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Nutritional support for mental health

Editorial

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The human brain consumes about 20% of the energy at rest, although it represents only 2 % of the body mass. Brain cells need two times more energy than other cells in the body; the generation of the electric signal for the communication throughout the nervous system uses half of it. Glucose and oxygen have to be transported in sufficient quantities together with the micronutrients that are used for its metabolism. A shortage of one of the required nutrients may have

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An alliance of the European food supplement industry

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negative consequences for the performance of the brain. It is, therefore, not surprising that dietary supplements improve mental health in circumstances where the supply is short. This may be the case for disabled people, for elderly, or for persons on a restrictive diet.

In a double-blind, randomized, placebo-controlled trial 225 patients aged 65 and older received either a placebo or a supplement providing 995 kcal and 100% of the reference nutrient intake for vitamins A, C, E, B₁, B₂, B₆, B₁₂, folic acid, niacin, biotin, pantothenic acid, potassium, magnesium, calcium, phosphorous, iron, zinc, iodine, copper, manganese, and selenium daily during 6 weeks. The main end points were nutritional status and quality of life that has been assessed at the beginning, 6 weeks and 6 months thereafter by means of the 36-item Short Form Survey (SF-36). This questionnaire consists of four physical and mental components each comparing the relative burden of diseases. Among the mental components, the scale 'social function' reflecting interference with normal social activities was significantly improved in the supplemented group in addition to two components of physical health. Thus, the quality of life for older people could substantially be enhanced by improving the nutritional status (Gariballa S, Forster S. Dietary supplementation and quality of life of older patients: a randomized, double-blind, placebo-controlled trial. *J Am Geriatr Soc.* 2007; 55: 2030-4).

Among all the nutrients, folic acid and n-3 fatty acids are of special interest. Although the former is consumed in a great number of food items, there is no major source with the exception of the liver. Nevertheless, methylation of proteins and phospholipids are crucial for a proper functioning of the brain. Several studies found an inverse relationship between folate intake and the impairment of brain diseases such as dementia. Thus, folate supplementation either alone or in combination with other B-vitamins may improve memory loss during ageing (Mischoulon D, Raab MF. The role of folate in depression and dementia. *J Clin Psychiatry* 2007; 68 Suppl 10:28-33).

A meta-analysis combining placebo-controlled clinical trials with n-3 fatty acids supports the use of n-3 PUFAs in the treatment of mood disorders. Furthermore, n-3 PUFAs reduce the symptoms of depression and they might be beneficial in anxiety and attentional disorders as well. One major conclusion of this review is the safety aspect: none of the studies reported serious side effects of supplemented n-3 PUFAs (Ross BM, Seguin J, Sieswerda LE. Omega-3 fatty acids as treatments for mental illness: which disorder and which fatty acid? *Lipids Health Dis.* 2007; 6: 21).

Taken all this evidence together it can be concluded that the brain deserves more attention in order to prevent attention deficits.

U. Moser, Editor

POLYHERBAL FOR THE RELIEF OF OSTEOARTHRITIS

Reparagen and glucosamine sulfate improve adverse conditions of osteoarthritis

Intervention

The efficacy and safety of reparagen, a polyherbal consisting of 300 mg of vincaria (*Uncaria guianensis*) and 1500 mg of RNI 249 (*Lepidium meyenii*), was compared to glucosamine sulfate in osteoarthritis subjects in a randomized, double-blind study. Volunteers received either glucosamine sulfate (n =47, 1500

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mg/day) or reparaGen (n =48, 1800 mg/day), administered orally, twice daily. Primary efficacy variable: response rate based on a 20% improvement in WOMAC pain scores. Additional outcomes: WOMAC scores for pain, stiffness and function, visual analog score (VAS) for pain, with assessments at 1, 2, 4, 6 and 8 weeks.

Results: The response rates (20% reduction in WOMAC pain) were substantial for both glucosamine (89%) and reparaGen (94%) and supported by investigator and subject assessments. Using related criteria response rates to reparaGen were favorable when compared to glucosamine. Compared to baseline both treatments showed significant benefits in WOMAC and VAS outcomes within one week ($P < 0.05$), with a similar, progressive improvement over the course of the 8 weeks treatment protocol (45-62% reduction in WOMAC or VAS scores).

