

LE Magazine June 2005

## ABSTRACTS

### Beta-sitosterol

#### **EFFECT OF RESVERATROL AND BETA-SITOSTEROL IN COMBINATION ON REACTIVE OXYGEN SPECIES AND PROSTAGLANDIN RELEASE BY.**

The objective of this project was to identify some possible mechanisms by which two common phytochemicals, resveratrol and beta-sitosterol, inhibit the growth of human prostate cancer PC-3 cells. These mechanisms include the effect of the phytochemicals on apoptosis, cell cycle progression, prostaglandin synthesis and the production of reactive oxygen species (ROS). Prostaglandins have been known to play a role in regulating cell growth and apoptosis. PC-3 cells were supplemented with 50 microM resveratrol or 16 microM beta-sitosterol alone or in combination for up to 5 days. Phytochemical supplementation resulted in inhibition in cell growth. beta-Sitosterol was more potent than resveratrol and the combination of the two resulted in greater inhibition than supplementation with either alone. Long-term supplementation with resveratrol or beta-sitosterol elevated basal prostaglandin release but beta-sitosterol was much more potent than resveratrol in this regard. beta-Sitosterol was more effective than resveratrol in inducing apoptosis and the combination had an intermediate effect after 1 day of supplementation. Cells supplemented with resveratrol were arrested at the G1 phase and at the G2/M phase in the case of beta-sitosterol while the combination resulted in cell arrest at the two phases of the cell cycle. beta-Sitosterol increased ROS production while resveratrol decreased ROS production. The combination of the two phytochemicals resulted in an intermediate level of ROS. The observed changes in prostaglandin levels and ROS production by these two phytochemicals may suggest their mediation in the growth inhibition. The reduction in ROS level and increase by resveratrol supplementation in PC-3 cells reflects the antioxidant properties of resveratrol. It was concluded that these phytochemicals may induce the inhibition of tumor growth by stimulating apoptosis and arresting cells at different locations in the cell cycle and the mechanism may involve alterations in ROS and prostaglandin production.

Prostaglandins Leukot Essent Fatty Acids. 2005 Mar;72(3):219-26

#### **BETA-SITOSTEROLS FOR BENIGN PROSTATIC HYPERPLASIA.**

**OBJECTIVES:** This systematic review aimed to assess the effects of beta-sitosterols (B-sitosterol) on urinary symptoms and flow measures in men with of benign prostatic hyperplasia (BPH). **SEARCH STRATEGY:** Trials were searched in computerized general and specialized databases (MEDLINE, EMBASE, Cochrane Library, Phytodok), by checking bibliographies, and by contacting manufacturers and researchers. **SELECTION CRITERIA:** Trials were eligible for inclusion provided they (1) randomized men with BPH to receive B-sitosterol preparations in comparison to placebo or other BPH medications, and (2) included clinical outcomes such as urologic symptom scales, symptoms, or urodynamic measurements. **DATA COLLECTION AND ANALYSIS:** Information on patients, interventions, and outcomes was extracted by at least two independent reviewers using a standard form. Main outcome measure for comparing the effectiveness of B-sitosterols with placebo and standard BPH medications was the change in urologic symptom scale scores. Secondary outcomes included changes in nocturia as well as urodynamic measures (peak and mean urine flow, residual volume, prostate size). Main outcome measure for side effects was the number of men reporting side effects. **MAIN RESULTS:** 519 men from 4 randomized, placebo-controlled, double-blind trials, (lasting 4 to 26 weeks) were assessed. 3 trials used non-glucosidic B-sitosterols and one utilized a preparation that contained 100% B-sitosteryl-B-D-glucoside. B-Sitosterols improved urinary symptom scores and flow measures. The weighted mean difference (WMD) for the IPSS was -4.9 IPSS points (95%CI = -6.3 to -3.5, n = 2 studies). The WMD for peak urine flow was 3.91 ml/sec (95%CI = 0.91 to 6.90, n = 4 studies) and the WMD for residual volume was -28.62 ml (95%CI = -41.42 to -15.83, n = 4 studies). The trial using 100% B-sitosteryl-B-D-glucoside (WA184) show improvement in urinary flow measures. B-sitosterols did not reduce prostate size. Withdrawal rates for men assigned to B-sitosterol and placebo were 7.8% and 8.0%, respectively. **REVIEWER'S CONCLUSIONS:** The evidence suggests non-glucosidic B-sitosterols improve urinary symptoms and flow measures. Their long term effectiveness, safety and ability to prevent BPH complications are not known.

