

Antiarrhythmic effects of increasing the daily intake of magnesium and potassium in patients with frequent ventricular arrhythmias.

Zehender M, Meinertz T, Faber T, et al. *J Am Coll Cardiol* 1997;29:1028-1034.

OBJECTIVES: This study sought to assess potential antiarrhythmic effects of an increase in the daily oral intake of magnesium and potassium in patients with frequent ventricular arrhythmias. **BACKGROUND:** Magnesium and potassium contribute essentially to the electrical stability of the heart. Despite experimental and clinical evidence for the antiarrhythmic properties of the two minerals, controlled data in patients with stable ventricular arrhythmias are lacking. **METHODS:** In a randomized, double-blind study, 232 patients with frequent ventricular arrhythmias (> 720 ventricular premature beats [VPBs]/24 h) confirmed at baseline and after 1 week of placebo therapy were subsequently treated over 3 weeks with either 6 mmol of magnesium/12 mmol of potassium-DL-hydrogenaspartate daily or placebo. **RESULTS:** Compared with placebo pretreatment, active therapy resulted in a median reduction of VPBs by -17.4% ($p = 0.001$); the suppression rate was 2.4 times greater than that in patients randomized to 3 weeks of placebo therapy (-7.4%, $p = 0.038$). The likelihood of a $\geq 60\%$ (predefined criterion) or $\geq 70\%$ suppression rate (calculated from the placebo-controlled run-in period) was 1.7 (25% vs. 15%, $p = 0.044$) and 1.5 times greater in the active than in the placebo group (20% vs. 13%, $p = 0.085$), respectively. No effect of magnesium and potassium administration was observed on the incidence of repetitive and supraventricular arrhythmias and clinical symptoms of the patients. **CONCLUSIONS:** To our knowledge, this study is the first to provide controlled data on the antiarrhythmic effect of oral administration of magnesium and potassium salts when directed to patients with frequent and stable ventricular tachyarrhythmias. A 50% increase in the recommended minimum daily dietary intake of the two minerals for 3 weeks results in a moderate but significant antiarrhythmic effect. However, with the given therapeutic regimen, repetitive tachyarrhythmias and patient symptoms remain unchanged.

Clinical symptoms of mitral valve prolapse are related to hypomagnesemia and attenuated by magnesium supplementation.

Lichodziejewska B, Klos J, Rezler J, et al. *Am J Cardiol* 1997;79:768-772.

Mitral valve prolapse syndrome (MVP) is a frequent disorder characterized by a number of complaints which lessen the quality of life. The pathogenesis of MVP symptoms has not been fully elucidated. Hyperadrenergic activity and magnesium deficiency have been suggested. This study was designed to verify the concept that heavily symptomatic MVP is accompanied by hypomagnesemia and to elucidate whether magnesium supplementation alleviates the symptoms and influences adrenergic activity. We assessed serum magnesium in 141 subjects with heavily symptomatic primary MVP and in 40 healthy controls. Decreased serum magnesium was found in 60% of patients and in 5% of controls ($p < 0.0001$). Patients with low serum magnesium were subjected to magnesium or placebo supplementation in a double-blind, crossover fashion. Typical symptoms of MVP ($n = 13$), intensity of anxiety, and daily excretion of catecholamines were determined. After 5 weeks, the mean number of symptoms per patient decreased from 10.4 ± 2.1 to 5.6 ± 2.5 ($p < 0.0001$), and a significant reduction in weakness, chest pain, dyspnea, palpitations, and anxiety was observed. Increased noradrenaline excretion before and after magnesium was seen in 63% and 17% of patients, respectively ($p < 0.01$). Mean daily excretion of noradrenaline and adrenaline was significantly diminished after magnesium. It is concluded that many patients with heavily symptomatic MVP have low serum magnesium, and supplementation of this ion leads to improvement in most symptoms along with a decrease in catecholamine excretion.

The impact of vitamin A supplementation on physical growth of children is dependent on season.

Bahl R, Bhandari N, Taneja S, Bhan MK. *Eur J Clin Nutr* 1997;51:26-29.

