

Effects of vitamin K2 on osteoporosis.

Iwamoto J, Takeda T, Sato Y. *Curr Pharm Des* 2004;10:2557-2576.

Vitamin K2 is a cofactor of gamma-carboxylase, which converts the glutamic acid (Glu) residue in osteocalcin molecules to gamma-carboxyglutamic acid (Gla), and is, therefore, essential for gamma-carboxylation of osteocalcin. Available evidence suggests that vitamin K2 also enhances osteocalcin accumulation in the extracellular matrix of osteoblasts in vitro. Osteocalcin-knockout mice develop hyperostosis, suggesting that the Gla-containing osteocalcin promotes normal bone mineralization. Although the precise role of osteocalcin in bone mineralization remains obscure, it probably regulates the growth of hydroxyapatite crystals. Furthermore, vitamin K2 also inhibits the expression of the osteoclast differentiation factor (ODF)/RANK ligand, tartrate-resistant acid phosphatase activity, and mononuclear cell formation, and induces osteoclast apoptosis in vitro. There is some evidence indicating that vitamin K2 prevents bone resorption in ovariectomized rats, retards the increase in bone turnover in orchidectomized rats, ameliorates the increase in bone resorption and decrease in bone formation in sciatic neurectomized rats, and prevents the decrease in bone formation in glucocorticoid-treated rats. These findings suggest that vitamin K2 may not only stimulate bone formation but also suppress bone resorption in vivo. Clinically, vitamin K2 sustains the lumbar bone mineral density (BMD) and prevents osteoporotic fractures in patients with age-related osteoporosis, prevents vertebral fractures in patients with glucocorticoid-induced osteoporosis, increases the metacarpal BMD in the paralytic upper extremities of patients with cerebrovascular disease, and sustains the lumbar BMD in patients with liver-dysfunction-induced osteoporosis. Vitamin K deficiency, as indicated by an increased circulating level of undercarboxylated osteocalcin, may contribute to osteoporotic fractures. Even though the effect of vitamin K2 on the BMD is quite modest, this vitamin may have the potential to regulate bone metabolism and play a role in reducing the risk of osteoporotic fractures. No randomized well-controlled prospective studies conducted on a sufficiently large number of patients have been reported yet, therefore, further studies are needed to confirm the efficacy of vitamin K2 in the treatment of osteoporosis.

Inflammation-induced endothelial dysfunction involves reduced nitric oxide bioavailability and increased oxidant stress.

Clapp BR, Hingorani AD, Kharbanda RK, et al. *Cardiovasc Res* 2004;64:172-178.

OBJECTIVES: Our aim was to investigate mechanisms of inflammation-induced endothelial dysfunction in humans. **METHODS:** Endothelial function in twenty-one healthy human volunteers was measured using forearm venous plethysmography before and 8 h after administration of typhoid vaccination to generate an inflammatory response. Basal and stimulated endothelial nitric oxide (NO) bioavailability was assessed by measurement of the responses to intra-arterial N(G)-monomethyl-L-arginine (L-NMMA) and bradykinin, respectively. The effects of supplementation with L-arginine or ascorbic acid were assessed to probe the effects of substrate deficiency and oxidative stress, respectively. Systemic effects were determined by measuring cytokine response, total anti-oxidant status (TAOS) and urinary protein excretion. **RESULTS:** Vaccination induced a cytokine response, a fall in total anti-oxidant status and increased urinary albumin excretion (UAE). There was a reduction in the response to bradykinin (BK, $P < 0.005$) and L-NMMA ($P < 0.0001$) with no effect on the response to glyceryl trinitrate (GTN) and norepinephrine (NE). Following vaccination blood flow response to BK (but not GTN) was partially returned to pre-vaccine levels by infusion of ascorbic acid ($P = 0.01$). Supplementation with L-arginine had no effect. **CONCLUSION:** Inflammation causes widespread endothelial dysfunction, reduces vascular NO bioavailability and increases oxidative stress. These actions are partially reversible with local anti-oxidants. These findings suggest a role for reactive oxygen species in inflammation-induced endothelial dysfunction.

A report of high-dose selenium supplementation: response and toxicities.

Reid ME, Stratton MS, Lillico AJ, et al. *J Trace Elem Med Biol* 2004;18:69-74.

Concerns about the toxicity of selenium has limited the doses used in chemoprevention. Based on previous studies, intakes of 400 microg/day and plasma selenium of 1000 ng/ml (Dietary Reference Intakes, Academy Press, New York, 2000, p. 384) were established as the no observed adverse effect level (NOAEL). This investigation summarizes the plasma response and toxicity reports from 24 men with biopsy-proven prostate cancer who were randomized to either 1600 or 3200 microg/day of selenized yeast as part of a controlled clinical trial testing selenium as a chemopreventive agent for prostate cancer progression. Subjects were on these doses for averages of almost 12 months. Plasma selenium levels were monitored throughout the course of follow-up. Symptoms of selenium toxicity were assessed by patient interview with specific questions regarding breath, hair and nail changes. Several liver and kidney function tests and hematology were measured at 6-month intervals. 8 subjects were randomized to the 1600 microg/day and 16 to the 3200 microg/day group. The mean plasma selenium levels achieved with supplementation were 492.2 ng/ml (SD = 188.3) and 639.7 ng/ml (SD = 490.7) for the 1600 and 3200 microg/day doses, respectively. The 3200 microg/day group reported more selenium-related side effects. Blood chemistry and hematology results were all within normal limits for both treatment groups. More subjects on 3200 microg/day reported symptoms of selenium toxicity; however, these reports did not correspond to peaks in plasma selenium levels. We observed no obvious selenium-related serious toxicities. As selenium is used in more chemoprevention and therapeutic settings, additional information on selenium species, sequestration of selenium in specific organs, excretion, and toxicities is needed.

Stone forming risk of calcium citrate supplementation in healthy postmenopausal women.

Sakhaee K, Poindexter JR, Griffith CS, Pak CY. *J Urol* 2004;172:958-961.

PURPOSE: We evaluated the effect of calcium citrate supplementation alone or in combination with potassium citrate on the stone forming propensity in healthy postmenopausal women. **MATERIALS AND METHODS:** A total of 18 postmenopausal women without stones underwent a randomized trial of 4 phases comprised of 2 weeks of treatment with placebo, calcium citrate (400 mg calcium twice daily), potassium citrate (20 mEq twice daily), and calcium citrate and potassium citrate (at same doses). During the last 2 days of each phase urine was collected in 24-hour pools for complete stone risk analysis. **RESULTS:** Compared to placebo, calcium citrate increased urinary calcium and citrate but decreased urinary oxalate and phosphate. Urinary saturation of calcium oxalate, brushite and undissociated uric acid did not change. Potassium citrate decreased urinary calcium, and increased urinary citrate and pH. It decreased urinary saturation of calcium oxalate and undissociated uric acid, and did not change the saturation of brushite. When calcium citrate was combined with potassium citrate, urinary calcium remained high, urinary citrate increased even further and urinary oxalate remained reduced from the calcium citrate alone, thereby marginally decreasing the urinary saturation of calcium oxalate. Urinary pH increased, decreasing urinary undissociated uric acid. The increase in pH increased the saturation of brushite despite the decrease in urinary phosphorus. **CONCLUSIONS:** Calcium citrate supplementation does not increase the risk of stone formation in healthy postmenopausal women. The co-administered potassium citrate may provide additional protection against formation of uric acid and calcium oxalate stones.

