooms and joint effects of mushrooms and green tea on breast cancer, a case-control study was conducted in southeast China in 2004-2005. The incident cases were 1,009 female patients aged 20-87 years with histologically confirmed breast cancer. The 1,009 age-matched controls were healthy women randomly recruited from outpatient breast clinics. Information on frequency and quantity of dietary intake of mushrooms and tea consumption, usual diet, and lifestyle were collected by face-to-face interview using a validated and reliable questionnaire. Compared with nonconsumers, the Odds ratios (Ors) were 0.36 (95% CI = 0.25-0.51) and 0.53 (0.38-0.73) for daily intake of ≥ 10 g fresh mushrooms and ≥ 4 g dried mushrooms, based on multivariate logistic regression analysis adjusting for established and potential confounders. There were dose-response relationships with significant tests for trend ($p = 0.05$ g dried green tea leaves per day). The corresponding linear trends were statistically significant for joint effect ($p < 0.001$). We conclude that higher dietary intake of mushrooms decreased breast cancer risk in pre- and postmenopausal Chinese women and an additional decreased risk of breast cancer from joint effect of mushrooms and green tea was observed. More research is warranted to examine the effects of dietary mushrooms and mechanism of joint effects of phytochemicals on breast cancer.

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*. 2009 Apr; 89(4): 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:** 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.

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

Endometrial

Gierach, GL, S. C. Chang, L. A. Brinton, et al. **Physical Activity, Sedentary Behavior, and Endometrial Cancer Risk in the NIH-AARP Diet and Health Study.** *International Journal of Cancer*. 2009 May 1; 1249: 2139-2147. Consistent with a strong hormonal etiology, endometrial cancer is thought to be influenced by both obesity and physical activity. Although obesity has been consistently related to risk, associations with physical activity have been inconclusive. We examined relationships of activity patterns with endometrial cancer incidence in the NIH-AARP Diet and Health Study cohort, which included 109,621 women, ages 50-71, without cancer history, who in 1995-1996 completed a mailed baseline questionnaire capturing daily routine and vigorous (defined as any period of ≥ 20 min of activity at work or home causing increases in breathing, heart rate, or sweating) physical activity. A second questionnaire, completed by 70,351 women, in 1996-1997 collected additional physical activity information. State cancer registry linkage identified 1,052 primary incident endometrial cancers from baseline through December 31, 2003. In multivariate proportional hazards models, vigorous activity was inversely associated with endometrial cancer in a dose-response manner (p for trend = 0.02) (relative risk (RR) for ≥ 5 times/week vs. never/rarely = 0.77, 95% confidence interval (CI): 0.63-0.95); this association was more pronounced among overweight and obese women (body mass index ≥ 25 ; RR = 0.61, 95% CI: 0.47-0.79) than among lean women (body mass index < 25 ; RR = 0.76, 95% CI: 0.52-1.10; p for interaction = 0.12). Although we observed no associations with light/moderate, daily routine or occupational physical activities, risk did increase with number of hours of daily sitting (p for trend = 0.02). Associations with vigorous activities, which may interact with body mass index, suggest directions for future research to clarify underlying biologic mechanisms, including those relating to hormonal alterations. (c) 2008 Wiley-Liss, Inc.

Lung

Lam, TK, A. J. Cross, D. Consonni, et al. **Intakes of Red Meat, Processed Meat, and Meat Mutagens Increase Lung Cancer Risk.** *Cancer Res*. 2009 Feb 1; 69(3): 932-939. Red and processed meat intake may increase lung cancer risk. However, the epidemiologic evidence is inconsistent and few studies have evaluated the role of meat mutagens formed during high cooking temperatures. We investigated the association of red meat, processed meat, and meat mutagen intake with lung cancer risk in Environment And Genetics in Lung cancer Etiology, a population-based case-control study. Primary lung cancer cases ($n = 2,101$) were recruited from 13 hospitals within the Lombardy region of Italy examining approximately 80% of the cases from the area. Noncancer population controls ($n = 2,120$), matched to cases on gender, residence, and age, were randomly selected from the same catchment area. Diet was assessed in 1,903 cases and 2,073 controls and used in conjunction with a meat mutagen database to estimate intake of heterocyclic amines (HCA) and benzo(a)pyrene (BaP). Multivariable odds ratios (OR) and 95% confidence intervals (95% CI) for sex-specific tertiles of intake were calculated using unconditional logistic regression. Red and processed meat were positively associated with lung cancer risk (highest-versus-lowest tertile: OR, 1.8; 95% CI, 1.5-2.2; P trend < 0.001 and OR, 1.7; 95% CI, 1.4-2.1; P trend < 0.001 , respectively); the risks were strongest among never