Cochrane Database Syst Rev. 2000;(2):CD001043

#### **IN VITRO AND IN VIVO (SCID MICE) EFFECTS OF PHYTOSTEROLS ON THE GROWTH AND DISSEMINATION OF HUMAN PROSTATE CANCER PC-3 CELLS.**

The dietary effect of phytosterols (PS) versus cholesterol on the growth and metastasis of the PC-3 human prostate cancer cells in SCID mice was studied. Also, their direct effect on the growth and migration of these cells in vitro was analysed. In the in vivo experiment, SCID mice were fed a diet containing 2% of either PS mixture or cholesterol plus 0.2% cholic acid and implanted with  $2 \times 10^6$  tumour cells per mouse. Tumour growth was monitored for 8 weeks post inoculation. Animals fed the PS diet had tumours 40-43% smaller than those fed the cholesterol diet. Furthermore, the number of mice with lymph node and lung metastasis was almost one-half that of the cholesterol-fed group. In the in vitro studies, both beta-sitosterol and campesterol inhibited the growth of PC-3 cells by 70% and 14%, respectively, while cholesterol supplementation increased the growth by 18% when compared with controls. PS inhibited the invasion of PC-3 cells into Matrigel-coated membranes by 78% while cholesterol increased it by 43% as compared with the cells in the control media. Migration of tumour cells through 8 microm pore membranes was reduced by 60-93% when the PC-3 cells were in PS media, as compared with a 67% increase after cholesterol supplementation. PS supplementation reduced the binding of PC-3 cells to laminin by 15-38% and fibronectin by 23% while cholesterol increased binding to type IV collagen by 36%. It was concluded that PS indirectly (in vivo as a dietary supplement) and directly (in tissue culture media) inhibited the growth and metastasis of PC-3 cells. beta-Sitosterol was more effective than campesterol in offering this protection in most of the parameters studied.

Eur J Cancer Prev. 2001 Dec;10(6):507-13

### **TREATMENT OF SYMPTOMATIC BENIGN PROSTATIC HYPERPLASIA WITH BETA-SITOSTEROL: AN 18-MONTH FOLLOW-UP.**

**OBJECTIVES:** To determine the long-term effects of phytotherapy with beta-sitosterol (the trade name for beta-sitosterol used in this study is Harzol(R)) for symptomatic benign prostatic hyperplasia (BPH). **Patient and methods** At 18 months after enrolment in a 6-month multicentre double-blind placebo-controlled clinical trial with beta-sitosterol (reported previously), patients were re-evaluated using the modified Boyarsky score, the International Prostate Symptom Score and quality-of-life index, the maximum urinary flow rate (Qmax) and postvoid residual urine volume (PVR). In this open extension of the original trial (after 6 months of treatment or placebo), patients were free to chose their further treatment for BPH. **RESULTS:** In all, 117 patients (59%) were eligible for analysis during the follow-up. Of the former beta-sitosterol group, 38 patients who continued beta-sitosterol treatment had stable values for all outcome variables between the end of the double-blind study and after 18 months of follow-up. The 41 patients choosing no further therapy had slightly worse symptom scores and PVR, but no changes in Qmax. Of the former placebo group, 27 patients who started beta-sitosterol after the double-blind trial improved to the same extent as the treated group for all outcome variables. The 18 patients choosing no further therapy showed no signs of improvement. **CONCLUSION:** The beneficial effects of beta-sitosterol treatment recorded in the 6-month double-blind trial were maintained for 18 months. Further clinical trials should be conducted to confirm these results before concluding that phytotherapy with beta-sitosterol is effective.

