

# Abstracts

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## Recently Published Abstracts

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### **St. John's wort in mild to moderate depression: the relevance of hyperforin for the clinical efficacy.**

Laakmann G, Schule C,  
Baghai T, Kieser M.  
*Pharmacopsychiatry*  
1998;31:S54-S59.

In a randomized, double-blind, placebo-controlled, multicenter study, the clinical efficacy and safety of two different extracts of St. John's wort were investigated in 147 male and female outpatients suffering from mild or moderate depression according to DSM-IV criteria. Following a placebo run-in period of three to seven days, the patients were randomized to one of three treatment groups: During the 42-day treatment period, they received 3 x 1 tablets of either placebo, Hypericum extract WS 5573 (300 mg, with a content of 0.5% hyperforin), or Hypericum extract WS 5572 (300 mg, with a content of 5% hyperforin). The manufacturing process for the two Hypericum preparations was identical, so that they differed only in their hyperforin content. Efficacy regarding depressive symptoms was assessed on days 0, 7, 14, 28, and 42, using the Hamilton Rating Scale for Depression (HAMD, 17-item version) and the Depression Self-Rating Scale (D-S) according to von Zerssen. In addition, the severity of illness was also rated by the investigators on days 0 and 42 using the Clinical Global Impression (CGI) scale. The last observation of patients withdrawn from the trial prematurely was carried forward. At the end of the treatment period (day 42), the patients receiving WS 5572 (5% hyperforin) exhibited the largest HAMD reduction versus day 0 (10.3 +/- 4.6 points; mean +/- SD), followed by the WS 5573 group (0.5% hyperforin; HAMD reduction 8.5 +/- 6.1 points) and the placebo group (7.9 +/- 5.2 points). As regards the change in the HAMD total score between day 0 and treatment end and its relationship to the hyperforin dose, a significant monotonic trend was demonstrated in the Jonckheere-Terpstra test ( $p = 0.017$ ). In pairwise comparisons, WS 5572 (5% hyperforin) was superior to placebo in alleviating depressive symptoms according to HAMD reduction (Mann-Whitney U-test:  $p = 0.004$ ), whereas the clinical effects of WS 5573 (0.5% hyperforin) and placebo were descriptively comparable. These results show that the therapeutic effect of St. John's Wort in mild to moderate depression depends on its hyperforin content.

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### **Enhanced synovial production of hyaluronic acid may explain rapid clinical response to high-dose glucosamine in osteoarthritis.**

McCarty MF. *Med Hypotheses* 1998;50:507-510.

Anecdotal reports of rapid symptomatic response to high-dose glucosamine in osteoarthritis are not credibly explained by the traditional view that glucosamine promotes synthesis of cartilage proteoglycans. An alternative or additional possibility is that glucosamine stimulates synovial production of hyaluronic acid (HA), which is primarily responsible for the lubricating and shock-absorbing properties of synovial fluid. Many clinical and veterinary studies have shown that intra-articular injections of high-molecular-weight HA produce rapid pain relief and improved mobility in osteoarthritis. HA has anti-inflammatory and analgesic properties, and promotes anabolic behavior in chondrocytes. The concentration and molecular weight of synovial fluid HA are decreased in osteoarthritis; by reversing this abnormality, high-dose glucosamine may provide rapid symptomatic benefit, and in the longer term aid the repair of damaged cartilage.

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### **Increased diurnal plasma concentrations of dehydroepiandrosterone in depressed patients.**

Heuser I, Deuschle M, Luppa P, et al. *J Clin Endocrinol Metab* 1998;83:3130-3133.

Activation of the hypothalamus-pituitary-adrenocortical system is a biological core symptom of depression. Although the regulation of cortisol secretion is well studied in this condition, there is no information about the diurnal activity of dehydroepiandrosterone (DHEA) secretion. Therefore, we studied 24-h DHEA plasma concentrations (every 30 min) in severely depressed patients (n = 26) and healthy controls (n = 33). We found depression to significantly increase diurnal minimal and mean DHEA plasma concentrations, whereas there was no effect on the diurnal maximal plasma concentration and the diurnal amplitude of DHEA. In particular, we found a parallel increase in mean DHEA (5.8 +/- 3.6 vs. 3.4 +/- 1.9 nmol/L; P < 0.003), cortisol (286 +/- 65 vs. 184 +/- 29 nmol/L; P < 0.0001) and ACTH (7.14 +/- 2.06 vs. 5.72 +/- 1.36 pmol/L; P < 0.002) plasma concentrations. The novel finding of parallel increases in diurnal DHEA and cortisol plasma concentrations in depressed patients has important implications for the regulation of the hypothalamus-pituitary-adrenocortical system in conditions of chronic stress and for the rationale of DHEA treatment in depressed patients.