OBJECTIVE: To determine the impact of vitamin A supplementation on physical growth in young children. **DESIGN:** Randomized, double blind, placebo controlled trial. **SETTING:** Urban slum community clinic. **SUBJECTS:** 900 children, aged 12-59 months, attending the community clinic with diarrhea of ≤ 7 d were included in the trial. **INTERVENTION:** Each child was given a single dose capsule containing 200,000 IU vitamin A or placebo at enrollment. **MAIN OUTCOME MEASURES:** Mean increments in weight and height during the 90 d period post supplementation. **RESULTS:** In all children, the mean increments in weight following supplementation were 0.66 kg (s.d. 0.5) and 0.64 kg (s.d. 0.6) in the vitamin A and placebo groups ($P = 0.5$). The mean increments in height were also similar in the two treatment groups ($P = 0.5$). Serum vitamin A was measured in 40 randomly selected children in each group; the proportion of subclinical deficiency (serum retinol < 20 micrograms/dl) was 62.5% in those enrolled during summer (April through July) as compared to 21.1% in those enrolled during the remaining cooler months of the year ($P = 0.02$). In the children supplemented with vitamin A during summer, the mean increment in weight was 140 g more than those who received placebo (95% confidence interval CI 30-250); there was also a significant reduction in the proportion of children who were wasted (< -2 weight-for-height Z-score) at end study (Odds Ratio 0.53, 95% CI 0.28-1.0, $P = 0.03$). There was no significant impact of vitamin A on height increments in children supplemented during summer. **CONCLUSION:** Vitamin A supplementation in 12-59 month old children improves weight gain in the subsequent three months only in the summer season, but not during the rest of the year.

The long term efficacy of glycyrrhizin in chronic hepatitis C patients.

Arase Y, Ikeda K,
Murashima N, et al. *Cancer*
1997;79:1494-1500.

BACKGROUND: Hepatocellular carcinoma (HCC) occurs in patients with hepatitis C virus-RNA positive chronic liver disease. It is important to prevent HCC with drug administration. **METHODS:** A retrospective study was undertaken to evaluate the long term preventive effect of Stronger Neo-Minophagen C (SNMC) on HCC development. SNMC is a Japanese medicine that is commonly administered to patients with chronic hepatitis C to improve the serum alanine aminotransferase (ALT) level. Of 453 patients diagnosed with chronic hepatitis C retrospectively in the study hospital between January 1979 and April 1984, 84 patients (Group A) had been treated with SNMC; SNMC was given at a dose of 100 mL daily for 8 weeks, then 2-7 times a week for 2-16 years (median, 10.1 years). Another group of 109 patients (Group B) could not be treated with SNMC or interferon for a long period of time (median, 9.2 years) and were given other herbal medicine (such as vitamin K). The patients were retrospectively monitored, and the cumulative incidence of HCC and risk factors for HCC were examined. **RESULTS:** The 10th-year rates of cumulative HCC incidence for Groups A and B were 7% and 12%, respectively, and the 15th-year rates were 12% and 25%. By Cox regression analysis, the relative risk of HCC incidence in patients not treated with SNMC (Group B) was 2.49 compared with that of patients treated with SNMC (Group A). **CONCLUSIONS:** In this study, long term administration of SNMC in the treatment of chronic hepatitis C was effective in preventing liver carcinogenesis.

Abstracts

Recently Published Abstracts

Dexfenfluramine. An updated review of its therapeutic use in the management of obesity.

Davis R, Faulds D. *Drugs* 1996;52:696-724.