BJU Int. 2000 May;85(7):842-6

### **ASSOCIATIONS BETWEEN DIET AND CANCER, ISCHEMIC HEART DISEASE, AND ALL-CAUSE MORTALITY IN NON-HISPANIC WHITE CALIFORNIA SEVENTH-DAY ADVENTISTS.**

Results associating diet with chronic disease in a cohort of 34192 California Seventh-day Adventists are summarized. Most Seventh-day Adventists do not smoke cigarettes or drink alcohol, and there is a wide range of dietary exposures within the population. About 50% of those studied ate meat products <1 time/wk or not at all, and vegetarians consumed more tomatoes, legumes, nuts, and fruit, but less coffee, doughnuts, and eggs than did nonvegetarians. Multivariate analyses showed significant associations between beef consumption and fatal ischemic heart disease (IHD) in men [relative risk (RR) = 2.31 for subjects who ate beef > or =3 times/wk compared with vegetarians], significant protective associations between nut consumption and fatal and nonfatal IHD in both sexes (RR approximately 0.5 for subjects who ate nuts > or =5 times/wk compared with those who ate nuts <1 time/wk), and reduced risk of IHD in subjects preferring whole-grain to white bread. The lifetime risk of IHD was reduced by approximately 31% in those who consumed nuts frequently and by 37% in male vegetarians compared with nonvegetarians. Cancers of the colon and prostate were significantly more likely in nonvegetarians (RR of 1.88 and 1.54, respectively), and frequent beef consumers also had higher risk of bladder cancer. Intake of legumes was negatively associated with risk of colon cancer in nonvegetarians and risk of pancreatic cancer. Higher consumption of all fruit or dried fruit was associated with lower risks of lung, prostate, and pancreatic cancers. Cross-sectional data suggest vegetarian Seventh-day Adventists have lower risks of diabetes mellitus, hypertension, and arthritis than nonvegetarians. Thus, among Seventh-day Adventists, vegetarians are healthier than nonvegetarians but this cannot be ascribed only to the absence of meat.

Am J Clin Nutr. 1999 Sep;70(3 Suppl):532S-538S

## ABSTRACTS

### Sun protection

#### **SUNSCREENS—THE ULTIMATE COSMETIC.**

One decade ago, a sun protection factor (SPF) of 15 was considered a complete blocker of ultraviolet radiation (UV). The logic behind that cutoff point was that sunscreens with this SPF number would always prevent erythema and that preventing erythema would prevent all the ill effects of UV exposure. Today, we know that both of these assumptions were wrong and we tend to recommend higher SPF. Consumers apply only about one-quarter to one-half thickness of the layer of sunscreen material used to measure the SPF in the laboratory. That means that less than 50% of the SPF number claimed on the label is spread on the consumer's skin, meaning that a sunscreen with an SPF 30 will give the real protection of an SPF of 15. Therefore, recommend 60 when you want a real protection of 30! Significant injury, DNA damage, mutations, and carcinogenesis can and do occur also with cumulative suberythral UV exposure. Thus, erythema induction, a criterion that defines SPF, is not a good indicator of UV damage. We also need higher SPF values to prevent the damage caused by suberythral doses of UV. The value of the SPF claimed on the label is diminished by environmental factors that are not taken into account during SPF measurements in the laboratory, such as sweating, water immersion, rubbing off, and photodegradation. There are some misunderstandings and confusion about the mode of action of physical sunscreens. It was originally considered that, in contrast to organic sunscreens, the inorganic metal oxides (zinc oxide and titanium dioxide) acted as scatterers or reflectors of UV light, as a mirror. This is not the case with modern micronized forms of metal oxides. It has been shown that both zinc oxide and titanium dioxide mobilize electrons within their atomic structure while absorbing UV radiation. Thus, although metallic oxides are not inert per se, in their coated form they are stable, non-toxic, and safe and they act as highly efficient UV attenuators. Therefore, we recommend our patients to use this type of sunscreens. We should exert all our influence upon our patients not to expose themselves to excessive sunlight, to routinely use generous layers of sunscreen agents, and to wear protective clothing. To wait for the dust to settle around the issue of the effectiveness of sunscreens in preventing melanoma, while the ideal sunscreens—topical, systemic, whatever—are at our disposal, is a luxury we cannot afford.