Tolerability was excellent, no serious adverse events were noted and safety parameters were unchanged. Rescue medication use was significantly lower in the reparaGen group ($p < 0.01$) at each assessment period. Serum IGF-1 levels were unaltered by treatments.

Conclusion

ReparaGen and glucosamine sulfate produced a steady reduction in osteoarthritis symptoms, particularly pain, with continued improvements upon sustained treatment. Use of the rescue medication was significantly less in reparaGen subjects, but otherwise responses were comparable between reparaGen and glucosamine sulfate groups. Both investigational agents were well tolerated and safe.

Source

Mehta K, Gala J, Bhasale S, Naik S, Modak M, Thakur H, Deo N, Miller MJ. Comparison of glucosamine sulfate and a polyherbal supplement for the relief of osteoarthritis of the knee: a randomized controlled trial [ISRCTN25438351]. *BMC Complement Altern Med.* 2007; 7: 34

SUPPLEMENTS TO REDUCE RISK FOR CHRONIC DISEASES

Supplement users are more likely to have optimal concentrations of chronic disease-related biomarkers

Observation

Information for this cross-sectional study was obtained by online questionnaires and physical examination (fasting blood, blood pressure, body weight) from a convenience sample of long-term users of multiple dietary supplements manufactured by Shaklee Corporation (Multiple Supp users, n =278). Data for non-users (No Supp users, n =602) and multivitamin/mineral supplement users (Single Supp users, n =176) were obtained from the National Health and Nutrition Examination Survey (NHANES) 2001-2002 and NHANES III 1988-1994. Logistic regression methods were used to estimate odds ratios with 95% confidence intervals.

Dietary supplements consumed on a daily basis by more than 50% of Multiple Supp users included a multivitamin/mineral, B-complex, vitamin C, carotenoids, vitamin E, calcium with vitamin D, omega-3 fatty acids, flavonoids, lecithin, alfalfa, coenzyme Q10 with resveratrol, glucosamine, and a herbal immune supplement. The majority of women also consumed gamma linolenic acid and a probiotic supplement, whereas men also consumed zinc, garlic, saw palmetto,

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and a soy protein supplement. Serum nutrient concentrations generally increased with increasing dietary supplement use. After adjustment for age, gender, income, education and body mass index, greater degree of supplement use was associated with more favorable concentrations of serum homocysteine, C-reactive protein, high-density lipoprotein cholesterol, and triglycerides, as well as lower risk of prevalent elevated blood pressure and diabetes.

Conclusion

Long-term multiple dietary supplement users are more likely to have optimal concentrations of chronic disease-related biomarkers, and less likely to have suboptimal blood nutrient concentrations, elevated blood pressure, and diabetes compared to non-users and multivitamin/mineral users. These findings should be confirmed by studying the dietary supplement usage patterns, health, and nutritional status of other groups of heavy users of dietary supplements.

Source

Block G, Jensen CD, Norkus EP, Dalvi TB, Wong LG, McManus JF, Hudes ML. Usage patterns, health, and nutritional status of long-term multiple dietary supplement users: a cross-sectional study. *Nutr J.* 2007; 6: 30.

Vitamins lower oxidative DNA damage

Intervention

80 volunteers received either one multivitamin capsule daily for 4 weeks (11 vitamins plus 10 minerals) or a placebo in a double-blind randomized trial. Peripheral blood lymphocytes were isolated from fasting blood samples before and after the intervention. DNA damage (strand breaks and alkali-labile sites) has been detected by the Comet assay and expressed as tail moment (TM). The TM is defined as the product of DNA in the tail and the mean distance of migration in the tail and is calculated by multiplying tail intensity/sum Comet intensity by the tail's center of gravity-peak position. A higher percentage of tail DNA signifies a higher level of DNA damage. Intervention with multivitamins significantly decreased the level of DNA damage: $TM_{Wk0} = 1.63 \pm 0.19$; $TM_{Wk4} = 1.43 \pm 0.18$ ($p=0.03$). Exposing the lymphocytes *ex vivo* to 100 $\mu\text{mol/L}$ H_2O_2 induced the DNA breakage, however less in the supplemented group: $TM_{Wk0} = 2.35 \pm 0.20$; $TM_{Wk4} = 2.11 \pm 0.18$ ($p=0.001$). There was no difference between men and women and in the placebo group the DNA damage did not change between weeks 0 and 4.