Dexfenfluramine increases serotonergic activity by stimulating serotonin (5-hydroxytryptamine; 5-HT) release into brain synapses, inhibiting its reuptake into presynaptic neurons and by directly stimulating postsynaptic serotonin receptors. On the basis of the serotonin hypothesis of appetite control, these actions would be expected to reduce appetite and, consequently, bodyweight. Studies conducted in animals and in overweight patients with and without associated disorders have confirmed the weight-reducing efficacy and good tolerability of dexfenfluramine. In 3-month clinical studies in obese patients, weight reductions with dexfenfluramine 15mg twice daily combined with dietary support were significantly higher than those achieved with placebo and similar to those with ephedrine/caffeine 20/20mg 3 times daily, sibutramine 10mg once daily and fluoxetine 60 mg/day. Furthermore, dexfenfluramine recipients with non-insulin-dependent diabetes mellitus, hyperlipidaemia or hypertension consistently show improvements in glycaemic control, blood lipid profiles and blood pressure. 12-month trial results indicate that most weight loss occurs in the initial 6 months and appears to be maintained for a further 6 months. Weight regain after withdrawal of treatment in 12-month studies demonstrates that dexfenfluramine is effective in maintaining a stable bodyweight at a lower level than placebo and in limiting food intake over this time period. Commonly reported adverse events with dexfenfluramine include diarrhoea, tiredness, dry mouth and somnolence; these symptoms are generally mild and transient. Approximately 7 and 10% of dexfenfluramine recipients in short and long term studies withdrew because of adverse events. Dexfenfluramine was better tolerated than ephedrine/caffeine and fluoxetine in short term studies. Obesity is a chronic condition that is accompanied by a number of metabolic complications. It is a significant health problem in developed countries, and as a major risk factor for many chronic diseases, including diabetes and cardiovascular disease, the economic burden of this condition is considerable. As with other chronic conditions, there is a role for pharmacological intervention in patients with severe obesity. However, drugs should be considered as only one component of a weight-control programme, since additional lifestyle modification is required to maintain weight loss. The promising data on the long term efficacy and tolerability of dexfenfluramine as well as its favourable effects on risk factors associated with obesity requires confirmation in long term studies. In the meantime, dexfenfluramine should be considered a valuable adjunct to a reduced-calorie diet in the management of severe obesity, particularly in patients with associated disorders and those unsuccessful with conventional weight loss measures. Available data support the use of the drug for up to 1 year to maintain weight loss and thus dexfenfluramine should be considered for long term administration.

Vitamin E protects human skeletal muscle from damage during surgical ischemia-reperfusion.

Novelli GP, Adembri C, Gandini E, et al. *Am J Surg* 1997;173:206-209.

PURPOSE: The biochemical and morphological alterations induced in lower limb skeletal muscle by ischemia-reperfusion (I-R) during aortic surgery and the effect of vitamin E pretreatment were investigated. **METHODS:** Two groups of patients undergoing aortic aneurysm resection, one untreated and one treated with vitamin E, were examined. Quadriceps muscle biopsies were taken after induction of anesthesia, at the end of ischemia, and after reperfusion. The malondialdehyde (MDA) content and morphology of biopsies were examined to assess peroxidative processes. **RESULTS:** Ischemia did not induce an increase in MDA content but did increase neutrophil infiltration in muscle fibers of untreated patients. Reperfusion led to a significant increase in MDA content and to intermyofibrillar edema and mitochondrial swelling. The MDA content was not increased during ischemia and neutrophil infiltration was minimal in vitamin E treated patients. At reperfusion, the MDA content, the ultrastructural injuries and neutrophil infiltration were significantly reduced by the treatment. **CONCLUSIONS:** Vitamin E is effective in reducing the oxidative muscle damage occurring after a period of I-R.

Contemporaneous melatonin administration modifies the circadian response to nocturnal bright light stimuli.

Cagnacci A, Soldani R, Yen SS. *Am J Physiol* 1997;272:R482-486.

We investigated whether the contemporaneous administration of melatonin can modify circadian phase shifts induced by bright light stimuli. After a baseline evaluation, 10 women were exposed for three consecutive nights to a 4-h bright light stimulus (>3,000 lx) initiated at the time of the estimated core body temperature (BT(c)) nadir. Along with light, each woman orally received, randomly and in a double-blind fashion, placebo (n = 5) or melatonin (n = 5; 1 mg 30 min before and 0.75 mg 120 min after the start of light exposure). Daily rhythms were reevaluated at the end of treatment. Bright light phase advanced, by about 90-120 min, BT(c) (P < 0.01), cortisol (P < 0.05), and melatonin (P < 0.01) rhythms. Contemporaneous administration of melatonin antagonized the phase advances of the cortisol and BT(c) rhythms, as well as the melatonin peak and melatonin offset. The phase advance of the melatonin onset was instead enhanced (P < 0.05). Contemporaneous melatonin administration modifies the capability of light to induce circadian phase shifts.

Abstracts

Recently Published Abstracts

The pineal hormone melatonin in hematology and its potential efficacy in the treatment of thrombocytopenia.