Magnesium prophylaxis for arrhythmias after cardiac surgery: a meta-analysis of randomized controlled trials.

Shiga T, Wajima Z, Inoue T, Ogawa R. *Am J Med* 2004;117:325-333.

BACKGROUND: Magnesium supplementation may reduce the incidence of arrhythmias, which often occur after cardiac surgery; however, recent findings of the effectiveness of magnesium prophylaxis have yielded discrepant results. **METHODS:** We searched electronic databases for randomized controlled trials of magnesium for the prevention of arrhythmias after cardiac surgery. The primary outcomes comprised the incidence of supraventricular and ventricular arrhythmias, and the secondary outcomes comprised serum magnesium concentration, length of hospital stay, myocardial infarction, and mortality. Effect sizes were estimated using a random-effects model. **RESULTS:** Seventeen trials (n=2069 patients) met the inclusion criteria. Pooled serum magnesium concentration at 24 hours after surgery in the treatment group was significantly higher than that in the control group (weighted mean difference=0.45 mmol/L [1.1 mg/dL]; 95% confidence interval [CI]: 0.30 to 0.59 mmol/L [0.7 to 1.4 mg/dL]; P <0.001). Magnesium supplementation reduced the risk of supraventricular arrhythmias (relative risk [RR]=0.77; 95% CI: 0.63 to 0.93; P=0.002) and ventricular arrhythmias (RR = 0.52; 95% CI: 0.31 to 0.87; P <0.0001), but had no effect on the length of hospital stay (weighted mean difference=-0.28 days; 95% CI: -0.70 to 1.27 days; P=0.48), the incidence of perioperative myocardial infarction (RR=1.03; 95% CI: 0.52 to 2.05; P = 0.99), or mortality (RR=0.97; 95% CI: 0.43 to 2.20; P=0.94). **CONCLUSION:** Administration of prophylactic magnesium reduced the risk of supraventricular arrhythmias after cardiac surgery by 23% (atrial fibrillation by 29%) and of ventricular arrhythmias by 48%. Supplementation had no notable benefit with respect to length of hospitalization, incidence of myocardial infarction, or mortality.

Folate deficiency inhibits the proliferation of primary human CD8+ T lymphocytes in vitro.

Courtemanche C, Elson-Schwab I, Mashiyama ST, et al. *J Immunol* 2004;173:3186-3192.

Folate is required for one-carbon transfer reactions and the formation of purines and pyrimidines for DNA and RNA synthesis. Deficiency of folate can lead to many clinical abnormalities, including macrocytic anemia, cardiovascular diseases, birth defects, and carcinogenesis. The nucleotide imbalance due to folate deficiency causes cell cycle arrest in the S phase and uracil misincorporation into DNA, which may result in DNA double-strand breaks during repair. The role of folate in the immune system has not been fully characterized. We cultured PHA-activated human T lymphocytes in varying concentrations of folate, and measured proliferation, cell cycle, apoptosis, uracil misincorporation, and proportions of Th cells (CD4(+)) and cytotoxic T (CD8(+)) cells. Folate deficiency reduced proliferation of T lymphocytes, induced cell cycle arrest in the S phase, induced apoptosis, and increased the level of uracil in DNA. Folate deficiency also increased the CD4(+) to CD8(+) ratio due to a marked reduction of CD8(+) cell proliferation. Folate or nucleoside repletion of folate-deficient cells rapidly restored T lymphocyte proliferation and normal cell cycle, reduced the DNA uracil content, and lowered the CD4(+) to CD8(+) ratio. These data suggest that folate status may affect the immune system by reducing the capacity of CD8(+) cells to proliferate in response to activation.

Prospective, comparative cohort studies and their contribution to the benefit assessments of therapeutic options: heart failure treatment with and without Hawthorn special extract WS 1442.

Habs M. *Forsch Komplementarmed Klass Naturheilkd* 2004;11 Suppl 1:36-39.

BACKGROUND: In addition to testing a drug for its efficacy, pharmacological quality and safety, current policies are increasingly demanding evaluations of the therapeutic benefits provided by a drug in general practice with “non-selected” patients and increasingly restrictive economic considerations. **OBJECTIVE:** One of the trials which addresses this task is the WISO cohort study (Efficacy and socio-economic relevance of treatment of chronic heart failure stage NYHA II with Crataegus extract WS 1442). It compares two different therapeutic strategies in the treatment of heart failure stage NYHA II, i.e. a conventional medication and a therapy which also includes hawthorn special extract WS 1442 (Crataegutt novo 450) in addition to chemical-synthetic drugs. In contrast to clinical trials, the patients in cohort studies are expressly not randomised and the physician in charge independently chooses the administered treatment. This comparative, non-interventional observation provides well-founded evidence of the “real-world effectiveness” of the tested preparation. **PATIENTS AND METHODS:** 952 patients with heart failure (NYHA II) were enrolled in the study by 217 general practitioners. 588 patients received Crataegus special extract WS 1442 (Crataegutt novo 450) either as an add-on therapy or as a monotherapy (Crataegus cohort) and 364 patients received therapy without hawthorn (comparative cohort). These two groups had the same indication (heart failure NYHA II) but were significantly different regarding gender, age and concomitant cardiovascular disease. Basically, in view of the free choice of therapy made by the physician in charge, such differences are to be expected in comparative observational studies. A sufficient degree of patient comparability was provided by means of the matched-pairs technique,

which replaced the randomisation procedure normally used in clinical studies. After 2 years, 130 patient pairs generated by this technique could be included in the interim assessment. **RESULTS:** The clinical symptoms with regard to all parameters investigated showed the same or a more pronounced improvement in the Crataegus cohort in the course of 2 years. After 2 years, the three cardinal symptoms of heart failure—fatigue ($p = 0.036$), stress dyspnoea ($p = 0.020$) and palpitations ($p = 0.048$)—were significantly less marked in the Crataegus cohort than in the comparative cohort. **DISCUSSION:** The particular design of the cohort study also provides valuable additional information: (1) Hawthorn special extract WS 1442 was prescribed in registered cardiological practices for the treatment of patients with heart failure stage NYHA II, partly as an alternative and partly as a supplement to the used chemical-synthetic drugs. (2) Favourable effects on the clinical symptoms were achieved although the patients in the Crataegus cohort received markedly fewer chemical-synthetic drugs than the patients in the comparative cohort (ACE-inhibitors: 36 vs. 54%, $p = 0.004$; cardiac glycosides: 18 vs. 37%, $p = 0.001$; diuretics: 49 vs. 61%, $p = 0.061$; beta-blockers: 22 vs. 33%, $p = 0.052$). **CONCLUSION:** The data show a clear benefit for patients with heart failure stage NYHA II treated with WS 1442. The single or add-on administration in addition to a chemical-synthetic medication resulted in objective improvements at comparable costs.