Conclusion

This study suggests that the consumption of a multivitamin reduces the oxidative DNA damage and thus the risk of mutations. Although there are some limitations of the study since data about biomarkers and food consumption are lacking, senior residents might benefit from these results. A significant raise in oxidative damage has been found in elderly volunteers (mean age 51 years) compared to a younger sample (mean age 35 years): $TM_{51} = 1.62 \pm 0.15$; $TM_{35} = 0.80 \pm 0.12$.

Source

Ribeiro ML, Arçari DP, Squassoni AC, Pedrazzoli J Jr. Effects of multivitamin supplementation on DNA damage in lymphocytes from elderly volunteers. *Mech Ageing Dev.* 2007; 128: 577-80.

VITAMIN D AND PARATHORMONE IN PUBERTY**High-normal PTH with low-normal 25(OH) vitamin D stores may be beneficial for bones during puberty****Intervention**

119 children (64% female) between the ages of 8 and 13 years received either a calcium supplement (1000 mg) or a placebo for 24 months in a randomized trial. 69 had complete information on diet, 25(OH)D status and bone assessments at the baseline and 24 months of follow-up. The primary objective of the study was to evaluate the effect of sub-optimal serum concentrations of 25(OH)D on whole body bone mass accrual. The children have been divided into 3 groups according their 25(OH)D levels at baseline: low: <18 ng/L; medium: > 18, but ≤34 ng/L; high: >34 ng/L. Annualized gain in bone area, BMC and BMD was determined over the length of follow-up. 25(OH)D was negatively related to the gain in total body bone area ($p = 0.003$), BMC ($p = 0.005$) and BMD ($p = 0.15$). Individuals with consistently low serum 25(OH)D levels had an 8% higher gain in bone area, 11% higher gain in BMC and no difference in BMD compared to those with consistently adequate serum 25(OH)D levels (>34 ng/L) over the follow-up period. Those with low serum 25(OH)D levels had higher PTH ($p = 0.002$), but similar 24-hour urinary calcium excretion compared to those with the highest 25(OH)D levels. There was no association between 25(OH) vitamin D levels and markers of bone formation (osteocalcin) or resorption (deoxypyridinoline) at the baseline or 24 months follow-up or between treatment groups.

Conclusion

Higher normal parathormone level accompanied by lower 25(OH)-vitamin D levels with moderate to high calcium intake appear to have beneficial effects on the accrual of bone area and BMC secondary to growth for the whole body in pubertal children after controlling for gender, race, season measured, Tanner stage of pubertal development and use of calcium supplements.

Source

Tylavsky FA, Ryder KM, Li R, Park V, Womack C, Norwood J, Carbone LD, Cheng S. Preliminary findings: 25(OH)D levels and PTH are indicators of rapid bone accrual in pubertal children. *J Am Coll Nutr.* 2007; 26: 462-70.

NUTRIENTS AS SUPPORTIVE ADJUVANTS OF THERAPIES**β-Carotene, but not α-Tocopherol, reduce severe adverse effects of radiation therapy****Observation**

Head- and Neck Cancer (HNC) patients enrolled in a multicenter, double-blind, placebo-controlled, randomized chemoprevention trial with α-tocopherol and β-carotene supplements were prospectively analyzed for a possible relationship between the occurrence of severe acute adverse effects of radiation therapy and plasma levels or dietary intake of β-carotene and α-tocopherol. Baseline plasma levels of β-carotene and α-tocopherol were 0.14 μmol/l and 31.5 μmol/l (median). The occurrence of severe acute adverse effects of radiation therapy overall was observed in 117 of the 535 patients