Acta Dermatovenerol Croat. 2003;11(3):158-62

#### **PROTECTIVE EFFECTS OF CURCUMIN AGAINST OXIDATIVE DAMAGE ON SKIN CELLS IN VITRO: ITS IMPLICATION FOR WOUND HEALING.**

**BACKGROUND:** Curcumin, isolated from turmeric, has been known to possess many pharmacologic properties. It has been proven to exhibit remarkable anticarcinogenic, anti-inflammatory, and antioxidant properties. Turmeric curcumin may be a good potential agent for wound healing. **METHODS:** To further understand its therapeutic mechanisms on wound healing, the antioxidant effects of curcumin on hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and hypoxanthine-xanthine oxidase induced damage to cultured human keratinocytes and fibroblasts were investigated. Cell viability was assessed by colorimetric assay and quantification of lactate dehydrogenase release. **RESULTS:** Exposure of human keratinocytes to curcumin at 10 microg/mL showed significant protective effect against hydrogen peroxide. Interestingly, exposure of human dermal fibroblasts to curcumin at 2.5 microg/mL showed significant protective effects against hydrogen peroxide. No protective effects of curcumin on either fibroblasts or keratinocytes against hypoxanthine-xanthine oxidase induced damage were found in our present studies. **CONCLUSION:** The findings indicate that curcumin indeed possessed powerful inhibition against hydrogen peroxide damage in human keratinocytes and fibroblasts.

J Trauma. 2001 Nov;51(5):927-31

#### **SUN EXPOSURE, SUNSCREENS, AND SKIN CANCER PREVENTION: A YEAR-ROUND CONCERN.**

**OBJECTIVE:** To review the role of sunlight in skin aging and skin cancer formation, and to provide guidelines on the use of sunscreens to minimize the adverse effects of sun damage. **DATA SOURCES:** A MEDLINE search of applicable articles on ultraviolet (UV) radiation, melanoma, sunscreens, and skin cancer, evaluating both human and animal studies. Published and unpublished original research as well as clinical experience were also used. **DATA SYNTHESIS:** The interaction of UV radiation and skin type plays a central role in melanoma formation. Mortality from melanoma is highest in geographic locations near the equator, where UV intensity is greatest. The incidence of melanomas in light-complected individuals (skin types I-III) is several times higher than those with darker skin types (types IV-VI), even in similar geographic regions. The UVB portion of the spectrum appears to be primarily responsible for skin cancer formation and photoaging, while short wave UVA rays play a significant contributing role. Regular sunscreen use has been shown to reduce the formation of precancerous actinic keratoses (AK) lesions by 36%. A dose-response relationship has also been found between the amount of sunscreen used and AK formation. **CONCLUSIONS:** Sunscreens have now been shown to reduce the carcinogenic effects of sunlight in humans. Patients should be

advised of the long-term consequences of sun exposure and the benefits of regular sunscreen use.

Ann Pharmacother. 1996 Jun;30(6):662-73

### **SUNSCREEN ISN'T ENOUGH.**

Topical sunscreens act by absorbing or scattering UV radiation and are widely available for general public use as a consumer product. Surveys carried out in the UK find that sunscreen use is regarded as the most important, and by implication the most effective, sun protection measure. But is perception borne out by reality? Sunscreens applied at the thickness tested by manufacturers need only possess an SPF of 15 to prevent sunburn even for all day exposure in tropical sunshine. Yet behavioural studies show that high SPF (>15) sunscreens do not always prevent sunburn. That the protection achieved is often less than that expected depends upon a number of factors: application thickness and technique; type of sunscreen applied; resistance to water immersion and sand abrasion; and when, where and how often sunscreen is re-applied. These factors provide ample evidence that the numerical measure of protection indicated on the product pack is generally higher than achieved in practice. This mismatch between expectation and realisation may be one contributing factor why sunscreens have been reported to be a risk factor in melanoma.