L-arginine and hypertension.

Gokce N. *J Nutr* 2004;134:2807S-2811S.

Hypertension is a major healthcare problem afflicting nearly 50 million individuals in the United States. Despite its strong causal association with cardiovascular disease complications including myocardial infarction, heart failure, and stroke, the majority of patients with hypertension do not achieve optimal blood pressure control. The prevalence of hypertension is expected to increase with the aging population, growing obesity epidemic, and rising incidence of metabolic syndrome. Endothelial dysfunction and reduced nitric oxide (NO) bioactivity represent prominent pathophysiological abnormalities associated with hypertensive cardiovascular disease. Individuals with hypertension exhibit blunted epicardial and resistance vascular dilation to endothelium-derived nitric oxide (EDNO) agonists in the peripheral and coronary circulation that likely contributes to mechanisms of altered vascular tone in hypertension. The amino acid L-arginine serves as the principal substrate for vascular NO production. Numerous studies, though not uniformly, demonstrate a beneficial effect of acute and chronic L-arginine supplementation on EDNO production and endothelial function, and L-arginine has been shown to reduce systemic blood pressure in some forms of experimental hypertension. This brief review discusses the potential role of L-arginine in hypertension, and reviews possible mechanisms of L-arginine action including modulation of EDNO production, alteration of asymmetrical dimethylarginine (ADMA):L-arginine balance, and possible improvement of insulin sensitivity. In view of the rising prevalence of hypertension, randomized human clinical studies investigating the potential therapeutic role of L-arginine may be warranted.

Phase I clinical trial of oral curcumin: biomarkers of systemic activity and compliance.

Sharma RA, Euden SA, Platton SL, et al. *Clin Cancer Res* 2004;10:6847-6854.

Curcumin, a polyphenolic antioxidant derived from a dietary spice, exhibits anticancer activity in rodents and in humans. Its efficacy appears to be related to induction of glutathione S-transferase enzymes, inhibition of prostaglandin E(2) (PGE(2)) production, or suppression of oxidative DNA adduct (M(1)G) formation. We designed a dose-escalation study to explore the pharmacology of curcumin in humans. Fifteen patients with advanced colorectal cancer refractory to standard chemotherapies consumed capsules compatible with curcumin doses between 0.45 and 3.6 g daily for up to 4 months. Levels of curcumin and its metabolites in plasma, urine, and feces were analyzed by high-pressure liquid chromatography and mass spectrometry. Three biomarkers of the potential activity of curcumin were translated from preclinical models and measured in patient blood leukocytes: glutathione S-transferase activity, levels of M(1)G, and PGE(2) production induced ex vivo. Dose-limiting toxicity was not observed. Curcumin and its glucuronide and sulfate metabolites were detected in plasma in the 10 nmol/L range and in urine. A daily dose of 3.6 g curcumin engendered 62% and 57% decreases in inducible PGE(2) production in blood samples taken 1 hour after dose on days 1 and 29, respectively, of treatment compared with levels observed immediately predose ($P < 0.05$). A daily oral dose of 3.6 g of curcumin is advocated for Phase II evaluation in the prevention or treatment of cancers outside the gastrointestinal tract. PGE(2) production in blood and target tissue may indicate biological activity. Levels of curcumin and its metabolites in the urine can be used to assess general compliance.

Terminalia arjuna reverses impaired endothelial function in chronic smokers.

Bharani A, Ahirwar LK, Jain N.
Indian Heart J 2004;56:123-128.

BACKGROUND: Smoking, largely through increased oxidative stress, causes endothelial dysfunction which is an early key event in atherosclerosis. Smoking cessation and antioxidant vitamin therapy are shown to have beneficial role by restoring altered endothelial physiology. The present study was aimed to determine whether Terminalia arjuna, an Indian medicinal plant with potent antioxidant constituents, would improve endothelial dysfunction in smokers. **METHODS AND RESULTS:** Eighteen healthy male smokers (age 28.16±9.45 years) and equal number of age-matched non-smoker controls participated in the study. The baseline brachial artery reactivity studies were performed using high frequency ultrasound according to standard protocol under identical conditions to determine endothelium-dependent, flow-mediated dilation and endothelium-independent nitroglycerine-mediated dilation. The two groups were matched regarding age, body mass index, blood pressure, serum cholesterol, mean resting vessel diameters and post-occlusion flow velocities (all p=NS). While flow-mediated dilation was significantly impaired amongst smokers compared to controls (4.71±2.22 v. 11.75±5.94%, p<0.005), the nitroglycerine-mediated dilation was similar in the two groups (20.35±3.89 v. 19.68±3.74%, p=NS). Subsequently the smokers were given Terminalia arjuna (500 mg q8h) or matching placebo randomly in a double blind cross-over design for two weeks each, followed by repetition of brachial artery reactivity studies to determine various parameters including flow-mediated dilation after each period. There was no significant difference as regards vessel diameter and flow velocities between the two therapies. However, the flow-mediated dilation showed significant improvement from baseline values after Terminalia arjuna therapy but not with placebo (9.31±3.74 v. 5.17±2.42%, p<0.005). **CONCLUSIONS:** Smokers have impaired endothelium-dependent but normal endothelium-independent vasodilation as determined by brachial artery reactivity studies. Further, Terminalia arjuna therapy for two weeks leads to significant regression of this endothelial abnormality amongst smokers.

The probiotic effect of Saccharomyces boulardii in a pediatric age group.

Erdeve O, Tiras U, Dallar Y. *J Trop Pediatr* 2004;50:234-236.

The aim of this study was to determine the efficacy of *S. boulardii* in diarrhea associated with commonly used antibiotics such as sulbactam-ampicillin (SAM) and azithromycin (AZT). Four hundred and sixty-six patients were assigned to four different groups as follows: group 1:117 patients receiving SAM alone; group 2:117 patients receiving SAM and *S. boulardii*; group 3:105 patients receiving AZT alone; group 4:127 patients receiving AZT and *S. boulardii*. Antibiotic-associated diarrhea was seen in 42 of the 222 patients (18.9 per cent) receiving an antibiotic without the probiotic, and in 14 of the 244 patients (5.7 per cent) who received both the probiotic and the antibiotic (p < 0.05). In the group receiving SAM where *S. boulardii* use was found to be significant, the use of *S. boulardii* decreased the diarrhea rate from 32.3 to 11.4 per cent in the 1-5 years age group (p < 0.05). This is a pioneering study investigating combined antibiotic and probiotic use in pediatric diarrhea patients.