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### **Oral glutamine reduces the duration and severity of stomatitis after cytotoxic cancer chemotherapy.**

Anderson PM, Schroeder G, Skubitz KM. *Cancer* 1998;83:1433-1439.

**BACKGROUND:** Mouth sores and/or difficulty swallowing are common and painful consequences of cytotoxic chemotherapy for cancer. In previous studies oral glutamine was found to protect animals from the effects of whole abdominal radiation and methotrexate-induced enteritis. Glutamine also was found to reduce oral mucositis in a nonrandomized pilot study in humans. Therefore, the authors attempted to determine the efficacy of oral glutamine in a randomized, double blind, crossover trial in cancer patients receiving chemotherapy. **METHODS:** Twenty-four patients (16 children and 8 adults) received glutamine or placebo (glycine) suspension (2 g amino acid/M<sup>2</sup>/dose twice daily) to swish and swallow on days of chemotherapy administration and for at least 14 additional days. Patients completed a calendar indicating days of mouth pain associated with each chemotherapy course and the effect of mouth pain on oral intake. **RESULTS:** Paired data indicated significant amelioration of stomatitis associated with glutamine administration after chemotherapy. The duration of mouth pain was 4.5 days less in chemotherapy courses in which glutamine supplementation was compared with placebo (Wilcoxon's signed rank test, P=0.0005). The severity of oral pain also was reduced significantly when glutamine was provided with chemotherapy (the amount of days mucositis restricted oral intake to soft foods [ $>$  or  $=$ Grade 2; Modified Eastern Cooperative Oncology Group grading system] was 4 days less with glutamine compared with placebo; Wilcoxon's signed rank test, P=0.002). **CONCLUSIONS:** Low dose oral glutamine supplementation during and after chemotherapy significantly reduced both the duration and severity of chemotherapy-associated stomatitis. Oral glutamine appears to be a simple and useful measure to increase the comfort of many patients at high risk of developing mouth sores as a consequence of intensive cancer chemotherapy.

**Dietary intake and blood levels of lycopene: association with cervical dysplasia among non-Hispanic, black women.**

Kantesky PA, Gammon MD, Mandelblatt J, et al. *Nutr Cancer* 1998;31:31-40.

We examined whether elevated levels of retinoids, carotenoids, folate, and vitamin E protected against cervical dysplasia among non-Hispanic, black women. We enrolled 32 women with incident cervical dysplasia, including cervical intraepithelial neoplasia (CIN) I, CIN II, and CIN III/carcinoma in situ, and 113 control women with normal cervical cytology in case-control study. Micronutrient levels were estimated from a food-frequency questionnaire (FFQ) and measured from blood samples. Information on risk factors for cervical neoplasia was elicited by interview. Hybrid capture was used to determine infection with human papillomavirus. After adjustment for potential confounders, analysis of micronutrient levels estimated from the FFQ suggested that women in the upper tertile of lycopene and vitamin A intake were one-third (odds ratio = 0.32, 95% confidence interval = 0.8-1.3) and one-fourth (odds ratio = 0.24, 95% confidence interval = 0.05-1.2) as likely, respectively, to have dysplasia as women in the lower tertile. Borderline protective trends ( $p < \text{or} = 0.10$ ) were apparent. Elevated levels of serum lycopene also suggested some protection against dysplasia. Results were not significant at  $\alpha = 0.05$  because of the small number of case women enrolled. Overall, correlations between estimates from the FFQ and serum levels were poor. This study indicates that, among black women, lycopene and perhaps vitamin A may play a protective role in the early stages of cervical carcinogenesis.

### **Iodine deficiency in cardiovascular diseases.**

Molnar I, Magyari M, Stief L. *Orv Hetil* 1998;139:2071-2073.

