Abstracts

Recently Published Abstracts

Folate, vitamin B12, and homocysteine in major depressive disorder.

Fava M, Borus JS, Alpert JE, et al. *Am J Psychiatry* 1997;154:426-428

OBJECTIVE: The authors examined the relationships between levels of three metabolites (folate, vitamin B12, and homocysteine) and both depressive subtype and response to fluoxetine treatment in depressed patients. METHOD: Fluoxetine, 20 mg/day for 8 weeks, was given to 213 outpatients with major depressive disorder. At baseline, depressive subtypes were assessed, and a blood sample was collected from each patient. Serum metabolite levels were assayed. Response to treatment was determined by percentage change in score on the 17-item Hamilton Depression Rating Scale. RESULTS: Subjects with low folate levels were more likely to have melancholic depression and were significantly less likely to respond to fluoxetine. Homocysteine and B12 levels were not associated with depressive subtype or treatment response. CONCLUSIONS: Overall, the results are consistent with findings linking low folate levels to poorer response to antidepressant treatment. Folate levels might be considered in the evaluation of depressed patients who do not respond to antidepressant treatment.

State of the art of the production of the antimalarial compound artemisinin in plants.

Van Geldre E, Vergauwe A, Van den Eeckhout E. *Plant Mol Biol* 1997;33:199-209

For more than three centuries we have relied on the extracts of the bark of Cinchona species to treat malaria. Now, it seems we may be changing to the leaves of a Chinese weed, Artemisia annua, and its active compound artemisinin. Artemisinin-derived drugs have been proved particularly effective treatments for severe malaria, even for multidrug-resistant malaria. However, this promising antimalarial compound remains expensive and is hardly available on a global scale. Therefore, many research groups have directed their investigations toward the enhancement of artemisinin production in A. annua cell cultures or whole plants in order to overproduce artemisinin or one of its precursors. This article provides a brief review of the state of art of the different aspects in A. annua research.

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Effect of treatment on bone mass, mineral metabolism, and body composition in untreated celiac disease patients.

Mautalen C, Gonzalez D, Mazure R, et al. *Am J Gastroenterol* 1997;92: 313-318

BACKGROUND/AIMS: Osteopenia is a common complication of celiac disease. The aims of this study were to evaluate whether treatment produces bone remineralization and whether calcium and vitamin D supplementation are necessary to reduce osteopenia. METHODS: Bone mineral density and biochemical parameters of bone and mineral metabolism were measured in 14 newly diagnosed adult celiac disease patients. All patients were treated with a gluten-free diet and were randomized to receive diet only (n = 7) or diet plus calcium (1.0 g/day) and vitamin D (32,000 IU/wk) supplementation (n = 7). Bone density was measured at baseline and at 6 and 12 months of follow-up. Tests for biochemical determinations were repeated every 3 months. RESULTS: At diagnosis, 11 patients had evidence of osteopenia (> 1 SD below normality) in the spine and total skeleton. After 12 months of gluten restriction, overall bone mass had increased 5.0% ($p < 0.01$) in the lumbar spine and 5.0% ($p < 0.002$) in the total skeleton. When one only considers those 11 patients who strictly followed gluten restriction, bone density increased 8.4% in the lumbar spine and 7.7% in the total skeleton. Remineralization occurred throughout the skeleton but was more pronounced in the axial than in the peripheral skeleton. The increase in bone mass was independent of age or menopause. Remineralization in patients treated with diet only was similar to that of patients treated with diet and supplements. Basal biochemical parameters showed a high bone turnover with secondary hyperparathyroidism. Treatment induced a decrease in bone turnover activity. However, a complete restoration of biochemical parameters was not achieved. CONCLUSIONS: Strict gluten avoidance promoted a significant increase in bone mineral density. However, values still remain markedly low after 1 yr in several patients. Although calcium and vitamin D supplementation did not provide additional benefit to that obtained by diet alone in the doses administered, our results do not preclude a possible effect of vitamin D at higher dose.

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Parenteral zinc supplementation in adult humans during the acute phase response increases the febrile response.

Braunschweig CL, Sowers M, Kovacevich DS, et al. *J Nutr* 1997;127: 70-74.