Extract of Rhodiola rosea radix reduces the level of C-reactive protein and creatinine kinase in the blood.

Abidov M, Grachev S, Seifulla RD, Ziegenfuss TN. *Bull Exp Biol Med* 2004;138:63-64. [Article in English, Russian]

The effects of extracts of *Rhodiola rosea* radix on blood levels of inflammatory C-reactive protein and creatinine kinase were studied in healthy untrained volunteers before and after exhausting exercise. *Rhodiola rosea* extract exhibited an antiinflammatory effect and protected muscle tissue during exercise.

Antidiabetic effect of Pycnogenol French maritime pine bark extract in patients with diabetes type II.

Liu X, Wei J, Tan F, et al. *Life Sci* 2004;75:2505-2513.

A double-blind, placebo-controlled, randomized, multi-center study was performed with 77 diabetes type II patients to investigate anti-diabetic effects of the French maritime pine bark extract, Pycnogenol. Supplementation with 100 mg Pycnogenol for 12 weeks, during which a standard anti-diabetic treatment was continued, significantly lowered plasma glucose levels as compared to placebo. HbA1(c) was also lowered; however, the difference as compared to placebo was statistically significant only for the first month. In the Pycnogenol-group endothelin-1 was significantly decreased, while 6-ketoprostaglandin F(1a) in plasma was elevated compared to placebo. Nitric oxide levels in plasma increased during treatment in both groups, but, differences did not reach statistical significance. Pycnogenol was well-tolerated with ECG, electrolytes, creatinine and blood urea nitrogen remaining unchanged in both groups. Mild and transient unwanted effects were reported for both groups without significant differences. Supplementation of Pycnogenol to conventional diabetes treatment lowers glucose levels and improves endothelial function.

Vitamin K, bone turnover, and bone mass in girls.

Kalkwarf HJ, Khoury JC, Bean J, Elliot JG. *Am J Clin Nutr* 2004;80:1075-1080.

BACKGROUND: Vitamin K has been suggested to have a role in bone metabolism, and low vitamin K intake has been related to low bone density and increased risk of osteoporotic fracture. **OBJECTIVE:** The objective of this study was to determine whether phylloquinone (vitamin K(1)) intake and biochemical indicators of vitamin K status are related to bone mineral content (BMC) and markers of bone formation and bone resorption in girls. **DESIGN:** Vitamin K status [plasma phylloquinone concentration and percentage of undercarboxylated osteocalcin (%ucOC)] was measured at baseline in a study of 245 healthy girls aged 3-16 y. Cross-linked N-telopeptide of type 1 collagen (NTx) breakdown, osteocalcin, and bone-specific alkaline phosphatase were measured to reflect bone resorption and formation. BMC of the total body, lumbar spine, and hip and dietary phylloquinone intake were measured annually for 4 y. **RESULTS:** Phylloquinone intake (median: 45 microg/d) was not consistently associated with bone turnover markers or BMC. Better vitamin K status (high plasma phylloquinone and low %ucOC) was associated with lower bone resorption and formation. Plasma phylloquinone was inversely associated with NTx and osteocalcin concentrations ($P < 0.05$), and %ucOC was positively associated with NTx and bone-specific alkaline phosphatase concentrations ($P < 0.05$). Indicators of vitamin K status were not consistently associated with current BMC or gain in BMC over the 4-y study period. **CONCLUSIONS:** Better vitamin K status was associated with decreased bone turnover in healthy girls consuming a typical US diet. Randomized phylloquinone supplementation trials are needed to further understand the potential benefits of phylloquinone on bone acquisition in growing children.

Alpha lipoic acid inhibits human T-cell migration: Implications for multiple sclerosis.

Marracci GH, McKeon GP, Marquardt WE, et al. *J Neurosci Res* 2004;78:362-370.

We have demonstrated previously the ability of the antioxidant alpha lipoic acid (ALA) to suppress and treat a model of multiple sclerosis (MS), relapsing experimental autoimmune encephalomyelitis (EAE). We describe the effects of ALA and its reduced form, dihydrolipoic acid (DHLA), on the transmigration of human Jurkat T cells across a fibronectin barrier in a transwell system. ALA and DHLA inhibited migration of Jurkat cells in a dose-dependent fashion by 16-75%. ALA and DHLA reduced matrix metalloproteinase-9 (MMP-9) activity by 18-90% in Jurkat cell supernatants. GM6001, a synthetic inhibitor of MMP, reduced Jurkat cell migration, but not as effectively as ALA and DHLA did. Both ALA and DHLA downmodulated the surface expression of the alpha4beta1 integrin (very late activation-4 antigen; VLA-4), which binds fibronectin and its endothelial cell ligand vascular cell adhesion molecule-1 (VCAM-1). Moreover, ALA, but not DHLA, reduced MMP-9-specific mRNA and extracellular MMP-9 from Jurkat cells and their culture supernatants as detected by relative reverse transcriptase-polymerase chain reaction (RT-PCR) and enzyme-linked immunosorbent assay (ELISA), respectively. ALA and DHLA inhibited Jurkat cell migration and have different mechanisms for inhibiting MMP-9 activity. These data, coupled with its ability to treat relapsing EAE, suggest that ALA warrants investigation as a therapy for MS.

Green tea (*Camellia sinensis*) extract does not alter cytochrome p450 3A4 or 2D6 activity in healthy volunteers.

Donovan JL, Chavin KD, Devane CL, et al. *Drug Metab Dispos* 2004;32:906-908.

Green tea extract is a widely used dietary supplement. The objective of this study was to assess the influence of a decaffeinated green tea (DGT; *Camellia sinensis*) extract on the activity of the drug-metabolizing enzymes cytochrome P-450 2D6 and 3A4. Probe drugs dextromethorphan (30 mg, CYP2D6 activity) and alprazolam (ALPZ; 2 mg, CYP3A4 activity) were administered orally to healthy volunteers (n = 11) at baseline, and again after treatment with four DGT capsules/day for 14 days. Each DGT capsule contained 211 +/- 25 mg of green tea catechins and <1 mg of caffeine. Dextromethorphan metabolic ratios (DMRs) and alprazolam pharmacokinetics were determined at baseline and after DGT treatment. There were no significant differences in ALPZ pharmacokinetics at baseline and after DGT treatment (all P values >= 0.05; maximum concentration in plasma, 33 +/- 8 versus 34 +/- 13 ng/ml; time to reach maximum concentration in plasma, 1.4 +/- 1.2 versus 1.4 +/- 1.2 h; area under the plasma concentration versus time curve, 480 +/- 119 versus 510 +/- 107 h. ng. ml(-1); half-life of elimination, 12.3 +/- 1.7 versus 13.1 +/- 3.4 h). The DMR was 0.053 +/- 0.045 at baseline and 0.041 +/- 0.032 after DGT supplementation (P > 0.05). The plasma concentration of the green tea flavonoid, (-)-epigallocatechin gallate, reached 1.3 +/- 1.8 microM 2 h after DGT treatment. Our results indicate that DGT is unlikely to alter the disposition of medications primarily dependent on the CYP2D6 or CYP3A4 pathways of metabolism.