smokers (OR, 2.4; 95% CI, 1.4-4.0; P trend = 0.001 and OR, 2.5; 95% CI, 1.5-4.2; P trend = 0.001, respectively). HCAs and BaP were significantly associated with increased risk of lung cancer. When separated by histology, significant positive associations for both meat groups were restricted to adenocarcinoma and squamous cell carcinoma but not small cell carcinoma of the lung. In summary, red meat, processed meat, and meat mutagens were independently associated with increased risk of lung cancer.

Renal

Grieb, SM, R. P. Theis, D. Burr, D. Benardot, T. Siddiqui and N. R. Asal. **Food Groups and Renal Cell Carcinoma: Results from a Case-Control Study.** *J Am Diet Assoc.* 2009 Apr; 1094: 656-667.

BACKGROUND: The role of diet in renal cell carcinoma risk has been inconclusive. This study uses an integrative approach to assess the role of food groups and food items in renal cell carcinoma risk. **DESIGN:** A case-control study was conducted from 2003-2006. **SUBJECTS/SETTING:** Incident cases (n=335) were identified from hospital records and the Florida cancer registry, and population controls (n=337) frequency matched by age (+/-5 years), sex, and race were identified through random-digit dialing. Eating habits were assessed through the use of the 70-item Block food frequency questionnaire. **STATISTICAL ANALYSES:** Odds ratios (ORs), 95% confidence intervals (CIs), and tests for trends were calculated using logistic regression, controlled for age, sex, race, income, body mass index, and pack-years of smoking. **RESULTS:** Decreased renal cell carcinoma risk was observed among the total sample and for men for vegetable consumption (all subjects: OR 0.56, 95% CI 0.35, 0.88; men: OR 0.49, 95% CI 0.25, 0.96) but not for fruit consumption. Tomato consumption decreased renal cell carcinoma risk for the total population and for men (all subjects: OR 0.50, 95% CI 0.31, 0.81; men: OR 0.47, 95% CI 0.24, 0.95). Increased risk of renal cell carcinoma was observed among all subjects and among women with increased consumption of red meat (all subjects: OR 4.43, 95% CI 2.02, 9.75; women: OR 3.04, 95% CI 1.60, 5.79). White bread consumption increased renal cell carcinoma risk among women only (OR 3.05, 95% CI 1.50, 6.20), as did total dairy consumption (OR 2.36, 95% CI 1.21, 4.60). **CONCLUSIONS:** The protective role of vegetables and the increased risk of renal cell carcinoma with meat consumption are supported. The protective role of fruits is not. Novel findings include the increased risk of renal cell carcinoma with white bread and white potato consumption and the decreased risk of renal cell carcinoma with tomato consumption.

Esophageal

Pandeya, N, G. Williams, A. C. Green, P. M. Webb and D. C. Whiteman. **Alcohol Consumption and the Risks of Adenocarcinoma and Squamous Cell Carcinoma of the Esophagus.** *Gastroenterology.* 2009 April; 1364: 1215-1224.e2. **Background and Aims:** Alcohol has been declared a carcinogen for cancers of the esophagus, although the evidence relates largely to the squamous subtype. Evidence for an effect on adenocarcinomas is scant and inconsistent. **Methods:** We compared nationwide samples of patients with esophageal adenocarcinoma (EAC) (n = 365) or esophagogastric junction adenocarcinoma (EGJAC) (n = 426) or esophageal squamous cell carcinoma (ESCC) (n = 303) with

controls sampled from a population register (n = 1580). We used generalized additive models to assess nonlinear effects of self-reported alcohol intake on cancer risk, and calculated odds ratios (ORs) and 95% confidence intervals (CIs) using multivariate logistic and piecewise regression. **Results:** We observed no association between average weekly alcohol intake and EAC or EGJAC risk. For ESCC, the relationship with alcohol was nonlinear. At intakes of less than 170 g/wk there was no significant association; at greater than this level, there was a significant linear effect (OR, 1.03; 95% CI, 1.02-1.05 per 10 g alcohol/wk). For ESCC, but not EAC or EGJAC, a statistically significant multiplicative interaction between smoking and alcohol was observed (P = .02). In analyses by beverage type, ESCC risks, but not EAC or EGJAC, increased linearly with beer intake (OR, 1.05; 95% CI, 1.04-1.07). Those who drank modest levels of wine (<50-90 g/wk) or port or spirits (<10-20 g/wk) had significantly lower risks of all 3 cancers than nondrinkers; higher intakes were associated with increased risks of ESCC only. **Conclusions:** Alcohol intake above the recommended US dietary guidelines significantly increases the risk of ESCC, but not EAC or EGJAC. Smoking modifies the effect of alcohol intake on ESCC risk. copyright 2009 AGA Institute.