Lissoni P, Tancini G, Barni S, et al. *Recenti Prog Med* 1996;87:582-585.

Recent experimental studies suggested that hematopoietic cell proliferation and differentiation are under a neuroendocrine control and that they change in relation to the 24-hour period. Moreover, it has been shown that the pineal hormone melatonin (MLT) plays a role in mediating the influence of the psychoendocrine system and of the lighting conditions on the hematopoiesis. Finally, MLT has appeared to regulate hematopoietic cell growth by influencing apoptosis-related mechanisms. In particular, preliminary studies have shown that the pineal hormone MLT may determine some benefits in blood cell disorders, mainly platelet diseases. On this basis, a pilot phase II study of MLT therapy was performed in patients suffering from persistent thrombocytopenia due to different causes. The study included 14 patients, and thrombocytopenia was due to bone metastatic involvement in 5, hypersplenism in 3, myelodysplastic syndrome in 3, DIC in 1, genetic factors in 1, and Werlhof's disease in the last case. MLT was given orally at 20 mg/day in the evening for 2 months. No MLT-related toxicity occurred. A normalization of platelet number was achieved in 8/14 (57%), and platelet mean number significantly increased on MLT therapy. This preliminary study would suggest that MLT may be effective in the treatment of thrombocytopenia due to different reasons, for which no effective standard therapy is available.

Retardation of myelination due to dietary vitamin B12 deficiency: cranial MRI findings.

Lovblad K, Ramelli G, Remonda L, et al. *Pediatr Radiol* 1997;27:155-158.

Vitamin B12 deficiency is known to be associated with signs of demyelination, usually in the spinal cord. Lack of vitamin B12 in the maternal diet during pregnancy has been shown to cause severe retardation of myelination in the nervous system. We report the case of a 14(1)/2-month-old child of strictly vegetarian parents who presented with severe psychomotor retardation. This severely hypotonic child had anemia due to insufficient maternal intake of vitamin B12 with associated megaloblastic anemia. MRI of the brain revealed severe brain atrophy with signs of retarded myelination, the frontal and temporal lobes being most severely affected. It was concluded that this myelination retardation was due to insufficient intake of vitamin B12 and vitamin B12 therapy was instituted. The patient responded well with improvement of clinical and imaging abnormalities. We stress the importance of MRI in the diagnosis and follow-up of patients with suspected diseases of myelination.

Selenium-induced thyroid dysfunction.

Hofbauer LC, Spitzweg C, Magerstadt RA, Heufelder AE. *Postgrad Med J* 1997;73:103-104.

Administration of the anti-oxidative trace element selenium is currently being evaluated for its benefits in patients with inflammatory diseases. However, little is known about the risks of selenium. We report on a patient in whom, along with standard therapy, administration of large intravenous doses of selenite for sepsis secondary to pneumonia resulted in development of marked hypothyroidism. In addition, severe iodine deficiency was noted, and supplementation with iodine led to normalisation of thyroid function.

Abstracts

Recently Published Abstracts

Pervasive occult gastrointestinal bleeding in an Alaska native population with prevalent iron deficiency. Role of *Helicobacter pylori* gastritis.

Yip R, Limburg PJ, Ahlquist DA, et al. *JAMA* 1997;277:1135-1139.

OBJECTIVE: To confirm prevalent iron deficiency among Yupik Eskimos living in Alaska and to explore the frequency of and potential lesions accounting for occult gastrointestinal bleeding. **DESIGN:** Descriptive survey. **SETTING:** Rural Arctic community. **SUBJECTS:** A total of 140 adult volunteers from 3 villages in the Yukon-Kuskokwim Delta region of western Alaska. **MAIN OUTCOME MEASURES:** Daily iron intake, hematologic and biochemical indexes of iron status, fecal hemoglobin levels, stool parasites, and endoscopic findings. **RESULTS:** While dietary iron intake by Yupiks was similar to that of a reference population, iron deficiency prevalence was increased 13-fold in Yupik men and 4-fold in Yupik women. Fecal hemoglobin levels were elevated in 90% of subjects contrasted with only 4% of a reference group; median levels were 5.9 and 0.5 mg of hemoglobin per gram of stool, respectively. Among 70 Yupik subjects with elevated fecal hemoglobin levels who had endoscopy performed, 68 (97%) had an abnormal gastric appearance consisting of erythema, mucosal thickening, diffuse mucosal hemorrhages, erosions, or ulcerations. Gastric biopsies revealed chronic gastritis with associated *Helicobacter pylori* in 68 (99%) of 69. No other hemorrhagic gastrointestinal disease was detected. **CONCLUSIONS:** Based on this study sample, occult gastrointestinal bleeding appears to be pervasive in the Yupik population and likely underlies the prevalent iron deficiency. An atypical hemorrhagic gastritis associated with *H pylori* infection is present almost universally and may represent the bleeding source.