Further evaluation of docosahexaenoic acid in patients with retinitis pigmentosa receiving vitamin A treatment: subgroup analyses.

Berson EL, Rosner B, Sandberg MA, et al. *Arch Ophthalmol* 2004;122:1306-1314.

OBJECTIVE: To determine whether docosahexaenoic acid will slow the course of retinal degeneration in subgroups of patients with retinitis pigmentosa who are receiving vitamin A. **DESIGN:** A cohort of 208 patients with retinitis pigmentosa, aged 18 to 55 years, were randomly assigned to 1200 mg of docosahexaenoic acid plus 15 000 IU/d of vitamin A given as retinyl palmitate (DHA + A group) or control fatty acid plus 15 000 IU/d of vitamin A (control + A group) and followed up over 4 years. Seventy percent of the patients in each group were taking vitamin A, 15 000 IU/d, prior to entry. We compared rates of decline in ocular function in the DHA + A vs control + A groups among the subgroups defined by use or nonuse of vitamin A prior to entry. We also determined whether decline in ocular function was related to red blood cell phosphatidylethanolamine docosahexaenoic acid level, dietary omega-3 fatty acid intake, or duration of vitamin A use. Main outcome measures were Humphrey Field Analyzer visual field sensitivity, 30-Hz electroretinogram amplitude, and visual acuity. **RESULTS:** Among patients not taking vitamin A prior to entry, those in the DHA + A group had a slower decline in field sensitivity and electroretinogram amplitude than those in the control + A group over the first 2 years ($P = .01$ and $P = .03$, respectively); these differences were not observed in years 3 and 4 of follow-up or among patients taking vitamin A prior to entry. In the entire cohort, red blood cell phosphatidylethanolamine docosahexaenoic acid level was inversely related to rate of decline in total field sensitivity over 4 years (test for trend, $P = .05$). This was particularly evident over the first 2 years among those not on vitamin A prior to entry (test for trend, $P = .003$). In the entire control + A group, dietary omega-3 fatty acid intake was inversely related to loss of total field sensitivity over 4 years (intake, <0.20 vs $> \text{or} = 0.20$ g/d; P

$= .02$). The duration of vitamin A supplementation prior to entry was inversely related to rate of decline in electroretinogram amplitude ($P = .008$). **CONCLUSIONS:** For patients with retinitis pigmentosa beginning vitamin A therapy, addition of docosahexaenoic acid, 1200 mg/d, slowed the course of disease for 2 years. Among patients on vitamin A for at least 2 years, a diet rich in omega-3 fatty acids ($> \text{or} = 0.20$ g/d) slowed the decline in visual field sensitivity.

Betaine in human nutrition.

Craig SA. *Am J Clin Nutr* 2004;80:539-549.

Betaine is distributed widely in animals, plants, and microorganisms, and rich dietary sources include seafood, especially marine invertebrates (approximately 1%); wheat germ or bran (approximately 1%); and spinach (approximately 0.7%). The principal physiologic role of betaine is as an osmolyte and methyl donor (transmethylation). As an osmolyte, betaine protects cells, proteins, and enzymes from environmental stress (eg, low water, high salinity, or extreme temperature). As a methyl donor, betaine participates in the methionine cycle—primarily in the human liver and kidneys. Inadequate dietary intake of methyl groups leads to hypomethylation in many important pathways, including 1) disturbed hepatic protein (methionine) metabolism as determined by elevated plasma homocysteine concentrations and decreased S-adenosylmethionine concentrations, and 2) inadequate hepatic fat metabolism, which leads to steatosis (fatty accumulation) and subsequent plasma dyslipidemia. This alteration in liver metabolism may contribute to various diseases, including coronary, cerebral, hepatic, and vascular diseases. Betaine has been shown to protect internal organs, improve vascular risk factors, and enhance performance. Databases of betaine content in food are being developed for correlation with population health studies. The growing body of evidence shows that betaine is an important nutrient for the prevention of chronic disease.

Carotenoids, vitamin A and risk of adenomatous polyp recurrence in the polyp prevention trial.

Steck-Scott S, Forman MR, Sowell A, et al. *Int J Cancer* 2004;112:295-305.

One trial reported beta-carotene supplementation was protective of adenomatous polyp recurrence in nonsmokers. We now examine the relation of serum and dietary carotenoids and vitamin A to adenomatous polyp recurrence in a subcohort of 834 participants in a low fat, high fiber, high fruit and vegetable dietary intervention, the Polyp Prevention Trial. Multivariate odds ratio (OR) and 95% confidence intervals (CI) of polyp recurrence were obtained using baseline or the average (first 3 years of the trial) carotenoid and vitamin A values after adjustment for covariates. Compared to the lowest quartile of baseline alpha-carotene concentrations, the OR of multiple polyp recurrence for the highest quartile was 0.55 (95% CI = 0.30-0.99) and the OR of right-sided recurrence was 0.60 (95% CI = 0.37-0.95). Baseline dietary intakes of alpha-carotene and vitamin A from food with/without supplements were inversely associated with any recurrence (p for linear trend = 0.03-alpha-carotene; $p = 0.004$ and $p = 0.007$ -intakes of vitamin A). Compared to the lowest quartile of averaged beta-carotene concentrations, the OR of multiple adenomas for the highest quartile was 0.40 (95% CI = 0.22-0.75) with an inverse trend ($p = 0.02$). The risk was inversely related to averaged: alpha-carotene concentrations and right-sided polyps; alpha-carotene intake and recurrence of any, multiple and right-sided polyps; beta-carotene intake and multiple adenoma recurrence; vitamin A from food (with supplements) and each adverse endpoint. Thus, alpha-carotene and vitamin A may protect against recurrence in nonsmokers and nondrinkers or be indicative of compliance or another healthy lifestyle factor that reduces risk.

Celiac disease and its endocrine and nutritional implications on male reproduction.