The acute phase response (APR) that follows injury or infection is characterized by a decrease in serum zinc concentrations, which we hypothesized benefits the host. Additionally, we proposed that preventing this decline by supplementing zinc would result in an exaggerated APR as indicated by elevated temperatures, increased serum cytokine concentrations, interleukin 6 and the acute phase protein (ceruloplasmin). A prospective, randomized, double-blinded, clinical trial was conducted. Patients on home parenteral nutrition with a diagnosis of catheter sepsis and patients with a diagnosis of pancreatitis, also on total parenteral nutrition (TPN), were recruited for the study. Following enrollment, block randomization was used to assign patients to receive 0 mg (n = 23) or 30 mg (n = 21) of zinc per day for the first 3 d of TPN. Blood samples for measurement of serum zinc, copper, ceruloplasmin and interleukin-6 were obtained upon enrollment and on d 1 through 3 of TPN. The highest temperatures reported on these days in the medical record were also recorded. Repeated measures ANOVA was used to determine differences in the primary outcome variables over time. No significant differences between groups were observed in serum interleukin-6 or ceruloplasmin concentrations. A significantly higher (P = 0.035) temperature was observed in the zinc-supplemented group compared with the control group on d 3 of parenteral nutrition. We conclude that parenteral zinc supplementation in patients experiencing a mild APR resulted in an exaggerated APR as evidenced by a significantly higher febrile response.

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The role of folic acid in deficiency states and prevention of disease.

Swain RA, St Clair L. *J Fam Pract* 1997;44: 138-144.

Folic acid, a water-soluble vitamin, has been used since the 1940s to treat some cases of macrocytic anemia without neurologic disease. Folate deficiency is best diagnosed with red blood cell folate levels along with macrocytosis and/or megaloblastic anemia. In addition to reversing overt deficiency, the vitamin may reduce the incidence of neural tube defects by 45% in women who receive 400 micrograms per day. It is recommended that all women of childbearing age take 400 micrograms of folate per day. Elevations in homocysteine levels, a metabolite intimately associated with folate, are also being found with increasing regularity in those with cardiovascular diseases. Homocysteine levels are reduced by folic acid administration. Therefore, there is some biologic plausibility, but not currently direct proof, for the assumption that folate supplements may prevent heart disease, stroke, and peripheral arterial disease. Controlled trials should take place before widespread food supplementation with folate is carried out on a large scale because of the possibility of outbreaks of permanent B12-related neurologic damage in those with undiagnosed pernicious anemia. However, if a patient has a premature cardiovascular event and has minimal risk factors, ordering a test to determine homocysteine level may be advisable, and if elevated, treating with folic acid supplement as long as B12 deficiency does not coexist.

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Plasma methylmalonic acid in relation to serum cobalamin and plasma homocysteine in a psychogeriatric population and the effect of cobalamin treatment.

Nilsson K, Gustafson L, Faldt R, et al. *Int J Geriatr Psychiatry* 1997;12:67-72

Cobalamin deficiency seems to be a relatively common condition in psychogeriatric patients. To elucidate the diagnostic possibility of cobalamin deficiency we have in this study analysed three markers for cobalamin deficiency, plasma methylmalonic acid, plasma homocysteine and serum cobalamin, in 96 psychogeriatric patients. Patients were divided into four groups according to serum cobalamins above or below 150 pmol/l and normal (< 19.9 mumol/l) or increased plasma homocysteine. The upper reference limit (95th percentile) for plasma methylmalonic acid in 100 healthy subjects was established to 0.42 mumol/l. The mean value of methylmalonic acid was increased only in the group of patients with serum cobalamin below 150 pmol/l and increased plasma homocysteine compared to the other groups. In this group six (46%) out of 13 patients exhibited increased plasma methylmalonic acid, whereas in the other groups the frequency of increased plasma methylmalonic acid only varied from 10 to 13%. During cobalamin supplementation the most pronounced decrease of plasma methylmalonic acid also occurred in the group of patients with low serum cobalamin levels and increased plasma homocysteine. Only 39% of the initial mean value for plasma methylmalonic acid was noted after 7-10 days of cobalamin administration.

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Effect of garlic and fish-oil supplementation on serum lipid and lipoprotein concentrations in hypercholesterolemic men.