The thyroid hormone deficiency on cardiovascular function can be characterized with decreased myocardial contractility and increased peripheral vascular resistance as well as with the changes in lipid metabolism. 42 patients with cardiovascular disease (mean age 65 +/- 13 yr, 16 males) were investigated if iodine insufficiency can play a role as a risk factor for the cardiovascular diseases. The patients were divided in 5 subgroups on the ground of the presence of hypertension, congestive heart failure, cardiomyopathy, coronary disfunction and arrhythmia. Urine iodine concentration (5.29 +/- 4.52 micrograms/dl) was detected with Sandell-Kolthoff colorimetric reaction. The most decreased urine iodine concentration was detected in the subgroups with arrhythmia and congestive heart failure (4.7 +/- 4.94 micrograms/dl and 4.9 +/- 4.81 micrograms/dl, respectively). An elevated TSH level was found by 3 patients (5.3 +/- 1.4 mIU/l). An elevation in lipid metabolism (cholesterol, triglyceride) associated with all subgroups without arrhythmia. In conclusion, the occurrence of iodine deficiency in cardiovascular disease is frequent. Iodine supplementation might prevent the worsening effect of iodine deficiency on cardiovascular disease.

### **Induction of apoptosis in prostate cancer cell lines by the green tea component, (-)-epigallocatechin-3-gallate.**

Paschka AG, Butler R, Young CY. *Cancer Lett* 1998;130:1-7.

Green tea components exert many biological effects, including antitumor and cancer preventive activities. In the search for anticancer agents for prostate cancer the inhibitory effects of green tea components were tested on the prostate cancer cell lines LNCaP, PC-3 and DU145. (-)-Epigallocatechin-3-gallate (EGCG) proved to be the most potent catechin at inhibiting cell growth. The inhibition induced by EGCG was found to occur via apoptotic cell death as shown by changes in nuclear morphology and DNA fragmentation. Thus, we report the first evidence that EGCG is the active component in green tea and induces apoptosis in human prostate cancer cells.

### **Current pharmacotherapies for Alzheimer's disease.**

Knopman DS. *Geriatrics* 1998;53:S31-S34.

This brief overview will describe some of the current anti-Alzheimer's disease (AD) agents. The relevance of the cholinergic deficit in AD is well-established. Cholinesterase inhibitor (CEI) drugs represent the only FDA-approved primary treatment options for AD as of April 1998. Modest efficacy for AD now has been shown in well-designed clinical trials for six separate CEI agents. Only two, tacrine and donepezil, are currently on the market in the United States, but several others, including rivastigmine (ENA-713), metrifonate, and physostigmine-CR could be available by the end of 1998. Three other treatment strategies are being pursued. Estrogen replacement therapy as a treatment for AD in postmenopausal women is under active investigation. Analogously, clinical studies provide evidence that individuals using anti-inflammatory agents have a lower probability of developing AD. The success of alpha-tocopherol and selegiline in a recently conducted 2-year, double-blinded, placebo-controlled trial supports the hypothesis that oxidative stress plays a role in AD.

### **Effect of ultrahigh-dose methylcobalamin on compound muscle action potentials in amyotrophic lateral sclerosis: a double-blind controlled study.**

Kaji R, Kodama M, Imamura A, et al. *Muscle Nerve* 1998;21:1775-1778.

To develop a symptomatic treatment for amyotrophic lateral sclerosis, we compared the effects of ultrahigh-dose and low-dose (25 and 0.5 mg/day, intramuscularly, for 14 days) methylcobalamin on averaged compound muscle action potential amplitudes (CMAPs) in a double-blind trial. No significant changes in CMAP amplitude were found in 12 patients who had the low-dose treatment at either 2 or 4 weeks after start of treatment. By contrast, 12 patients assigned to the ultrahigh-dose group demonstrated a significant increase at 4 weeks. This method may provide a clinically useful measure to improve or retard muscle wasting, if a larger extended trial fulfills its promise.

### **Selenium, systemic immune response syndrome, sepsis, and outcome in critically ill patients.**

Forceville X, Vitoux D, Gauzit R, et al. *Crit Care Med* 1998;26:1536-1544.