Can the fast bone loss in osteoporotic and osteopenic patients be stopped with active vitamin D metabolites?

Dambacher MA, Kranich M, Schacht E, Neff M. *Calcif Tissue Int* 1997;60:115-118.

The aim of this study was to evaluate whether fast trabecular bone loss in osteoporotic and osteopenic patients can effectively be treated with active vitamin D metabolites. Thirty-one osteoporotic and osteopenic patients were monitored between 4 and 22 months before and between 8 and 18 months during the treatment. Fast bone losers were designated as osteoporotic or osteopenic patients with a loss of trabecular bone density in the radius of 3% or more calculated for 1 year. For this differentiation, the high precise peripheral quantitative computed tomography system (DENSISCAN 1000) was used (reproducibility 0.3% in mixed collectives). The pretreatment loss and the "gain" under treatment with active vitamin D metabolites was calculated for 1 year. The treatment consisted of either 0.5 micro;g calcitriol daily or 1 micro;g of alfacalcidol daily. Before treatment, the trabecular bone loss in the radius/year was $-6.6 \pm 0.5\%$ (mean \pm SEM). After treatment with vitamin D metabolites, the trabecular bone gain in the radius/year was $0.01 \pm 0.6\%$ (mean \pm SEM). The difference was highly significant ($P < 0.001$). In contrast to this, the loss of cortical bone density before treatment was $-1.8 \pm 0.3\%$ (mean \pm SEM) and the reduced loss after treatment $-0.2 \pm 0.4\%$ (mean \pm SEM), both values calculated for 1 year. This difference was less significant ($P < 0.05$). This study shows that the treatment with active vitamin D metabolites is very effective in slowing fast trabecular bone loss in osteoporotic and osteopenic patients.

Abstracts

Recently Published Abstracts

Modulated mitogenic proliferative responsiveness of lymphocytes in whole-blood cultures after a low-carotene diet and mixed-carotenoid supplementation in women.

Kramer TR, Burri BJ. *Am J Clin Nutr* 1997;65:871-875.

To determine the effects of dietary carotenes on the mitogenic proliferative responsiveness of blood lymphocytes in vitro, nine premenopausal women were fed a low-carotene diet for 120 d. Low-dose beta-carotene (0.5 mg/d) was given to five subjects on days 1-60, while four received a placebo. All subjects received a low-dose beta-carotene (0.5 mg/d) supplement on days 61-120, plus a carotenoid complex on days 101-120. The mean (+/-SEM) serum beta-carotene concentration for the combined beta-carotene supplemented and placebo subjects (n = 9) was not significantly reduced from that on day 1 (1.27 +/- 0.24 mumol/L) on days 60 (0.66 +/- 0.14 mumol/L) and 100 (0.91 +/- 0.38 mumol/L), but on day 120 (3.39 +/- 0.44 mumol/L) it was increased above that on days 1, 60, and 100. Maximum mitogenic proliferative responsiveness of blood lymphocytes in vitro to optimal dose phytohemagglutinin (PHA) was reduced on days 60 (P = 0.025) and 100 (P < 0.0001), but corrected itself on day 120 to a value above those on day 1 (P = 0.04), day 60 (P = 0.0001), and day 100 (P < 0.0001). Present findings show that a diet low in carotene had a suppressive effect on the maximum mitogenic proliferative responsiveness of blood lymphocytes in vitro, which was not corrected with low-dose beta-carotene supplementation but was with a carotenoid complex from vegetables rich in carotenoids.

Is metabolic evidence for vitamin B-12 and folate deficiency more frequent in elderly patients with Alzheimer's disease?