Adler AJ, Holub BJ. *Am J Clin Nutr* 1997;65:445-450

This study examined the effects of garlic and fish-oil supplementation (alone and in combination) on fasting serum lipids and lipoproteins in hypercholesterolemic subjects. After an initial run-in phase, 50 male subjects with moderate hypercholesterolemia were randomly assigned for 12 wk to one of four groups: 1) 900 mg garlic placebo/d + 12 g oil placebo/d; 2) 900 mg garlic/d + 12 g oil placebo/d; 3) 900 mg garlic placebo/d + 12 g fish oil/d, providing 3.6 g n-3 fatty acids/d; and 4) 900 mg garlic/d + 12 g fish oil/d. In the placebo group, mean serum total cholesterol, low-density-lipoprotein cholesterol (LDL-C), and triacylglycerols were not significantly changed in relation to baseline. Mean group total cholesterol concentrations were significantly lower with garlic+fish oil (-12.2%) and with garlic (-11.5%) after 12 wk but not with fish oil alone. Mean LDL-C concentrations were reduced with garlic+fish oil (-9.5%) and with garlic (-14.2%) but were raised with fish oil (+8.5%). Mean triacylglycerol concentrations were reduced with garlic+fish oil (-34.3%) and fish oil alone (-37.3%). The garlic groups (with and without fish oil) had significantly lower ratios of total cholesterol to high-density-lipoprotein cholesterol (HDL-C) and LDL-C to HDL-C. In summary, garlic supplementation significantly decreased both total cholesterol and LDL-C whereas fish-oil supplementation significantly decreased triacylglycerol concentrations and increased LDL-C concentrations in hypercholesterolemic men. The combination of garlic and fish oil reversed the moderate fish-oil-induced rise in LDL-C. Coadministration of garlic with fish oil was well-tolerated and had a beneficial effect on serum lipid and lipoprotein concentrations by providing a combined lowering of total cholesterol, LDL-C, and triacylglycerol concentrations as well as the ratios of total cholesterol to HDL-C and LDL-C to HDL-C.

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Low serum vitamin B-12 concentrations are associated with faster human immunodeficiency virus type 1 (HIV-1) disease progression.

Tang AM, Graham NM, Chandra RK, Saah AJ. *J Nutr* 1997;127:345-351

We conducted a nonconcurrent prospective cohort study to examine associations between serum concentrations of vitamin B-6, vitamin B-12 and folate and the risk of progression to first acquired immunodeficiency syndrome (AIDS) diagnosis and CD4+ cell decline to < 2 x 10(8) cells/L. The study population was drawn from a cohort of homosexual and bisexual men in the Baltimore-Washington, DC area. Eligible subjects were human immunodeficiency virus type 1 (HIV-1)-seropositive at study entry and had serum available in the serum repository from their 1984 baseline study visit. Serum micronutrient levels were assessed in 310 subjects. The follow-up period (April 1984 through December 1993) was approximately 9 y. In Kaplan-Meier analyses, participants with low serum vitamin B-12 concentrations (< 120 pmol/L) had significantly shorter AIDS-free time than those with adequate vitamin B-12 concentrations (median AIDS-free time = 4 vs. 8 y, respectively, P = 0.004). This effect persisted in Cox proportional hazards models after adjusting for HIV-1-related symptoms, CD4+ cell count, age, serum albumin, use of antiretroviral therapy before AIDS, frequency of alcohol consumption and serum folate concentration [relative hazard (RH) = 1.89, 95% confidence interval (CI) = 1.15-3.10]. To further explore the temporal relation between low serum vitamin B-12 concentrations and disease progression, additional analyses were performed excluding subjects with more advanced disease at baseline. In these analyses, the increase in risk of progression to AIDS for those with low serum vitamin B-12 concentrations remained significant (RH = 2.21, 95% CI = 1.13-4.34), providing further evidence that low vitamin B-12 concentrations preceded disease progression. In contrast, low serum concentrations of vitamin B-6 and folate were not associated with either progression to AIDS or decline in CD4+ lymphocyte count. Intervention studies are needed to determine whether correction of low serum vitamin B-12 concentrations in early HIV-1 infection will influence the natural history of disease progression.

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Activation of immune function by dehydroepiandrosterone (DHEA) in age-advanced men.