**OBJECTIVES:** To confirm early, marked decrease in plasma selenium concentrations in patients admitted to a surgical and medical intensive care unit (ICU), and to study this decrease according to the presence or absence of systemic inflammatory response syndrome (SIRS), sepsis, or direct ischemia-reperfusion. **DESIGN:** Prospective, observational study. **SETTINGS:** Collaboration between the adult ICU of a 1,100-bed general hospital and a biochemical research laboratory of a university medical center. **PATIENTS:** One hundred thirty-four consecutive surgical and medical ICU patients. **INTERVENTIONS:** None. **MEASUREMENTS AND MAIN RESULTS:** In the first 31 patients, plasma and urine selenium concentrations were measured by electrothermal atomic absorption spectrometry on admission and once weekly during their ICU stay. These values were compared first with severity scores, criteria for SIRS, sepsis, and organ system failure taken on admission, and then with nosocomial infection, organ system failure during ICU stay, and hospital mortality. An early, low mean plasma selenium concentration was observed in these patients compared with selenium laboratory reference values. Plasma selenium, measured on ICU admission, inversely correlated with Acute Physiology and Chronic Health Evaluation II or Simplified Acute Physiology II scores. Patients with SIRS had lower selenium concentrations than those without SIRS. Mean urine selenium losses were normal in the first 31 patients. Plasma selenium concentration was low in all patients with severe sepsis and septic shock (range 0.20 to 0.72 micromol/L) and in those patients with ischemia-reperfusion from aortic cross-clamping (range 0.34 to 0.68 micromol/L). Despite recommended specific selenium supplementation, plasma selenium concentrations remained low for >2 wks in patients with SIRS. However, there was a slight increase in plasma selenium concentrations in surviving SIRS patients, whereas plasma selenium concentrations decreased in nonsurviving patients. The frequency of ventilator-associated pneumonia, organ system failure, and mortality was three times higher in patients with low plasma selenium concentration at the time of admission (selenium < or =0.70 micromol/L) than for the other patients. **CONCLUSIONS:** In severely ill ICU patients with SIRS, we observed an early 40% decrease in plasma selenium concentrations, reaching values observed in deleterious nutritional selenium deficiency. This prolonged decrease in selenium concentrations could explain the three-fold increase in morbidity and mortality rates in these patients compared with other ICU patients. The efficacy of selenium treatment in SIRS patients with a high gravity index score or hypoperfusion needs further investigation.

### **Vitamins in HIV disease progression and vertical transmission.**

Fawzi WW, Hunter DJ.

*Epidemiology* 1998;9:457-466.

Human immunodeficiency virus (HIV) infection is a major public health problem worldwide, but particularly in subsaharan Africa and Asia. Numerous observational studies report inverse associations between vitamin status, measured biochemically or as levels of dietary intake, and the risk of disease progression or vertical transmission. Evidence to support these findings has been obtained from a few randomized placebo-controlled trials. In this paper, we review studies that examined the role of vitamins A, B, C, D, and E in HIV disease progression and transmission, and we discuss the potential mechanisms of action of these vitamins. Adequate vitamin intake leads to enhancement of epithelial integrity and systemic immunity and could contribute to improved clinical condition among HIV-infected subjects and reduce vertical transmission by reducing the risk and severity of opportunistic infection and reducing viral load in blood. Adequate vitamin status may also reduce vertical transmission through the intrapartum and breastfeeding routes by reducing HIV viral load in lower genital secretions and breast milk, respectively. Vitamin supplements may be one of a few potential treatments that are inexpensive enough to be made available to HIV-infected persons in developing countries.

**Association between elevated plasma total homocysteine and increased common carotid artery wall thickness.**

Voutilainen S, Alfthan G, Nyyssonen K, et al. *Ann Med* 1998;30:300-306.

Homocysteine is increasingly recognized as a risk factor for atherothrombotic arterial diseases. We investigated the relation between plasma concentrations of total homocysteine (tHcy) and common carotid artery intima-media wall thickness, measured by B-mode ultrasonography, in 513 asymptomatic men and women from eastern Finland aged 45-69 years. The subjects were examined in 1994-95 at the baseline of the Antioxidant Supplementation in Atherosclerosis Prevention (ASAP) study, a randomized double-blind placebo-controlled two by two factorial trial on the effect of vitamin E and C supplementation in the prevention of atherosclerotic progression. The subjects were assigned into two categories according to the plasma tHcy concentration; concentration over 11.5 micromol/L (highest quartile) or concentration below 11.5 micromol/L. In this study population the mean plasma tHcy concentration was 10.0 micromol/L, and the prevalence of plasma tHcy concentration exceeding 11.5 micromol/L was 33% in men and 18% in women. The adjusted mean intima-media thickness of the right and left common carotid arteries was 1.12 mm in men with elevated plasma tHcy concentration and 1.02 mm in men with a plasma tHcy concentration below 11.5 micromol/L ( $P = 0.029$ ). In women there was no significant difference. We conclude that elevated plasma tHcy concentrations are associated with early atherosclerosis, as manifested by increased common carotid artery intima-media wall thickness, in middle-aged eastern Finnish men.