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(22%) during radiation therapy. Severe acute adverse effects were more often observed in patients with stage II cancer, in female patients, and in subjects with low dietary β -carotene intake. Severe acute adverse effects to specific sites were observed for 65 patients to the mucosa, for 60 patients to the larynx, and for 25 patients to other sites. A higher dietary intake of β -carotene was associated with approximately 40% lower frequencies of severe acute adverse effects of radiation therapy to specific sites and overall. The association was statistically significant for severe acute adverse effects to the larynx (OR = 0.56, 95% CI = 0.32-0.99) and overall (OR = 0.61, 95% CI = 0.40-0.93), whereas it was of borderline statistical significance for acute adverse effects to the mucosa (OR = 0.62, 95% CI = 0.36-1.07). A similar pattern of inverse relationships was observed between plasma β -carotene and severe acute adverse effects of radiation therapy, although statistical significance level was only achieved for adverse effects to the mucosa (OR = 0.55, 95% CI = 0.32-0.94). Patients randomized in the supplement arm who received both β -carotene and α -tocopherol had fewer severe acute adverse effects during radiation therapy (OR = 0.38, 95% CI = 0.20-0.74). Neither dietary- nor plasma α -tocopherol was associated with the occurrence of severe adverse effects of radiation therapy. Dietary β -carotene was not associated with local recurrence of the HNC (HR = 0.93, 95% CI = 0.63-1.38). On the other hand, patients with plasma β -carotene above the median of 0.14 $\mu\text{mol/l}$ had a significantly lower rate of local recurrence (HR = 0.67, 95% CI = 0.45-0.99). This effect was particularly marked in the supplementation arm of the trial (HR = 0.54, 95% CI = 0.32-0.91). Neither dietary- nor plasma α -tocopherol was associated with local recurrence of the HNC.

Conclusion

A high consumption of fruits and vegetables has been advocated for many years for cancer control. Dietary modifications following this recommendation increase beta carotene intake and its plasma level. Prospective studies suggest beneficial plasma levels above 0.40 $\mu\text{mol/l}$ for β -carotene and of 30 $\mu\text{mol/l}$ for α -tocopherol (Biesalski HK, et al. Antioxidant vitamins in prevention. Clin Nutr. 1997; 16: 151-5) [ed.note]. Subjects with dietary intakes in accordance with these recommendations have, when they develop head and neck cancer, a more favorable response to radiation therapy.

Source

Meyer F, Bairati I, Jobin E, G elinas M, Fortin A, Nabid A, T etu B. Acute adverse effects of radiation therapy and local recurrence in relation to dietary and plasma beta carotene and alpha tocopherol in head and neck cancer patients. Nutr Cancer. 2007; 59: 29-35.

Antioxidants positively interact with radiation therapy

Review

The use of antioxidants during cancer treatment remains controversial since many oncologists take the position that antioxidants by their nature undermine the free radical mechanism of chemotherapy and radiotherapy and should therefore generally be avoided during treatment. For their part, many integrative practitioners believe that antioxidants taken during cancer treatment not only alleviate some of the adverse effects of that treatment but also enhance the efficacy of cancer therapy. Until recently, research attention has focused primarily on the interaction of antioxidants with chemotherapy; relatively little attention has been paid to the interaction of antioxidants with radiotherapy. This article reviews the clinical literature that has addressed whether antioxi-

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Intervention

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dants do in fact interfere with radiation therapy. Studies have variously investigated the use of α -tocopherol for the amelioration of radiation-induced mucositis; pentoxifylline and vitamin E to correct the adverse effects of radiotherapy; melatonin alongside radiotherapy in the treatment of brain cancer; retinol palmitate as a treatment for radiation-induced proctopathy; a combination of antioxidants (and other naturopathic treatments) and external beam radiation therapy as definitive treatment for prostate cancer; and the use of synthetic antioxidants, amifostine, dexrazoxane, and mesna as radioprotectants. With few exceptions, most of the studies draw positive conclusions about the interaction of antioxidants and radiotherapy.

Conclusion

The preponderance of data suggests that antioxidants do not conflict with the effectiveness of radiotherapy and may in fact significantly mitigate the adverse effects of that treatment.