J Photochem Photobiol B. 2001 Nov 15;64(2-3):105-8

### **EFFECT OF DAILY VERSUS INTERMITTENT SUNSCREEN APPLICATION ON SOLAR SIMULATED UV RADIATION-INDUCED SKIN RESPONSE IN HUMANS.**

**BACKGROUND:** Acute and chronic skin damage occurs as a consequence of solar UV radiation exposure. To diminish such skin damage, the dermatologic community advocates the daily use of sunscreens as part of a sun avoidance strategy. **OBJECTIVE:** We determined the effectiveness of a sunscreen product with a sunscreen protection factor (SPF) of 15 applied daily in preventing UV-induced histologic damage in human skin compared with the protection afforded by sunscreens with equal or higher SPF applied intermittently. **METHODS:** Twenty-four subjects were exposed to 2 minimal erythema doses of solar-simulated UV on 4 consecutive days. Three sunscreen products were applied to the buttock of each subject. One SPF 15 product was applied daily before exposure to UV and, to simulate intermittent product use, an SPF 15 or SPF 29 product was applied on 3 of 4 days, with one missed application on days 2, 3, or 4. Skin biopsy specimens were taken and processed for routine and immunohistochemical staining. Changes in number of sunburn cells and Langerhans cells as well as degree of inflammatory infiltrate and lysozyme immunostaining were determined. **RESULTS:** There was a statistically significant increase in the number of sunburn cells, degree of inflammation, and intensity of lysozyme staining, and there was a decrease in the number of Langerhans cells at sites where sunscreen application was missed as compared with unirradiated control and daily SPF 15 sunscreen-treated sites. **CONCLUSION:** Our data suggest that daily use of a sunscreen reduces the skin damage produced by UV exposure compared with intermittent use of equal or higher SPF products. The daily application of sunscreens in appropriate quantities reduces the harmful effects of solar UV radiation on skin. Compliance is essential for maximal benefit of sunscreens.

J Am Acad Dermatol. 2000 Oct;43(4):610-8

**ABSTRACTS****Hormone testing****EFFECT OF DHEA ON ABDOMINAL FAT AND INSULIN ACTION IN ELDERLY WOMEN AND MEN: A RANDOMIZED CONTROLLED TRIAL.**

**CONTEXT:** Dehydroepiandro-sterone (DHEA) administration has been shown to reduce accumulation of abdominal visceral fat and protect against insulin resistance in laboratory animals, but it is not known whether DHEA decreases abdominal obesity in humans. DHEA is widely available as a dietary supplement without a prescription. **OBJECTIVE:** To determine whether DHEA replacement therapy decreases abdominal fat and improves insulin action in elderly persons. **DESIGN AND SETTING:** Randomized, double-blind, placebo-controlled trial conducted in a US university-based research center from June 2001 to February 2004. **PARTICIPANTS:** Fifty-six elderly persons (28 women and 28 men aged 71 [range, 65-78] years) with age-related decrease in DHEA level. **INTERVENTION:** Participants were randomly assigned to receive 50 mg/d of DHEA or matching placebo for 6 months. **MAIN OUTCOME MEASURES:** The primary outcome measures were 6-month change in visceral and subcutaneous abdominal fat measured by magnetic resonance imaging and glucose and insulin responses to an oral glucose tolerance test (OGTT). **RESULTS:** Of the 56 men and women enrolled, 52 underwent follow-up evaluations. Compliance with the intervention was 97% in the DHEA group and 95% in the placebo group. Based on intention-to-treat analyses, DHEA therapy compared with placebo induced significant decreases in visceral fat area (-13 cm<sup>2</sup> vs +3 cm<sup>2</sup>, respectively;  $P = .001$ ) and subcutaneous fat (-13 cm<sup>2</sup> vs +2 cm<sup>2</sup>,  $P = .003$ ). The insulin area under the curve (AUC) during the OGTT was significantly reduced after 6 months of DHEA therapy compared with placebo (-1119  $\mu$ U/mL per 2 hours vs +818  $\mu$ U/mL per 2 hours,  $P = .007$ ). Despite the lower insulin levels, the glucose AUC was unchanged, resulting in a significant increase in an insulin sensitivity index in response to DHEA compared with placebo (+1.4 vs -0.7,  $P = .005$ ). **CONCLUSION:** DHEA replacement could play a role in prevention and treatment of the metabolic syndrome associated with abdominal obesity.