Joosten E, Lesaffre E, Riezler R, et al. *J Gerontol A Biol Sci Med Sci* 1997;52:M76-79.

BACKGROUND: It is still unclear whether there is an association between Alzheimer's disease and vitamin B-12 or folate deficiency. This study was designed to investigate whether patients with Alzheimer's disease are particularly prone to metabolically significant cobalamin or folate deficiency as compared to nondemented hospitalized controls and healthy elderly controls living at home. **METHODS:** Evaluation for the diagnosis of Alzheimer's disease, routine laboratory tests, serum folate and vitamin B-12, serum methylmalonic acid (MMA), total homocysteine (tHcy), and radiological tests was performed in 52 patients with Alzheimer's disease (AD), 50 nondemented hospitalized controls, and 49 healthy elderly subjects living at home. **RESULTS:** Serum vitamin B-12 and folate levels are comparable between patients with AD, hospitalized control patients, and subjects living at home. Patients with AD have the highest serum MMA and tHcy levels. The MMA levels of patients with AD and hospitalized controls are not different, but the mean tHcy level is significantly higher in patients with AD as compared to nondemented patients or subjects living at home. **CONCLUSION:** The interpretation of the vitamin B-12 and folate status in patients with AD depends largely on the methodology (i.e., serum vitamin vs metabolite levels) and the selection of the control group. Although patients with AD have the highest tHcy and MMA levels, metabolically significant vitamin B-12 and folate deficiency is also a substantial problem in nondemented elderly patients.

Effect of transdermal nitroglycerin or N-acetylcysteine, or both, in the long-term treatment of unstable angina pectoris.

Ardissino D, Merlini PA, Savonitto S, et al. *J Am Coll Cardiol* 1997;29:941-947.

OBJECTIVES: This study was designed to evaluate whether the addition of transdermal nitroglycerin or oral N-acetylcysteine, or both, to conventional medical therapy improves the natural history of unstable angina pectoris. **BACKGROUND:** Transdermal nitroglycerin is widely used to treat angina pectoris, but the development of tolerance is a major problem that may reduce its clinical efficacy. It has been suggested that the addition of N-acetylcysteine to nitroglycerin reverses the development of tolerance, potentiates the hemodynamic response to nitroglycerin and may improve in-hospital prognosis in unstable angina. **METHODS:** We assessed the efficacy of adding transdermal nitroglycerin or oral N-acetylcysteine, or both, to conventional medical therapy in a randomized, double-blind, placebo-controlled trial involving 200 patients with unstable angina who were followed up for 4 months. **RESULTS:** Outcome events—death, myocardial infarction or refractory angina requiring revascularization—occurred in 31% of patients receiving nitroglycerin, 42% of those receiving N-acetylcysteine, 13% of those receiving nitroglycerin plus N-acetylcysteine and 39% of those receiving placebo ($p = 0.0052$). Kaplan-Meier curves showed a higher probability ($p < 0.01$) of no failure of medical treatment in the group receiving both nitroglycerin and N-acetylcysteine than in those receiving placebo, N-acetylcysteine or nitroglycerin alone. The combination of nitroglycerin and N-acetylcysteine was associated with a high incidence of side effects (35%), mainly intolerable headache, which was almost twice as frequent as in patients receiving nitroglycerin alone. **CONCLUSIONS:** The combination of nitroglycerin and N-acetylcysteine, associated with conventional medical therapy in the long-term treatment of patients with unstable angina, reduces the occurrence of outcome events. However, the high incidence of side effects limits the clinical applicability of this therapeutic strategy at least at the dosage used in the present study.

The effect of acute glutathione treatment on sorbitol level in erythrocytes from diabetic patients.

Ciuchi E, Odetti P, Prando R. *Diabetes Metab* 1997;23:58-60.

This study evaluated the effect of acute intravenous glutathione (GSH) infusion on red blood cell (RBC) sorbitol levels in 21 diabetic subjects and 6 normal controls of similar age and body mass index (Kg/m²). All patients received 1,200 mg of GSH in 500 ml of isotonic saline solution during one-hour intravenous administration. At the end of acute infusion of GSH, sorbitol concentration decreased from 20.90 +/- 1.16 to 16.24 +/- 0.81 nmol/g Hb ($p < 0.001$) in RBCs of diabetic subjects. No significant changes were observed in controls. These data support the hypothesis that GSH depletion, by reducing glycolytic flux to pyruvate, may enhance the rate of glucose metabolism through the polyol pathway and worsen the metabolic imbalance of diabetic tissues. The administration of exogenous GSH could interrupt this vicious circle.