Khorram O, Vu L, Yen SS. *J Gerontol A Biol Sci Med Sci* 1997;52:M1-7

BACKGROUND: Substantial data from animal studies have demonstrated a stimulatory effect of dehydroepiandrosterone (DHEA) on immune function. However, little is known about the effects of DHEA on the human immune system. Since aging is associated with a decline in immune function and in DHEA production, we proposed that oral administration of DHEA to elderly men would result in activation of their immune system. METHODS: Nine healthy age-advanced men (mean age of 63 years) with low DHEA-sulfate levels participated in this study. They were treated nightly with an oral placebo for 2 weeks followed by DHEA (50 mg) for 20 weeks. Fasting (0800h-0900h) blood samples were obtained at 4- to 8-week intervals for immune function studies and hormone determinations. Freshly isolated peripheral lymphocytes were used for flow cytometric identification of lymphocyte subsets, cells expressing the IL-2 receptor (IL-2R), mitogen stimulation studies, and for determining natural killer (NK) cell number and cytotoxicity. Levels of interleukin-2 (IL-2) and IL-6 secreted from cultured lymphocytes were determined under basal and mitogen stimulated conditions. Sera were analyzed for soluble IL-2 Receptor (sIL-2R) levels, insulin-like growth factor-I (IGF-I) and IGF binding protein-I (IGFBP-I) concentrations. RESULTS: Baseline levels of serum DHEA sulfate (DHEAS), a stable marker of circulating DHEA levels, were 2 standard deviations below young adult values and increased 3-4 fold within 2 weeks. These levels were sustained throughout the duration of DHEA administration. When compared with placebo, DHEA administration resulted in a 20% increase ($p < .01$) in serum IGF-I, a decreasing trend in IGFBP-I, and a 32% increase in the ratio of IGF-I/IGFBP-I ($p < .01$). Activation of immune function occurred within 2-20 weeks of DHEA treatment. The number of monocytes increased significantly ($p < .01$) after 2 (45%) and 20 (35%) weeks of treatment. The population of B cells fluctuated with increases ($p < .05$) at 2 (35%) and 10 (29%) weeks of treatment. B cell mitogenic response increased 62% ($p < .05$) by 12 weeks unaccompanied by changes in serum IgG, IgA, and IgM levels. Total T cells and T cell subsets were unaltered. However, a 40% increase ($p < .05$) in T cell mitogenic response, 39% increase in cells expressing the IL-2R (CD25+) ($p < .05$), and 20% increase in serum sIL-2R levels ($p < .01$) were found at 12-20 weeks of DHEA treatment, suggesting a functional activation of T lymphocytes occurred. In vitro mitogen stimulated release of IL-2 and IL-6 was enhanced 50% ($p < .05$) and 30% ($p < .01$) respectively by 20 weeks of treatment without basal secretion being affected. NK cell number showed a 22-37% increase ($p < .01$) by 18-20 weeks of treatment with a concomitant 45% increase ($p < .01$) in cytotoxicity. There were no adverse effects noted with DHEA administration. CONCLUSION: Administration of oral DHEA at a daily dose of 50 mg to age-advanced men with low serum DHEAS levels significantly activated immune function. The mechanism(s) to account for the immunoenhancing properties of DHEA are unclear. Consideration is given to the potential role of an increase in bioavailable IGF-I, which by virtue of its mitogenic effects on immune cell function, may mediate the DHEA effects. While extended studies are required, our findings suggest potential therapeutic benefits of DHEA in immunodeficient states.

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Role of oxidative stress and antioxidant therapy in alcoholic and nonalcoholic liver diseases.