Ovarian

Wu, AH, C. L. Pearce, C. -C Tseng, C. Templeman and M. C. Pike. **Markers of Inflammation and Risk of Ovarian Cancer in Los Angeles County.** *International Journal of Cancer.* 2009 15 Mar; 1246:1409-1415. Factors that increase inflammation have been suggested to influence the development of ovarian cancer, but these factors have not been well studied. To further investigate this question, we studied the role of talc use, history of endometriosis and use of non-steroidal anti-inflammatory drugs (NSAIDs) and risk of ovarian cancer in a population-based case-control study in Los Angeles County involving 609 women with newly diagnosed epithelial ovarian cancer and 688 population-based control women. Risk of ovarian cancer increased significantly with increasing frequency and duration of talc use; compared to never users risk was highest among long-duration (20+ years), frequent (at least daily) talc users (adjusted relative risk (RR) = 2.08, 95% confidence interval (CI) = 1.34-3.23). A history of physician-diagnosed endometriosis was statistically significantly associated with risk (RR = 1.66, 95% CI =1.01-2.75). Women who were talc users and had a history of endometriosis showed a 3-fold increased risk (RR = 3.12, 95% CI =1.36-7.22), Contrary to the hypothesis that risk of ovarian cancer may be reduced by use of NSAIDs; risk increased with increasing frequency (per 7 times/week, RR = 1.27, 95% CI = 1.14-1.43) and years of NSAID use (per 5 years of use, RR = 1.25, 95% CI =1.10-1.42); this was consistent across types of NSAIDs. We conclude that risk of ovarian cancer is significantly associated with talc use and with a history of endometriosis, as has been found in previous studies. The NSAID finding was unexpected and suggests that factors associated with inflammation are associated with ovarian cancer risk. This result needs confirmation with careful attention to the reasons for NSAID use. copyright 2008 Wiley-Liss, Inc.

Nutrition

Liu, C-, Y. -H Hsu, M. -T Wu, et al. **Cured Meat, Vegetables, and Bean-Curd Foods in Relation to Childhood Acute Leukemia Risk: A Population Based Case-Control Study.**

Background: Consumption of cured/smoked meat and fish leads to the formation of carcinogenic N-nitroso compounds in the acidic stomach. This study investigated whether consumed cured/smoked meat and fish, the major dietary resource for exposure to nitrites and nitrosamines, is associated with childhood acute leukemia. Methods: A population-based case-control study of Han Chinese between 2 and 20 years old was conducted in southern Taiwan. 145 acute leukemia cases and 370 age- and sex-matched controls were recruited between 1997 and 2005. Dietary data were obtained from a questionnaire. Multiple logistic regression models were used in data analyses. Results: Consumption of cured/smoked meat and fish more than once a week was associated with an increased risk of acute leukemia (OR = 1.74; 95% CI: 1.15-2.64). Conversely, higher intake of vegetables (OR = 0.55; 95% CI: 0.37-0.83) and bean-curd (OR = 0.55; 95% CI: 0.34-0.89) was associated with a reduced risk. No statistically significant association was observed between leukemia risk and the consumption of pickled vegetables, fruits, and tea. Conclusion: Dietary exposure to cured/smoked meat and fish may be associated with leukemia risk through their contents of nitrites and nitrosamines among children and adolescents, and intake of vegetables and soy-bean curd may be protective. copyright 2009 Liu et al; licensee BioMed Central Ltd.

Lagiou, P, R. Talamini, E. Samoli, et al. **Diet and Upper-Aerodigestive Tract Cancer in Europe: The ARCADE Study.** *International Journal of Cancer.* 2009 Jun 1; 12411: 2671-2676.