Stazi AV, Mantovani A. *Minerva Med* 2004;95:243-254. [Article in Italian]

The problem of the interference of celiac disease (CD) with the male reproductive system is made evident both by the recognized adverse effects on female reproduction and by the multifactorial nature of the disease. It is important to consider CD as a multifactorial condition since its diverse effects can be modulated, besides gluten, by different concurrent genetic and environmental factors. The male CD patient has a greater risk of infertility and other reproductive disturbances, as well as a greater incidence of hypoandrogenism. In this paper the problems of CD associated to endocrine disorders and to deficiencies of micronutrients are discussed. Affected males show a picture of tissue resistance to androgens. Moreover, attention should be paid to increases of FSH and prolactin; these are not associated to infertility and/or impotence, but they may indicate an imbalance at hypothalamus-pituitary level, with general effects on health: an example is the increased risk of male osteoporosis in CD patients. Hormone alterations are reversible upon start of the gluten-free diet, emphasizing the importance of early diagnosis; this should be performed in the case of clinical suspicion, e.g., unexplained hypoandrogenism. As regards nutritional aspects, the folic acid deficiency of CD can affect rapidly proliferating tissues, such as the embryo and the seminiferous epithelium. More attention should be paid to deficiencies of fat-soluble vitamins, such as A and E, observed in CD. Vitamin A is important for Sertoli cell function as well as for early spermatogenic phases. Vitamin E supports the correct differentiation and function of epididymal epithelium, spermatid maturation and secretion of proteins by the prostate. Therefore, CD male patients should be considered as vulnerable subjects; thus, the detection of early biomarkers of andrological or endocrinological dysfunctions should trigger timely strategies for prevention and treatment.

Association of serum total homocysteine with the extent of ischemic heart disease in a Mediterranean cohort.

Vrentzos G, Papadakis JA, Malliaraki N, et al. *Angiology* 2004;55:517-524.

High total homocysteine (tHcy) concentrations increase coronary disease risk. Therefore, the authors examined the relation between tHcy concentrations and the number of stenotic arteries in patients with ischemic heart disease (IHD). They enrolled 155 patients with IHD (135 men) who had undergone selective coronary angiography during the previous 2 years. These patients were divided into 4 groups according to the number of vessels (0, 1, 2, and 3) with $\geq 70\%$ stenosis. They also reviewed the major coronary risk factors for each patient (age, gender, hypertension, diabetes mellitus, dyslipidemia, cigarette smoking, obesity), and measured serum concentrations of tHcy, folate, vitamin B12 and lipids. There was a significant positive correlation ($r_s = 0.19$; $p = 0.017$; $n = 155$) between tHcy serum concentration and the extent of coronary atherosclerosis, expressed by the number of coronary arteries with significant stenosis. Moreover, the number of affected vessels displayed a significant positive correlation with the presence of diabetes mellitus ($r_s = 0.30$; $p < 0.0001$; $n = 155$) and serum concentrations of lipoprotein (a) ($r_s = 0.25$; $p < 0.05$; $n = 67$) and a negative correlation with apolipoprotein A-I serum concentration ($r_s = -0.27$; $p < 0.01$; $n = 67$). In this study, the serum concentrations of tHcy correlated with the extent of coronary atherosclerosis, independently of other classical risk factors, with the exception of diabetes mellitus.

Vitamin B6 level is associated with symptoms of depression.

Hvas AM, Juul S, Bech P, Nexø E. *Psychother Psychosom* 2004 ;73:340-343.

BACKGROUND: A low level of vitamin B6 might theoretically cause depression as vitamin B6 is a cofactor in the tryptophan-serotonin pathway. In the present study, we examined the association between depression and the phosphate derivative of vitamin B6 in plasma, pyridoxal phosphate (PLP). **METHODS:** In 140 individuals, symptoms of depression were evaluated by the Major Depression Inventory, and biochemical markers of vitamin B deficiency were measured. **RESULTS:** We found that 18 (13%) individuals were depressed. A low plasma level of PLP was significantly associated with the depression score ($p=0.002$). No significant association was found between depression and plasma vitamin B12 ($p=0.13$), plasma methylmalonic acid ($p=0.67$), erythrocyte folate ($p=0.77$), and plasma total homocysteine ($p=0.16$). **CONCLUSION:** Our study suggests that a low level of plasma PLP is associated with symptoms of depression. Randomized trials are now justified and needed in order to examine whether treatment with vitamin B6 may improve symptoms of depression.

Efficacy and safety of Vitamin C vaginal tablets in the treatment of non-specific vaginitis; A randomised, double blind, placebo-controlled study.

Petersen EE, Magnani P. *Eur J Obstet Gynecol Reprod Biol* 2004;117:70-75.

Methods: This was a randomised, double-blind, placebo-controlled study to evaluate the efficacy and safety of Vitamin C vaginal tablets (250mg) given once a day in patients suffering from non-specific vaginitis. The total length of the study was 20 days, including a treatment phase of 6 days. The primary end-point was the presence in the two groups of non-specific vaginitis 1 and 2 weeks after the end of treatment, as assessed by at least 3 out of the 4 characteristic symptoms: discharge, fishy odour, vaginal [Formula: see text], and presence of clue cells. Secondary end-points were the individual symptoms and signs, above reported, and pruritus, fever, superinfections, microscopic findings on vaginal smear, and colposcopy. **Patients:** One hundred female patients aged 18 years or older and suffering from non-specific vaginitis were included in the study after giving their informed consent. Fifty were randomised to the active treatment and 50 to placebo. Seven patients, three in the Vitamin C group and four in the placebo group, were lost to follow-up and did not complete the treatment period. Two patients in the active group showed protocol deviations (age under 18 years and HIV-positive, respectively). The two groups resulted comparable for demographics, history and baseline clinical picture. **Results:** A cluster analysis of the four main symptoms showed a statistically significant difference between the active group and the placebo group; significantly more patients were still affected by non-specific vaginitis after placebo (35.7%) compared to patients treated with Vitamin C tablets (14.0%). The meaningful secondary variable, referring to the microscopic examination of vaginal smear, supported the trend for efficacy in the Vitamin C treated group. The clue cells disappeared in 79% of patients treated with the drug and in 53% of patients on placebo. Similarly, bacteria disappeared in 77 and 54%, respectively, while lactobacilli reappeared in 79.1 and 53.3%, respectively.

Vaginal pH values decreased significantly in both groups, but the frequency rate of subjects with [Formula: see text], as measured 1 week after the drug discontinuation, was significantly lesser in the Vitamin C group (16.3%) than in the placebo group (38.6%). Adverse events occurred in four patients, two on placebo (pruritus, cystitis) and two on Vitamin C (two candidiasis).

Lycopene: modes of action to promote prostate health.

Wertz K, Siler U, Goralczyk R. *Arch Biochem Biophys* 2004;430:127-134.