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### **Effectiveness of vitamin E in comparison with diclofenac sodium in treatment of patients with chronic polyarthritis.**

Wittenborg A, Petersen G, Lorkowski G, Brabant T. *Z Rheumatol* 1998;57:215-221.

In a randomized, double blind parallel group comparison the antiphlogistic and analgetic efficacy of high-dosed vitamin E (3 x 400 mg RRR-alpha-Tocopherolacetat/d) versus diclofenac-sodium has been investigated in hospitalized patients with established chronic rheumatoid arthritis. After 3 weeks of treatment the vitamin E group (n = 42) as well as the diclofenac group (n = 43) showed a significant improvement of all assessed clinical parameters. Duration of morning stiffness could be reduced under vitamin E treatment from 90 min to 68 min and under diclofenac treatment from 68 min to 30 min. The joint index according to Richie declined from 56 to 46 (vitamin E) and 49 to 34 (diclofenac). Grip strength increased in the vitamin E group as well as in the diclofenac group. In addition, the degree of pain, assessed by a 10 cm visual analogue scale, reduced significantly under vitamin E as well as under diclofenac. Regarding the therapeutical result both, physicians and patients, considered both drugs to be similarly effective. Especially regarding the risk profile of NSAR in long-term treatment of chronic rheumatoid arthritis intake of high-dosed vitamin E is a possible alternative in the treatment of inflammatory rheumatoid diseases.

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### **The efficacy of N-acetylcysteine as a hepatoprotective agent in liver transplantation.**

Thies JC, Teklote J, Clauer U, et al. *Transpl Int* 1998;11:S390-S392.

One of the most common complications after liver transplantation is primary graft dysfunction which results from severe deterioration of the microcirculation. The data obtained from our experimental studies indicate that N-acetylcysteine (NAC) is able to reduce the severity of ischemia/reperfusion injury and improves postoperative graft function after liver transplantation in rats. The aim of this pilot study was to evaluate the efficacy of NAC as a hepatoprotective agent under clinical conditions. A group of 30 liver transplanted patients were treated with NAC, and 30 patients (control group) were treated with a 5% solution of glucose only. In the NAC group we observed a distinct reduction in ischemia/reperfusion injury and improved liver function with less elevated peak transaminases, better macrocirculation, improved liver synthesis function and a lower incidence of primary nonfunction compared with the control group. We conclude that NAC is a very promising substance for reducing graft dysfunction in clinical liver transplantation.

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**Comparative study for assessing quality of life of patients with exogenous sleep disorders (temporary sleep onset and sleep interruption disorders) treated with a hops-valerian preparation and a benzodiazepine drug.**

Schmitz M, Jackel M. *Wien Med Wochenschr* 1998;148:291-298.

This randomized, double-blind, controlled clinical trial in parallel group design demonstrated equivalent efficacy and tolerability of a hop-valerian preparation compared with a benzodiazepine preparation in patients suffering from sleep disorders according to DSM-IV criteria. Sleep quality, fitness and quality of life were determined by psychometric tests, psychopathologic scales and sleep-questionnaires at the beginning of the therapy, end of therapy (duration 2 weeks) and then 1 week after cessation of therapy. Patients' state of health (4-point scale) and medication tolerability (occurrence of adverse events) were documented. Using the following as parameters "Alphabetischer Durchstreichtest, Feinmotoriktest, Befindlichkeitsskala, Beschwerdeliste, Schlafragebogen A and B" the differences between beginning and the end of the therapy were analyzed by simultaneous testing of the equality or superiority of the test preparation. The equivalence of both therapies according to sleep quality, fitness and quality of life was proven by a Mann-Whitney-Statistic of 0.50 with a lower boundary of the 95% confidence interval of 0.46. The patients' state of health improved during therapy while showing a deterioration after cessation with both preparations. Withdrawal symptoms, however, were documented with benzodiazepine. Only one adverse drug reaction was reported during this study, namely stomach complaints from both the test and reference medication. This study shows that the investigated hop-valerian preparation in the appropriate dose is a sensible alternative to benzodiazepine for the treatment of nonchronic and non-psychiatric sleep disorders.