There is suggestive, but inconclusive, evidence that dietary factors may affect risk of cancers of the upper aerodigestive tract (UADT). In the context of the alcohol-related cancers and genetic susceptibility in Europe study, we have examined the association of dietary factors with UADT cancer risk. We have analyzed data from 2,304 patients with UADT cancer and 2,227 control subjects recruited in 14 centers in 10 European countries. Dietary data were collected through a semi-quantitative food frequency questionnaire that also assessed preferred temperature of hot beverages. Statistical analyses were conducted through multiple logistic regression controlling for potential confounding variables, including alcohol intake and smoking habits. Consumption of red meat (OR per increasing tertile = 1.14, 95% CI: 1.05-1.25), but not poultry, was significantly associated with increased UADT cancer risk and the association was somewhat stronger for esophageal cancer. Consumption of fruits (OR per increasing tertile = 0.68, 95% CI: 0.62-0.75) and vegetables (OR per increasing tertile = 0.73, 95% CI: 0.66-0.81) as well as of olive oil (OR for above versus below median = 0.78, 95% CI 0.67-0.90) and tea (OR for above versus below median = 0.83, 95% CI 0.69-0.98) were significantly associated with reduced risk of UADT cancer. There was no indication that an increase in tea or coffee temperature was associated with increased risk of UADT overall or cancer of the esophagus; in fact, the association was, if anything, inverse. In conclusion, the results of this large multicentric study indicate that diet plays an important role in the etiology of UADT cancer

Exercise

Adamsen, L, C. Andersen, J. Midtgaard, T. Moller, M. Quist and M. Rorth. **Struggling with Cancer and Treatment: Young Athletes Recapture Body Control and Identity**

through Exercise: Qualitative Findings from a Supervised Group Exercise Program in Cancer Patients of Mixed Gender Undergoing Chemotherapy. *Scand J Med Sci Sports.*2009Feb;191:55-66. Cancer and treatment can negatively affect the body's performance and appearance. Exercise has been tested in a few studies for altered body image among middle-aged women with breast cancer. The aim of the study was to explore how young pre-cancer athletes of both genders experience disease- and treatment-related physical fitness and appearance changes while undergoing chemotherapy and participating in a 6-week group exercise intervention. A prospective, explorative study using semi-structured interviews was conducted before and at termination of the intervention. The study included 22 cancer patients (median age 28 years). The young athletes experienced a change from a high level of physical activity, body satisfaction and a positive self-identity to a low level of physical activity, body denial and a negative self-identity. In the program, the patients experienced increased physical strength and recapture of certain aspects of their former positive body perception. Deterioration of muscle functions caused by chemotherapy was particularly painful to these patients, independent of gender and age. Young physically active patients are heavily dependent on their physical capacity, body satisfaction and self-identity. This should be taken into account when designing programs to rehabilitate and encourage these patients through the often-strenuous antineoplastic treatments.

CAM of the Month

Julkunen, J, M. Gustavsson-Lilius and P. Hietanen. **Anger Expression, Partner Support, and Quality of Life in Cancer Patients.** *J Psychosom Res.* 2009 Mar; 663: 235-244. OBJECTIVE: Family members are the most important source of social support for cancer patients. The determinants of family support, however, are not well understood. In this study, the associations of anger-expression styles of both patients and their partners with patient-perceived partner support and the impact of these variables on long-term health-related quality of life (HRQL) of the patient were examined. METHOD: The baseline data were collected at the time of diagnosis; a follow-up survey was conducted at 8 months. Questionnaires included the Spielberger AX scale, the Family Support scale, and the RAND-36 Health Survey. The sample comprised 153 patients and their partners. The theoretical model was tested with a path analysis using structural equation modeling, and gender differences were tested using multivariate analysis of covariance. RESULTS: Path analyses indicated that partner support was an important mediator, partly explaining the associations between anger-expression styles and HRQL. As hypothesized, anger control had a positive relationship with perceived partner support, while habitual inhibition of anger (anger-in) showed a negative correlation with partner support. Analyses by gender revealed some clear differences: for the male patients, the wife's high level of anger expression (anger-out) was significantly positively related to patient mental HRQL, whereas for the female patients, their husband's anger-out was negatively correlated with the patient's mental HRQL. In addition, patient's own anger-out had a more pronounced negative effect on HRQL for women as compared to men. CONCLUSION: The anger-expression styles of both patients and their partners seem to modify the family atmosphere, and together, they are important determinants of the long-term quality of life of the cancer patients. Interventions for couples facing cancer should include a focus on ways of dealing with anger and thereby support dyadic coping with cancer.

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