Tardive dyskinesia exacerbated after ingestion of phenylalanine by schizophrenic patients.

Mosnik DM, Spring B, Rogers K, Baruah S. *Neuropsychopharmacology* 1997;16:136-146.

Despite continued research, the influences that promote or exacerbate tardive dyskinesia (TD) symptoms remain incompletely understood. Recent findings (Gardos et al. 1992; Richardson et al. 1989) suggest that ingestion of the dietary constituent, phenylalanine, might exacerbate TD symptoms, but a double-blind, placebo-controlled challenge had not previously been conducted in schizophrenic patients. On two different mornings, in counter-balanced order, 18 male schizophrenic patients with TD were challenged with either 100 mg/kg phenylalanine or placebo. Effects on abnormal involuntary movements, recall memory, and plasma phenylalanine were measured 90 minutes post-challenge. The results supported the hypothesis in that involuntary movements increased to a statistically and clinically meaningful degree after the phenylalanine challenge, but not after placebo. No effects on memory were detected. Significant order effects characterized the plasma findings but not the behavioral data. Results indicate that a dietary constituent, the amino acid phenylalanine, can potentially exacerbate tardive dyskinesia symptoms in schizophrenic patients. The influence of phenylalanine and other ingested substances on clinical symptomatology warrants further investigation.

Abstracts

Recently Published Abstracts

Effect of propionyl-L-carnitine on quality of life in intermittent claudication.

Brevetti G, Perna S, Sabba C, et al. *Am J Cardiol* 1997;79:777-780.

A double-blind, dose titration study was designed to assess the efficacy of propionyl-L-carnitine in intermittent claudication. The effect on walking capacity was described in a previous article. This study reports on the effect on quality of life, assessed by the McMaster Health Index Questionnaire (MHIQ). After 24 weeks of treatment, the global MHIQ score did not show any difference from baseline in patients randomized to placebo (n = 102). Conversely, it increased from 0.59 +/- 0.12 to 0.64 +/- 0.12 in those taking propionyl-L-carnitine (n = 85). Analysis of variance showed a significant difference between treatments (p = 0.018). Stepwise multiple regression analysis identified baseline maximal walking capacity (cutoff point 250 m) as a predictor of treatment outcome. In patients walking < 250 m, propionyl-L-carnitine significantly improved physical function (p = 0.027), emotional function (p = 0.002), and global MHIQ score (p = 0.002) compared with placebo. Also, for maximal walking capacity, group difference significantly favored propionyl-L-carnitine (p = 0.009). In patients with baseline maximal walking capacity > or = 250 m, propionyl-L-carnitine did not affect the MHIQ scores, nor improve walking performance. These data indicate that propionyl-L-carnitine exerts beneficial effects on quality of life and walking performance in patients with more severely limited walking capacity.

Taurine supplementation prevents hyperaminoacidemia in growing term infants fed high-protein cow's milk formula.

Raiha NC, Fazzolari-Nesci A, Boehm G. *Acta Paediatr* 1996;85:1403-1407.

Blood urea nitrogen (BUN) and plasma and urine amino acid concentrations were compared between three cohorts of healthy growing term infants who were breast-fed (BF) or randomly assigned to one of two formulas either taurine non-supplemented (FF) or taurine supplemented (FF + T). The infants were studied from 2 to 12 weeks of age. Weight gain and growth in length was normal and similar in all three feeding groups during the study interval. At 12 weeks BUN was significantly higher in the FF group than in the BF and FF + T groups, 16.5 mg/dl vs 7.0 and 7.3 mg/dl, respectively. Total plasma amino acids (FF group: 240.5 +/- 110.1 mumoles/dl; BF group 180.1 +/- 28.7 mumoles/dl; FF + T group: 182.3 +/- 89.4 mumoles/dl) and total essential amino acids (FF group: 89.8 +/- 37.3 mumoles/dl; BF group: 56.1 +/- 16.3 mumoles/dl; FF + T group: 53.0 +/- 24.2 mumoles/dl). The urine amino acid concentrations reflected the plasma levels in all groups. These results indicate that taurine supplementation to a high protein formula lowers BUN levels and the plasma urine amino acid concentrations by some yet unknown mechanism to concentrations similar to those found in breast-fed infants with a much lower protein intake.