### **Chemopreventive agents: selenium.**

Combs GF Jr., Gray WP.  
*Pharmacol Ther*  
1998;79:179-192.

The element selenium (Se) was recognized only 40 years ago as being essential in the nutrition of animals and humans. It is recognized as being an essential component of a number of enzymes, in which it is present as the amino acid selenocysteine. Se compounds have also been found to inhibit tumorigenesis in a variety of animal models, and recent studies indicate that supplemental Se in human diets may reduce cancer risk. The antitumorigenic activities have been associated with Se intakes that correct nutritionally deficient status in animals, as well as higher intakes that are substantially greater than those associated with maximal expression of the selenocysteine-containing enzymes. Therefore, it is proposed that while some cancer protection, particularly that involving antioxidant protection, involves selenoenzymes, specific Se metabolites, which are produced in significant amounts at relatively high Se intakes, also discharge antitumorigenic functions. According to this two-stage model of the roles of Se in cancer prevention, individuals with nutritionally adequate Se intakes may benefit from Se supplementation. Evidence for chemoprevention by Se and for the apparent mechanisms underlying these effects is reviewed to the end of facilitating the development of the potential of Se compounds as cancer chemopreventive agents.

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**The ‘age+5’ rule:  
comparisons of dietary  
fiber intake among 4- to  
10-year-old children.**

Hampl JS, Betts NM, Benes  
BA. *J Am Diet Assoc*  
1998;98:1418-1423.

**OBJECTIVE:** To determine children’s sources of dietary fiber and to identify the food group choices made by those who met the “age+5” rule, which recommends that children daily consume an amount of fiber that is equal to their age plus an additional 5 g fiber. **DESIGN:** This study used 24-hour dietary recalls and 1-day food records to assess the nutrient intake and food group choices of children who did and did not meet the recommendations of the age+5 rule. **SUBJECTS:** The 1989-1991 US Department of Agriculture Continuing Survey of Food Intakes by Individuals provided the study sample of 603 children between the ages of 4 and 6 years and 782 children between the ages of 7 and 10 years. **STATISTICAL ANALYSES:** Differences in nutrient and food group intakes between age categories were determined by t tests. **RESULTS:** Only 45% of 4- to 6-year-olds and 32% of 7- to 10-year-olds consumed adequate fiber to meet the age+5 rule. Those who met the age+5 rule did so by consuming significantly more high- and low-fiber breads and cereals, fruits, vegetables, legumes, nuts, and seeds. Children with low fiber intakes had significantly higher energy-adjusted intakes of fat and cholesterol, whereas those who met the age+5 rule had significantly higher energy-adjusted intakes of dietary fiber, vitamins A and E, folate, magnesium, and iron. **APPLICATIONS:** The majority of the children had low intakes of dietary fiber, suggesting that they are at risk for future chronic disease. Parents and school foodservice personnel should strive to offer fiber-rich foods to children so their acceptance and consumption of them will be increased.

### **L-carnitine supplementation in childhood epilepsy: current perspectives.**

De Vivo DC, Bohan TP, Coulter DL, et al. *Epilepsia* 1998;39:1216-1225.

In November 1996, a panel of pediatric neurologists met to update the consensus statement issued in 1989 by a panel of neurologists and metabolic experts on L-carnitine supplementation in childhood epilepsy. The panelists agreed that intravenous L-carnitine supplementation is clearly indicated for valproate (VPA)-induced hepatotoxicity, overdose, and other acute metabolic crises associated with carnitine deficiency. Oral supplementation is clearly indicated for the primary plasmalemmal carnitine transporter defect. The panelists concurred that oral L-carnitine supplementation is strongly suggested for the following groups as well: patients with certain secondary carnitine-deficiency syndromes, symptomatic VPA-associated hyperammonemia, multiple risk factors for VPA hepatotoxicity, or renal-associated syndromes; infants and young children taking VPA; patients with epilepsy using the ketogenic diet who have hypocarnitinemia; patients receiving dialysis; and premature infants who are receiving total parenteral nutrition. The panel recommended an oral L-carnitine dosage of 100 mg/kg/day, up to a maximum of 2 g/day. Intravenous supplementation for medical emergency situations usually exceeds this recommended dosage.