Epidemiological evidence strongly suggests that lycopene consumption contributes to prostate cancer risk reduction. Preclinical studies show that lycopene acts via different mechanisms, which have the potential to cooperate in reducing the proliferation of normal and cancerous prostate epithelial cells, in reducing DNA damage, and in improving oxidative stress defense. The mechanisms include inhibition of prostatic IGF-I signaling, IL-6 expression, and androgen signaling. Moreover, lycopene improves gap-junctional communication and induces phase II drug metabolizing enzymes as well as oxidative defense genes. These findings provide plausible explanations for the epidemiological findings how lycopene can contribute to reduced prostate cancer risk. The novel finding that lycopene reduces local androgen signaling in the prostate suggests also efficacy in prevention of benign prostate hyperplasia. Intervention trials in humans are required to finally prove clinical efficacy of the lycopene molecule in prostate health.

Soy isoflavone intake lowers serum LDL cholesterol: a meta-analysis of 8 randomized controlled trials in humans.

Zhuo XG, Melby MK, Watanabe S. *J Nutr* 2004;134:2395-2400.

Clinical trials have noted hypocholesterolemic effects of soy protein intake, but the components responsible are not known. This meta-analysis of 8 randomized controlled trials was conducted to more precisely evaluate the effects of isoflavones on blood LDL cholesterol concentration independently of soy protein level. PubMed was searched for English-language randomized controlled trial articles published from 1966 to 2003 that described the effects of soy protein isolate (SPI) intake with measured isoflavone levels on blood lipids in humans using the search terms soy protein, isoflavones, and cholesterol. From 31 articles identified by the search, 8 articles (with 10 low vs. high isoflavone comparisons) were selected for the meta-analysis. Subjects in each comparison consumed similar dietary fat, cholesterol, and fiber; the reported body weight of subjects did not change significantly during treatment. Serum LDL cholesterol concentration in subjects who consumed SPI (mean 50 g/d) with high isoflavone content (mean intake 96 mg/d) decreased by 0.15 mmol/L (95% CI: 0.08 to 0.23 mmol/L; $P < 0.0001$) compared with those who consumed the same SPI level with low isoflavone content (mean intake 6 mg/d). Decreases in serum LDL cholesterol concentration in hypercholesterolemic and normocholesterolemic subjects were 0.18 mmol/L (95% CI: 0.01 to 0.35 mmol/L; $P = 0.03$) and 0.14 mmol/L (95% CI: 0.06, 0.23 mmol/L; $P = 0.0008$), respectively. With identical soy protein intake, high isoflavone intake led to significantly greater decreases in serum LDL cholesterol than low isoflavone intake, demonstrating that isoflavones have LDL cholesterol-lowering effects independent of soy protein.

Magnesium treatment for sudden hearing loss.

Nageris BI, Ulanovski D, Attias J. *Ann Otol Rhinol Laryngol* 2004;113:672-675.

Magnesium treatment has been repeatedly shown to reduce the incidence of both temporary and permanent noise-induced hearing loss. We hypothesized that it might also improve the permanent threshold shift in patients with acute-onset hearing loss. In a prospective, randomized, double-blind, placebo-controlled trial, 28 patients with idiopathic sudden sensorineural hearing loss were treated with either steroids and oral magnesium (study group) or steroids and a placebo (control group). Compared to the controls, the magnesium-treated group had a significantly higher proportion of patients with improved hearing (>10 dB hearing level) across all frequencies tested, and a significantly greater mean improvement in all frequencies. Analysis of the individual data confirmed that more patients treated with magnesium experienced hearing improvement, and at a larger magnitude, than control subjects. Magnesium is a relatively safe and convenient adjunct to steroid treatment for enhancing the improvement in hearing, especially in the low-tone range, in patients with sudden sensorineural hearing loss.

Artemisinin induces apoptosis in human cancer cells.

Singh NP, Lai HC. *Anticancer Res* 2004;24:2277-2280.

BACKGROUND: Artemisinin is a chemical compound extracted from the wormwood plant, *Artemisia annua* L. It has been shown to selectively kill cancer cells in vitro and retard the growth of implanted fibrosarcoma tumors in rats. In the present research, we investigated its mechanism of cytotoxicity to cancer cells. **MATERIALS AND METHODS:** Molt-4 cells, in complete RPMI-1640 medium, were first incubated with 12 microM of human holotransferrin at 37 degrees C in a humid atmosphere of 5% CO₂ for one hour. This enhanced the iron supply to the cells. The cells were then pelleted and transferred to a complete RPMI-1640 containing 200 microM of an analog dihydroartemisinin (DHA) and incubation was started (0 h). In addition, some culture samples were treated with holotransferrin alone and some (controls) were assayed without neither holotransferrin nor DHA treatment. Cells were counted and DNA diffusion assay was used to evaluate apoptosis and necrosis in each sample at 0 h and at 1, 2, 4 and 8 h of incubation. **RESULTS:** DHA treatment significantly decreased cell counts and increased the proportion of apoptosis in cancer cells compared to controls ($\chi^2=4.5$, $df=1$, $p<0.035$). Addition of holotransferrin significantly further decreased cell counts ($\chi^2=4.5$, $df=1$, $p<0.035$) and increased apoptosis ($\chi^2=4.5$, $df=1$, $p<0.035$). No necrotic cells were observed. **CONCLUSION:** This rapid induction of apoptosis in cancer cells after treatment with DHA indicates that artemisinin and its analogs may be inexpensive and effective cancer agents.

Safety of Hypericum extract in mildly to moderately depressed outpatients; A review based on data from three randomized, placebo-controlled trials.

Trautmann-Sponsel RD, Dienel A. *J Affect Disord* 2004;82:303-307.

Rationale: Hypericum extracts have been regarded as antidepressant drugs without specific side effects by patients, medical professionals and researchers alike. Recently there has been discussion about potential interactions between St. John's wort and other drugs. **Objectives:** To investigate the tolerability of Hypericum extract by comparing adverse event rates observed during clinical trials with the herbal drug to those observed under placebo and synthetic antidepressants. **Methods:** A data review was performed based on the original data of three double-blind, randomised multicenter trials, during which 594 outpatients suffering from mild to moderate depression according to DSM-IV criteria received 3 x 300 mg/day Hypericum extract (WS(R) 5570, WS(R) 5572, WS(R) 5573) or placebo over a double-blind treatment period of 6 weeks. For the pooled data from the three trials, the risk ratios and risk differences versus placebo for single and grouped adverse events were determined along with their 95% confidence intervals. The data were inspected for relevant differences between Hypericum extract and placebo and were compared to trials involving the administration of several synthetic antidepressants. **Results:** For the pooled data of the three trials, the percentage of patients with any adverse events under Hypericum extract exposition was comparable to placebo. The drug was also found to be devoid of effects of sedation, anticholinergic reactions, gastrointestinal disturbances and sexual dysfunction often found in patients treated with tricyclic antidepressants or selective serotonin reuptake inhibitors. **Conclusion:** The analysis did not reveal any specific effects of Hypericum extract.

Effect of a Mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial.

Esposito K, Marfella R, Ciotola M, et al. *JAMA* 2004;292:1440-1446.