JAMA. 2004 Nov 10;292(18):2243-8

**THE EFFECT OF TESTOSTERONE REPLACEMENT ON ENDOGENOUS INFLAMMATORY CYTOKINES AND LIPID PROFILES IN HYPOGONADAL MEN.**

Testosterone has immune-modulating properties, and current *in vitro* evidence suggests that testosterone may suppress the expression of the proinflammatory cytokines TNF $\alpha$ , IL-1 $\beta$ , and IL-6 and potentiate the expression of the antiinflammatory cytokine IL-10. We report a randomized, single-blind, placebo-controlled, crossover study of testosterone replacement (Sustanon 100) vs. placebo in 27 men (age, 62  $\pm$  9 yr) with symptomatic androgen deficiency (total testosterone, 4.4  $\pm$  1.2 nmol/liter; bioavailable testosterone, 2.4  $\pm$  1.1 nmol/liter). Compared with placebo, testosterone induced reductions in TNF $\alpha$  (-3.1  $\pm$  8.3 vs. 1.3  $\pm$  5.2 pg/ml;  $P = 0.01$ ) and IL-1 $\beta$  (-0.14  $\pm$  0.32 vs. 0.18  $\pm$  0.55 pg/ml;  $P = 0.08$ ) and an increase in IL-10 (0.33  $\pm$  1.8 vs. -1.1  $\pm$  3.0 pg/ml;  $P = 0.01$ ); the reductions of TNF $\alpha$  and IL-1 $\beta$  were positively correlated ( $r(S) = 0.588$ ;  $P = 0.003$ ). In addition, a significant reduction in total cholesterol was recorded with testosterone therapy (-0.25  $\pm$  0.4 vs. -0.004  $\pm$  0.4 mmol/liter;  $P = 0.04$ ). In conclusion, testosterone replacement shifts the cytokine balance to a state of reduced inflammation and lowers total cholesterol. Twenty of these men had established coronary disease, and because total cholesterol is a cardiovascular risk factor, and proinflammatory cytokines mediate the development and complications associated with atheromatous plaque, these properties may have particular relevance in men with overt vascular disease.

J Clin Endocrinol Metab. 2004 Jul;89(7):3313-8

**CHANGES IN SEX HORMONE-BINDING GLOBULIN AND TESTOSTERONE DURING WEIGHT LOSS AND WEIGHT MAINTENANCE IN ABDOMINALLY OBESE MEN WITH THE METABOLIC SYNDROME.**

**BACKGROUND:** Mild hypoandrogenism in men, usually defined by low levels of testosterone, is a peculiar feature of abdominal obesity that independently predicts the development of insulin resistance and diabetes mellitus. Little is known about the short- and long-term effects of weight loss on sex steroids in abdominally obese men, however. **OBJECTIVES:** We assessed the effect of rapid weight loss and sustained weight maintenance on the plasma concentrations of testosterone and other sex hormones in 58 abdominally obese men (age, 46.3  $\pm$  7.5 years; body mass index, 36.1  $\pm$  3.8 kg/m<sup>2</sup>; waist girth, 121  $\pm$  10 cm) with the metabolic syndrome. **RESULTS:** The men lost on average 16.3  $\pm$  4.5 kg during a 9-week very low-calorie diet (VLCD) and maintained 14.3  $\pm$  9.1 kg weight loss after a 12-month maintenance period (vs. baseline,  $p < 0.001$ ). Sex hormone-binding globulin (SHBG) increased from 27.6  $\pm$  11.9 to 48.1  $\pm$  23.5 nmol/l during the VLCD but decreased to 32.6  $\pm$  12.9 nmol/l during weight maintenance, which was still higher than at baseline ( $p < 0.001$ ). Free testosterone (fT) increased from 185  $\pm$  66 to 208  $\pm$  70 pmol/l ( $p = 0.002$ ) during the VLCD and remained high after 1 year of weight maintenance (212  $\pm$  84 pmol/l,  $p = 0.002$ ). Total testosterone levels followed a pattern intermediate between fT and SHBG. Plasma estradiol and