**Efficacy and acceptability of tadenan (Pygeum africanum extract) in the treatment of benign prostatic hyperplasia (BPH): a multicentre trial in central Europe.**

Breza J, Dzurny O, Borowka A, et al. *Curr Med Res Opin* 1998;14:127-139.

Pygeum africanum extract is available as Tadenan in many countries, including those in central and eastern Europe, for the treatment of mild to moderate BPH. Its efficacy and acceptability have been demonstrated in numerous open and placebo-controlled studies in large populations. The present open three-centre efficacy and safety study was conducted according to common protocol at urology clinics in the Czech and Slovak Republics and in Poland, in order to confirm the therapeutic profile of Pygeum africanum in conditions of daily practice, using International Prostate Symptom Score (IPSS) and flowmetry assessments. Men aged 50-75 years and in compliance with the selection criteria (including IPSS  $\geq$  12, quality of life (QoL) score  $\geq$  3, and maximum urinary flow  $\leq$  15 ml/s) were first examined then recalled after two weeks during which no treatment was provided (washout and check of stability). If still compliant, they were entered at this point into a two-month period of treatment with Pygeum africanum extract 50 mg twice daily. There followed a further one-month period without treatment, the objective being to evaluate the persistence of any effects observed during the previous two months of Pygeum africanum administration. The primary efficacy parameter investigated was IPSS; the other efficacy parameters were QoL, nocturnal frequency, maximum urinary flow, average urinary flow, post-voiding residual volume and prostatic volume, after one and two months of Pygeum africanum treatment and one month after stopping treatment. A total of 85 patients were evenly distributed between the three centres and completed the entire study. At inclusion their mean IPSS was 16.17, QoL was 3.60 and nocturia was 2.6 times per night. The changes in subjective scores, IPSS and QoL after the two-month treatment period were highly statistically significant with mean improvements of 40% and 31%, respectively. Nocturnal frequency was reduced by 32% and the mean reduction was again highly statistically significant. Mean maximum urinary flow, average urinary flow and urine volume were also statistically significantly improved, but the modest improvement in post-voiding volume did not reach statistical significance. The improvements, which exceeded those observed with placebo in earlier studies, were maintained after one month without treatment indicating an interesting persistence of clinically useful activity. Prostatic volume and quality of sexual life remained unchanged throughout. No treatment-related adverse effects were observed. In conclusion, under conditions of daily practice, Pygeum africanum extract induces significant improvement in IPSS and uroflowmetry parameters. These positive effects are accompanied by a very satisfactory safety profile with the overall result of a substantial improvement in QoL.

### **Effects of different regimens of sodium fluoride treatment for osteoporosis on the structure, remodeling and mineralization of bone.**

Balena R, Kleerekoper M, Foldes JA, et al. *Osteoporos Int* 1998;8:428-435.

We compared initial and final bone histomorphometric findings in 66 osteoporotic patients treated with sodium fluoride (NaF) according to three regimens, and in 7 osteoporotic patients who did not receive NaF. Fourteen patients received continuous NaF 75 mg/day (high-dose) with calcium 1500 mg/day for a mean of 41 months. Twenty-six patients received continuous NaF 50 mg/day (low-dose) with calcium 2000 mg/day for a mean of 15 months, either with (10 patients) or without (16 patients) vitamin D. Twenty-six patients received cyclical low-dose NaF, alternating with vitamin D, for a mean of 15 months and a total treatment duration of 28 months, of whom 14 were and 12 were not on NaF at the time of the second biopsy. Disregarding differences between regimens, there were significant increases in total and mineralized bone volume and trabecular thickness and nonsignificant decreases in these measurements in the control group. Fluoride-induced bone formation was exclusively appositional with no evidence for the creation of new trabeculae. The effect of low-dose NaF on bone structure was the same when the same total dose was given continuously or intermittently, and when the patient was or was not taking vitamin D. The increases in total and mineralized bone volume but not trabecular thickness were greater with high-dose than with low-dose NaF. Low-dose NaF caused modest but significant increases in all osteoid indices, and modest but significant declines in adjusted apposition rate and osteoid maturation rate and no change in bone formation rate. With high-dose NaF, the increase in BV/TV was greater but all indices of osteoid accumulation were much higher and all indices of impaired osteoblast function and mineralization were much lower, and 12 of 14 patients had some form of osteomalacia. This occurred also in 3 of 30 patients treated with low-dose NaF who were not taking vitamin D; the mean increase in osteoid thickness was significantly greater in these patients than in 22 low-dose patients who were taking vitamin D. We conclude: (1) The inconsistent effect of NaF in increasing bone strength is partly due to failure to restore connectivity in patients with severe bone loss and partly due to substantial osteoid accumulation. (2) Even low-dose NaF causes impaired osteoblast function, but this is much greater with high-dose prolonged therapy. (3) There is an unexplained discrepancy between the increase in bone formation implied by increases in spinal bone mineral and the lack of increase in bone formation measured histomorphometrically. (4) Defective mineralization is more closely related to the total cumulative dose of NaF than to the duration of treatment, and with low-dose treatment may be preventable by vitamin D. (5) Future clinical trials should be carried out with smaller doses of NaF and before there has been substantial loss of horizontal trabeculae in the spine.