Nitric oxide scavenging by curcuminoids.

Sreejayan, Rao MN. *J Pharm Pharmacol* 1997;49:105-107.

Because curcumin, a compound with anti-inflammatory and anticancer activity, inhibits induction of nitric oxide synthase in activated macrophages and has been shown to be a potent scavenger of free radicals we have investigated whether it can scavenge nitric oxide directly. Curcumin reduced the amount of nitrite formed by the reaction between oxygen and nitric oxide generated from sodium nitroprusside. Other related compounds, e.g. demethoxycurcumin, bisdemethoxycurcumin and diacetylcucurmin were as active as curcumin, indicating that the methoxy and the phenolic groups are not essential for the scavenging activity. The results indicate curcumin to be a scavenger of nitric oxide. Because this compound is implicated in inflammation and cancer, the therapeutic properties of curcumin against these conditions might be at least partly explained by its free-radical scavenging properties, including those toward nitric oxide.

**Magnesium deficiency:
possible role in
osteoporosis associated
with gluten-sensitive
enteropathy.**

Rude RK, Olerich M.

Osteoporos Int 1996;6:453-461.

Osteoporosis and magnesium (Mg) deficiency often occur in malabsorption syndromes such as gluten-sensitive enteropathy (GSE). Mg deficiency is known to impair parathyroid hormone (PTH) secretion and action in humans and will result in osteopenia and increased skeletal fragility in animal models. We hypothesize that Mg depletion may contribute to the osteoporosis associated with malabsorption. It was our objective to determine Mg status and bone mass in GSE patients who were clinically asymptomatic and on a stable gluten-free diet, as well as their response to Mg therapy. Twenty-three patients with biopsy-proven GSE on a gluten-free diet were assessed for Mg deficiency by determination of the serum Mg, red blood cell (RBC) and lymphocyte free Mg²⁺, and total lymphocyte Mg. Fourteen subjects completed a 3-month treatment period in which they were given 504-576 mg MgCl₂ or Mg lactate daily. Serum PTH, 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D and osteocalcin were measured at baseline and monthly thereafter. Eight patients who had documented Mg depletion (RBC Mg²⁺ < 150 microM) underwent bone density measurements of the lumbar spine and proximal femur, and 5 of these patients were followed for 2 years on Mg therapy. The mean serum Mg, calcium, phosphorus and alkaline phosphatase concentrations were in the normal range. Most serum calcium values fell below mean normal and the baseline serum PTH was high normal or slightly elevated in 7 of the 14 subjects who completed the 3-month treatment period. No correlation with the serum calcium was noted, however. Mean serum 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D and osteocalcin concentrations were also normal. Despite only 1 patient having hypomagnesemia, the RBC Mg²⁺ (153 +/- 6.2 microM; mean +/- SEM) and lymphocyte Mg²⁺ (182 +/- 5.5 microM) were significantly lower than normal (202 +/- 6.0 microM, p < 0.001, and 198 +/- 6.8 microM, p < 0.05, respectively). Bone densitometry revealed that 4 of 8 patients had osteoporosis of the lumbar spine and 5 of 8 had osteoporosis of the proximal femur (T-scores < or = -2.5). Mg therapy resulted in a significant rise in the mean serum PTH concentration from 44.6 +/- 3.6 pg/ml to 55.9 +/- 5.6 pg/ml (p < 0.05). In the 5 patients given Mg supplements for 2 years, a significant increase in bone mineral density was observed in the femoral neck and total proximal femur. This increase in bone mineral density correlated positively with a rise in RBC Mg²⁺. This study demonstrates that GSE patients have reduction in intracellular free Mg²⁺, despite being clinically asymptomatic on a gluten-free diet. Bone mass also appears to be reduced. Mg therapy resulted in a rise in PTH, suggesting that the intracellular Mg deficit was impairing PTH secretion in these patients. The increase in bone density in response to Mg therapy suggests that Mg depletion may be one factor contributing to osteoporosis in GSE.