dehydroepiandrosterone sulphate concentrations changed only transiently or not at all. CONCLUSIONS: Rapid weight loss with successful weight maintenance in abdominally obese men with the metabolic syndrome brings about a sustained increase in fT levels. The dramatic increase in SHBG attenuated initially during weight maintenance but remained elevated. These findings may be important with regard to prevention of progressive metabolic decompensation and cardiovascular disease associated with obesity and the metabolic syndrome.

Diabetes Obes Metab. 2004 May;6(3):208-15

### **USE OF 5-ALPHA-REDUCTASE INHIBITORS IN THE PREVENTION OF PROSTATE CANCER.**

5-alpha-reductase inhibitors are now in widespread use for the treatment of benign prostatic hyperplasia (BPH) and these molecules have recently come under the spotlight in prostate cancer. Their peripheral "hormonal" action inducing reduced intraprostatic DHT synthesis seems to involve them in this hormone-dependant disorder. Finasteride evaluated in the treatment of BPH (PLESS study) was found to have a preventive effect on the incidence of cancer and this activity was assessed in a specific trial (PCPT study). Nevertheless, in the latter randomized study with a 7-year follow-up period, a reduction in the global incidence of the number of cases of cancers was associated with an increase in the number of high-grade cancers. A slight reduction in prostate cancer was also noted in the studies with dutasteride in BPH (ARIA3001, ARIA3002 and ARIB3003). An international multicenter study (REDUCE) is currently being conducted to confirm the preventive value of this molecule which has a more complete activity than finasteride with its inhibitory action on the two 5-alpha-reductase iso-enzymes, and may therefore have a clearer efficiency and rule out the risk of onset of high-grade cancer.

Ann Urol (Paris). 2004 Dec;38 Suppl 2:S35-42

### **SUBCLINICAL HYPOTHYROIDISM IS AN INDEPENDENT RISK FACTOR FOR ATHEROSCLEROSIS AND MYOCARDIAL INFARCTION IN ELDERLY WOMEN: THE ROTTERDAM STUDY.**

BACKGROUND: Overt hypothyroidism has been found to be associated with cardiovascular disease. Whether subclinical hypothyroidism and thyroid autoimmunity are also risk factors for cardiovascular disease is controversial. OBJECTIVE: To investigate whether subclinical hypothyroidism and thyroid autoimmunity are associated with aortic atherosclerosis and myocardial infarction in postmenopausal women. DESIGN: Population-based cross-sectional study. SETTING: A district of Rotterdam, The Netherlands. PARTICIPANTS: Random sample of 1149 women (mean age +/- SD, 69.0 +/- 7.5 years) participating in the Rotterdam Study. MEASUREMENTS: Data on thyroid status, aortic atherosclerosis, and history of myocardial infarction were obtained at baseline. Subclinical hypothyroidism was defined as an elevated thyroid-stimulating hormone level (>4.0 mU/L) and a normal serum free thyroxine level (11 to 25 pmol/L [0.9 to 1.9 ng/dL]). In tests for antibodies to thyroid peroxidase, a serum level greater than 10 IU/mL was considered a positive result. RESULTS: Subclinical hypothyroidism was present in 10.8% of participants and was associated with a greater age-adjusted prevalence of aortic atherosclerosis (odds ratio, 1.7 [95% CI, 1.1 to 2.6]) and myocardial infarction (odds ratio, 2.3 [CI, 1.3 to 4.0]). Additional adjustment for body mass index, total and high-density lipoprotein cholesterol level, blood pressure, and smoking status, as well as exclusion of women who took beta-blockers, did not affect these estimates. Associations were slightly stronger in women who had subclinical hypothyroidism and antibodies to thyroid peroxidase (odds ratio for aortic atherosclerosis, 1.9 [CI, 1.1 to 3.6]; odds ratio for myocardial infarction, 3.1 [CI, 1.5 to 6.3]). No association was found between thyroid autoimmunity itself and cardiovascular disease. The population attributable risk percentage for subclinical hypothyroidism associated with myocardial infarction was within the range of that for known major risk factors for cardiovascular disease. CONCLUSION: Subclinical hypothyroidism is a strong indicator of risk for atherosclerosis and myocardial infarction in elderly women.