Source

Moss RW. Do antioxidants interfere with radiation therapy for cancer? *Integr Cancer Ther.* 2007; 6: 281-92

Vitamin K improves stability of anticoagulant therapy**Intervention**

200 patients, who used a vitamin K antagonist, were randomized in double-blind, randomized, placebo-controlled trial to receive either phenprocoumon and 100 μ g vitamin K once daily or phenprocoumon and a placebo for 24 weeks. The primary outcome was the percentage of time the International Normalized Ratio (INR) was within the therapeutic range. The time in the therapeutic range was 85.5% in the placebo group and 89.5% in the vitamin K group (adjusted difference 3.6%; 95% CI -0.8% to 8.0%). The time below the therapeutic range was 3.1% in the placebo group and 2.1% in the vitamin K group (adjusted difference -0.7%; 95% CI -2.5% to 1.1%) and the time above the therapeutic range was 11.4% in the placebo group and 8.5% in the vitamin K group (adjusted difference -2.9%; 95% CI -6.9% to 1.1%). The relative risk (RR) of a maximal stability in the vitamin K group compared to the placebo group was 1.8 (95%, CI 1.1–2.7).

Conclusion

Supplementation of vitamin K antagonists with 100 μ g vitamin K improves stability of anticoagulant therapy. Because the risk of side effects is inversely related to anticoagulant stability, such an improvement is likely to reduce the number of bleeding and thrombotic events

Source

Rombouts EK, Rosendaal FR, Van Der Meer FJ. Daily vitamin K supplementation improves anticoagulant stability. *J Thromb Haemost.* 2007; 5: 2043-8.

Vitamin C improves erythropoietin response**Review**

Hemodialysis patients (HD) who are treated with recombinant human erythropoietin (epoetin) for an increased erythropoiesis exhibit often a poor response despite a normal iron status. Iron supplementation is not justified for this hypo responsiveness due to the potential hazards of iron overload aggravated by intravenous iron therapy. Furthermore, in vivo studies have indicated that the promising effect of intravenous iron medication to overcome iron-deficient erythropoiesis is not observed in iron-overloaded hemodialysis HD patients. Vitamin C, a water-soluble antioxidant as well as a reducing

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agent, has a number of associations with iron metabolism. Recent research highlights that vitamin C can potentiate the mobilization of iron from inert tissue stores and facilitates the incorporation of iron into protoporphyrin in HD patients being treated with epoetin. Interest has turned towards the use of vitamin C as an adjuvant therapy in this field. The important reason for adjuvant therapies is that they may help to reduce epoetin requirements or allow dialysis patients to achieve increased hemoglobin concentrations, and derive more cost-effectiveness and greater clinical benefits from epoetin treatment.

Conclusion

It is reasonable to start an adjuvant therapy with vitamin C in hemodialysis patients with poor response to epoetin. At the beginning, 100 mg vitamin C IV is administered at the end of the hemodialysis 3 times a week for 2-6 months. If no response is seen, the dose should be titrated up to a dose of 300 mg or 500 mg IV 3 times a week for 2-6 months with careful monitoring of potential adverse effects.

Source

Tarnag DC. Novel aspects of vitamin C in epoetin response. J Chin Med Assoc. 2007; 70: 357-60

ANTIOXIDANTS FOR CARDIOVASCULAR HEALTH

Low-dose antioxidants reduce platelet activation

Intervention

186 healthy volunteers participated in a randomized, double-blind, placebo-controlled trial. 100 subjects were in the antioxidant group and received daily a mixture of 120 mg ascorbic acid, 30 mg vitamin E, 6 mg β -carotene, 100 μ g selenium (as enriched yeast) and 20 mg zinc for 2 years 86 were in the placebo group. Baseline subject characteristics did not differ between the two groups. Blood concentrations of zinc (from 13.2 ± 1.6 to 14.9 ± 4.1 μ mol/l), selenium (from 1.06 ± 0.18 to 1.52 ± 0.24 μ mol/l), and β -carotene (from 0.51 ± 0.30 to 0.89 ± 0.59 μ mol/l) significantly increased between baseline and two years in the multi-antioxidant supplementation group supporting subject compliance ($p < 0.05$). At two years, the median urinary 11-dehydro TXB_{2/2,3} dinor 6 keto PGF_{1 α} ratio was significantly lower in the multi-antioxidant supplementation group (3.4 versus 2.78, $p = 0.015$). Serum selenium concentration was the only antioxidant studied that was significantly related to the urinary 11-dehydro TXB_{2/2,3} dinor 6 keto PGF_{1 α} ratio.