CONTEXT: The metabolic syndrome has been identified as a target for dietary therapies to reduce risk of cardiovascular disease; however, the role of diet in the etiology of the metabolic syndrome is poorly understood. **OBJECTIVE:** To assess the effect of a Mediterranean-style diet on endothelial function and vascular inflammatory markers in patients with the metabolic syndrome. **DESIGN, SETTING, AND PATIENTS:** Randomized, single-blind trial conducted from June 2001 to January 2004 at a university hospital in Italy among 180 patients (99 men and 81 women) with the metabolic syndrome, as defined by the Adult Treatment Panel III. **INTERVENTIONS:** Patients in the intervention group (n = 90) were instructed to follow a Mediterranean-style diet and received detailed advice about how to increase daily consumption of whole grains, fruits, vegetables, nuts, and olive oil; patients in the control group (n = 90) followed a prudent diet (carbohydrates, 50%-60%; proteins, 15%-20%; total fat, <30%). **MAIN OUTCOME MEASURES:** Nutrient intake; endothelial function score as a measure of blood pressure and platelet aggregation response to L-arginine; lipid and glucose parameters; insulin sensitivity; and circulating levels of high-sensitivity C-reactive protein (hs-CRP) and interleukins 6 (IL-6), 7 (IL-7), and 18 (IL-18). **RESULTS:** After 2 years, patients following the Mediterranean-style diet consumed more foods rich in monounsaturated fat, polyunsaturated fat, and fiber and had a lower ratio of omega-6 to omega-3 fatty acids. Total fruit, vegetable, and nuts intake (274 g/d), whole grain intake (103 g/d), and olive oil consumption (8 g/d) were also significantly higher in the intervention group (P<.001). The level of physical activity increased in both groups by approximately 60%, without difference between groups (P =.22). Mean (SD) body weight decreased more in patients in the intervention group (-4.0 [1.1] kg) than in those in the control group (-1.2 [0.6] kg)

(P<.001). Compared with patients consuming the control diet, patients consuming the intervention diet had significantly reduced serum concentrations of hs-CRP (P =.01), IL-6 (P =.04), IL-7 (P = 0.4), and IL-18 (P = 0.3), as well as decreased insulin resistance (P<.001). Endothelial function score improved in the intervention group (mean [SD] change, +1.9 [0.6]; P<.001) but remained stable in the control group (+0.2 [0.2]; P =.33). At 2 years of follow-up, 40 patients in the intervention group still had features of the metabolic syndrome, compared with 78 patients in the control group (P<.001). **CONCLUSION:** A Mediterranean-style diet might be effective in reducing the prevalence of the metabolic syndrome and its associated cardiovascular risk.

Coenzyme Q10 serum levels in Huntington's disease.

Andrich J, Saft C, Gerlach M, et al. *J Neural Transm Suppl* 2004;68:S111-S116.

Mitochondrial dysfunction contributes to the neurodegenerative process in Huntington's disease (HD). Coenzyme Q10 (CoQ10) enhances mitochondrial complex I activity and may therefore provide a therapeutic benefit in HD. We compared serum CoQ10 levels of previously untreated and treated HD patients with those of healthy controls. CoQ10 did not significantly (ANCOVA F(dF 2, dF 55) = 2.57; p=0.086) differ between all three groups. However, the post hoc analysis showed no significant (p = 0.4) difference between treated HD patients ([CoQ10]: 88.12 [mean]±24.44 [SD], [range] 48.75-146.32 [pg/million platelets]) and controls (93.71±20.72, 65.31-157.94), however previously untreated HD patients (70.10±21.12, 38.67-106.14) had marked (p = 0.051) lower CoQ10 results than treated HD patients and controls (p = 0.017). Our results support that CoQ10 supplementation in HD patients may reduce impaired mitochondrial function in HD.

Fish intake is associated with a reduced progression of coronary artery atherosclerosis in postmenopausal women with coronary artery disease.

Erkkila AT, Lichtenstein AH, Mozaffarian D, Herrington DM. *Am J Clin Nutr* 2004;80:626-632.

BACKGROUND: Higher intakes of fish and n-3 fatty acids are associated with a reduced risk of cardiovascular events and mortality. However, limited data exist on the effect of fish intake on actual measures of progression of coronary artery atherosclerosis. **OBJECTIVE:** The aim was to examine the association between fish intake and the progression of coronary artery atherosclerosis in women with coronary artery disease. **DESIGN:** This was a prospective cohort study of postmenopausal women (n = 229) participating in the Estrogen Replacement and Atherosclerosis trial. Usual fish intake was estimated at baseline with a food-frequency questionnaire. Quantitative coronary angiography was performed at baseline and after 3.2 +/- 0.6 (x +/- SD) y to evaluate changes in the mean minimum coronary artery diameter, the mean percentage of stenosis, and the development of new coronary lesions. **RESULTS:** Compared with lower fish intakes, consumption of > or =2 servings of fish or > or =1 serving of tuna or dark fish per week was associated with smaller increases in the percentage of stenosis (4.54 +/- 1.37% compared with -0.06 +/- 1.59% and 5.12 +/- 1.48% compared with 0.35 +/- 1.47%, respectively; P < 0.05 for both) in diabetic women after adjustments for age, cardiovascular disease risk factors, and dietary intakes of fatty acids, cholesterol, fiber, and alcohol. These associations were not significant in nondiabetic women. Higher fish consumption was also associated with smaller decreases in minimum coronary artery diameter and fewer new lesions. **CONCLUSIONS:** Consumption of fish is associated with a significantly reduced progression of coronary artery atherosclerosis in women with coronary artery disease.

The clinical study on the adjunctive effects of aqueous extract from Coptis root for the treatment of chronic periodontitis.

Wu YH, Jiang GS, Zhagn SZ, et al. *Shanghai Kou Qiang Yi Xue* 2004;13:252-255. [Article in Chinese]

PURPOSE: To make a therapeutic membrane with aqueous extract from coptis root and explore its adjunctive effects for treating chronic periodontitis. **METHODS:** Drug membrane from coptis root aqueous extract was developed; 4 teeth in 30 patients with moderate to advanced periodontitis were randomly divided into four groups: coptis root membrane, iodine glycerin, single drug membrane and blank control group. All parameters including plaque index(PI), probing depth(PD), attachment loss(AL) and bleeding on probing(BOP) were measured at baseline, 4 and 7 weeks after treatment. Analysis of variance and chi-square test were carried out for analysis. **RESULTS:** In all four groups, there were significant differences of PD, AL, BOP between baseline and 4,7 weeks after treatment(P<0.05), the treatment effect of coptis root membrane was significantly superior to that of other three groups(P<0.05). Moreover, all the parameters improved continuously. **CONCLUSION:** Use of coptis root membrane as an adjunctive method after scaling can significantly improve the treatment effect of periodontitis.