Ann Intern Med. 2000 Feb 15;132(4):270-8

**ABSTRACTS****CLA****DIETARY INTAKE OF CONJUGATED LINOLEIC ACIDS AND RISK OF PREMENOPAUSAL AND POSTMENOPAUSAL BREAST CANCER, WESTERN NEW YORK EXPOSURES AND BREAST CANCER STUDY (WEB STUDY).**

Specific fatty acids may have differential effects on breast cancer etiology. Animal studies have suggested that conjugated linoleic acids (CLA), a group of fatty acids found predominantly in dairy products and the meat of ruminants, have potent anticarcinogenic properties. We examined breast cancer risk and dietary CLA intake among 1,122 women with primary, incident, histologically confirmed breast cancer and 2,036 controls frequency matched to cases by age, race, and county of residence. Diet was assessed with a self-administered 104-item food frequency questionnaire and other relevant data were collected by detailed in-person interviews. We examined risk with intake of total CLAs and the 9c,11t-18:2 isomer of CLA (9,11 CLA). Odds ratios and 95% confidence intervals were estimated by unconditional logistic regression, adjusting for age, the residual of fat adjusted for energy, and other breast cancer risk factors. No association was observed between intakes of total CLA or 9,11 CLA and overall risk of premenopausal or postmenopausal breast cancer. We observed little association between CLA intakes and risk of estrogen receptor (ER)-negative or ER-positive tumors, although, compared with premenopausal women in the lowest quartile of 9,11 CLA intake, those in the highest quartile had a marginally significant reduction in risk of having an ER-negative tumor (odds ratio, 0.40; 95% confidence interval, 0.16-1.01). Our findings suggest that, although CLA intake was not related to overall breast cancer risk, there may be associations with tumor biology at least among premenopausal women.

Cancer Epidemiol Biomarkers Prev. 2004 Sep;13(9):1480-4

**AN OVERVIEW OF THE EFFECT OF LINOLEIC AND CONJUGATED-LINOLEIC ACIDS ON THE GROWTH OF SEVERAL HUMAN TUMOR CELL LINES.**

Both n-6 and n-3 polyunsaturated fatty acids are dietary fats important for cell function, being involved in several physiologic and pathologic processes, such as tumorigenesis. Linoleic acid and conjugated linoleic acid, its geometrical and positional stereoisomer, were tested on several human tumor cell lines originating from different tissues and with different degrees of malignancy. This was to provide the widest possible view of the impact of dietary lipids on tumor development. While linoleic acid exerted different effects, ranging from inhibitory to neutral, even promoting growth, conjugated linoleic acid inhibited growth in all lines tested and was particularly effective against the more malignant cells, with the exception of mammary tumor cells, in which behavior was the opposite, the more malignant cell line being less affected. The inhibitory effect of conjugated linoleic acid on growth may be accompanied by different contributions from apoptosis and necrosis. The effects of conjugated linoleic acid on growth or death involved positive or negative variations in PPARs. The important observation is that a big increase of PPARalpha protein occurred in cells undergoing strong induction of apoptosis, whereas PPARbeta/delta protein decreased. Although PPARalpha and PPARbeta/delta seem to be correlated to execution of the apoptotic program, the modulation of PPARgamma appears to depend on the type of tumor cell, increasing as protein content, when inhibition of cell proliferation occurred. In conclusion, CLA may be regarded as a component of the diet that exerts antineoplastic activity and its effect may be antiproliferative or pro-apoptotic.

Int J Cancer. 2004 Dec 20;112(6):909-19

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