**Total parenteral nutrition supplemented with medium-chain triacylglycerols prevents atrophy of the intestinal mucosa in septic rats.**

Iba T, Yagi Y, Kidokoro A, et al. *Nutrition* 1998;14:667-671.

Total parenteral nutrition (TPN) is associated with an increased incidence of bacterial translocation (BT) compared with enteral nutrition because of the disuse atrophy of the intestine. In this study, we assessed the effect of adding medium-chain triacylglycerols (MCT) to TPN for the prevention of mucosal atrophy in the intestine. Rats were subjected to either fat-free TPN, TPN with long-chain triacylglycerols (LCT), or TPN with MCT for 5 d and nutrition parameters were evaluated. In another set of rats receiving the same TPN regimen, 0.8 or 0.05 mg/kg endotoxin was administered on day 4. Survival was evaluated and BT to the mesenteric lymph nodes, liver, and systemic blood was measured 24 h later. The mucosal heights of the jejunum and ileum were evaluated concurrently. The survival rate was significantly improved in the MCT group ( $P < 0.05$ ) at the endotoxin dose of 0.8 mg/kg. The nutrition condition presented by phospholipid, total cholesterol, and total ketone body levels was the best in the MCT group compared to the other groups. The intestinal villous height in the ileum was significantly greater in the MCT group. However, the improvement of BT in MCT group was not statistically significant. In this endotoxin-challenged rat model, survival rate was improved by the supplementation of MCT. This effect may be presented in some part by the improvement in nutrition condition and by the prevention of mucosal atrophy in the intestine.

### **Effects of vitamin E and C supplementation on oxidative stress and viral load in HIV-infected subjects.**

Allard JP, Aghdassi E, Chau J, et al. *AIDS* 1998;12:1653-1659.

**OBJECTIVES:** The HIV-infected population is known to be oxidatively stressed and deficient in antioxidant micronutrients. Since in vitro replication of HIV is increased with oxidative stress, this study assessed the effect of antioxidant vitamin supplementation on lipid peroxidation, a measure of oxidative stress, and viral load in humans. **DESIGN:** A randomized placebo-controlled, double-blind study. **METHODS:** Forty-nine HIV-positive patients were randomized to receive supplements of both DL-alpha-tocopherol acetate (800 IU daily) and vitamin C (1000 mg daily), or matched placebo, for 3 months. Plasma antioxidant micronutrient status, breath pentane output, plasma lipid peroxides, malondialdehyde and viral load were measured at baseline and at 3 months. New or recurrent infections for the 6-month period after study entry were also recorded. **RESULTS:** The vitamin group (n = 26) had an increase in plasma concentrations of alpha-tocopherol (P < 0.0005) and vitamin C (P < 0.005) and a reduction in lipid peroxidation measured by breath pentane (P < 0.025), plasma lipid peroxides (P < 0.01) and malondialdehyde (P < 0.0005) when compared with controls (n = 23). There was also a trend towards a reduction in viral load (mean +/- SD changes over 3 months, -0.45 +/- 0.39 versus +0.50 +/- 0.40 log<sub>10</sub> copies/ml; P = 0.1; 95% confidence interval, -0.21 to -2.14). The number of infections reported was nine in the vitamin group and seven in the placebo group. **CONCLUSION:** Supplements of vitamin E and C reduce oxidative stress in HIV and produce a trend towards a reduction in viral load. This is worthy of larger clinical trials, especially in HIV-infected persons who cannot afford new combination therapies.