Conclusion

A low-dose multi-antioxidant supplementation contributes to a reduction in platelet activation which is beneficial for cardiovascular function.

Source

Arnaud J, Bost M, Vitoux D, Labarère J, Galan P, Faure H, Hercberg S, Bordet JC, Roussel AM, Chappuis P. Effect of low dose antioxidant vitamin and trace element supplementation on the urinary concentrations of thromboxane and prostacyclin metabolites. J Am Coll Nutr. 2007; 26: 405-11.

Flavonoids like epigallocatechin gallate improve endothelial function

Review

Endothelium-dependent flow-mediated dilation of the brachial artery has been improved two hours after consumption of black tea; this effect is sustained following daily consumption for four weeks in patients with proven coronary artery disease. This favorable effect can not be related to a systemic reduction in oxidative stress as reflected by plasma antioxidant capacity or other systemic

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markers of oxidative stress. However, it remains possible that flavonoids could have an antioxidant effect at the tissue level in the vasculature. The effect of tea consumption can not be attributed to caffeine or to non-specific effects on the function of vascular smooth muscle. The major component of green tea, epigallocatechingallate, activates eNOS that increases nitric oxide synthesis and produces endothelium- dependent relaxation of arterial segments. Thus, flavonoids activate specific signaling pathways in endothelial cells that improve multiple aspects of endothelial function.

Conclusion

Endothelial dysfunction contributes to the pathogenesis of cardiovascular disease. Epidemiological studies have shown that increased consumption of flavonoid-containing beverages and foods reduce cardiovascular risk. Flavonoids have powerful effects at the cellular level and offer a great deal of promise as a novel approach for the prevention and management of cardiovascular disease.

Source

Shenouda SM, Vita JA. Effects of flavonoid-containing beverages and EGCG on endothelial function *J AM Coll Nutr* 2007; 26: 366S-372S

FOLIC ACID LOWERS BLOOD ARSENIC

Folic acid facilitates arsenic methylation resulting in increased arsenic elimination

Intervention

Arsenic occurs in groundwater that is used for drinking in several countries increasing the risk of chronic diseases. 130 arsenic-exposed participants with low plasma folate levels (<9 nmol/L) have been enrolled in a randomized, double-blind, placebo-controlled trial. 68 received a folic acid supplement (400 μ g/d) and 62 a placebo for 12 weeks. Blood concentrations of total arsenic, inorganic arsenic, monomethylarsonic acid (MMA), and dimethylarsinic acid (DMA) have been evaluated before and after the supplementation period. MMA in blood was reduced by a mean \pm SE of $22.24 \pm 2.86\%$ in the folic acid supplementation group and by $1.24 \pm 3.59\%$ in the placebo group ($P < 0.0001$). There was no change in DMA in blood; DMA is rapidly excreted in urine as evidenced by an increase in urinary DMA ($P = 0.0099$). Total blood arsenic was reduced by 13.62% in the folic acid supplementation group and by 2.49% in the placebo group ($P = 0.0199$).

Conclusion

Folic acid supplementation to participants with low plasma concentrations of folate (< 9 nmol/L) lowered blood arsenic concentrations, primarily by decreasing blood monomethylarsonic acid and increasing urinary dimethylarsinic acid. Therapeutic strategies to facilitate arsenic methylation, particularly in populations with folate deficiency or hyperhomocysteinemia or both, may lower blood arsenic concentrations and thereby contribute to the prevention of arsenic-induced illnesses.

Source

Gamble MV, Liu X, Slavkovich V, Pilsner JR, Ilievski V, Factor-Litvak P, Levy D, Alam S, Islam M, Parvez F, Ahsan H, Graziano JH. Folic acid supplementation lowers blood arsenic *Am J Clin Nutr* 2007; 86: 1202-9