Lieber CS. *Adv Pharmacol* 1997;38:601-628

The main pathway for the hepatic oxidation of ethanol to acetaldehyde proceeds via ADH and is associated with the reduction of NAD to NADH; the latter produces a striking redox change with various associated metabolic disorders. NADH also inhibits xanthine dehydrogenase activity, resulting in a shift of purine oxidation to xanthine oxidase, thereby promoting the generation of oxygen-free radical species. NADH also supports microsomal oxidations, including that of ethanol, in part via transhydrogenation to NADPH. In addition to the classic alcohol dehydrogenase pathway, ethanol can also be reduced by an accessory but inducible microsomal ethanoloxidizing system. This induction is associated with proliferation of the endoplasmic reticulum, both in experimental animals and in humans, and is accompanied by increased oxidation of NADPH with resulting H2O2 generation. There is also a concomitant 4- to 10-fold induction of cytochrome P4502E1 (2E1) both in rats and in humans, with hepatic perivenular preponderance. This 2E1 induction contributes to the well-known lipid peroxidation associated with alcoholic liver injury, as demonstrated by increased rates of superoxide radical production and lipid peroxidation correlating with the amount of 2E1 in liver microsomal preparations and the inhibition of lipid peroxidation in liver microsomes by antibodies against 2E1 in control and ethanol-fed rats. Indeed, 2E1 is rather "leaky" and its operation results in a significant release of free radicals. In addition, induction of this microsomal system results in enhanced acetaldehyde production, which in turn impairs defense systems against oxidative stress. For instance, it decreases GSH by various mechanisms, including binding to cysteine or by provoking its leakage out of the mitochondria and of the cell. Hepatic GSH depletion after chronic alcohol consumption was shown both in experimental animals and in humans. Alcohol-induced increased GSH turnover was demonstrated indirectly by a rise in alpha-amino-n-butyric acid in rats and baboons and in volunteers given alcohol. The ultimate precursor of cysteine (one of the three amino acids of GSH) is methionine. Methionine, however, must be first activated to S-adenosylmethionine by an enzyme which is depressed by alcoholic liver disease. This block can be bypassed by SAMe administration which restores hepatic SAMe levels and attenuates parameters of ethanol-induced liver injury significantly such as the increase in circulating transaminases, mitochondrial lesions, and leakage of mitochondrial enzymes (e.g., glutamic dehydrogenase) into the bloodstream. SAMe also contributes to the methylation of phosphatidylethanolamine to phosphatidylcholine. The methyltransferase involved is strikingly depressed by alcohol consumption, but this can be corrected, and hepatic phosphatidylcholine levels restored, by the administration of a mixture of polyunsaturated phospholipids (polyenylphosphatidylcholine). In addition, PPC provided total protection against alcohol-induced septal fibrosis and cirrhosis in the baboon and it abolished an associated twofold rise in hepatic F2-isoprostanes, a product of lipid peroxidation. A similar effect was observed in rats given CCl4. Thus, PPC prevented CCl4- and alcohol-induced lipid peroxidation in rats and baboons, respectively, while it attenuated the associated liver injury. Similar studies are ongoing in humans.

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Double-blind, placebo-controlled, crossover trial of glycine adjuvant therapy for treatment-resistant schizophrenia.

Heresco-Levy U, Javitt DC, Ermilov M, et al. *Br J Psychiatry* 1996;169: 610-617

BACKGROUND: It has been proposed that schizophrenia is associated with underactivity of brain glutamatergic neurotransmission, especially at the level of the N-methyl-D-aspartate (NMDA) subtype of glutamate receptor. Glycine potentiates NMDA receptor-mediated neurotransmission, indicating that it may serve as an effective therapeutic agent in the treatment of schizophrenia. METHOD: Eleven treatment-resistant patients with chronic schizophrenia completed a double-blind, placebo-controlled, six-week, randomly assigned, crossover treatment trial of 0.8 g/kg body weight/day of glycine, added to their prior antipsychotic treatment. RESULTS: Glycine was well tolerated, resulted in significantly increased serum glycine levels and induced a mean 36 (7%) reduction in negative symptoms ($P < 0.0001$). Significant improvements were also induced in depressive and cognitive symptoms. The greatest reduction in negative symptoms was registered in the patients who had the lowest baseline serum glycine levels. CONCLUSIONS: These results extend previous findings and suggest an additional approach to the pharmacotherapy of negative symptoms and cognitive deficits in schizophrenia.

Folic acid and cervix dysplasia.

Zarcone R, Bellini P, Carfora E, et al. *Minerva Ginecol* 1996;48:397-400

The localized folate deficiency, which is sometimes misdiagnosed as cervical dysplasia, because of morphological similarities between the cytologic features of megaloblastosis seen with folate deficiency and the changes associated with dysplasia, could be a component of the dysplastic process. In this study we attempted the effect of oral folic in women with cervical dysplasia. A total of 154 subjects with grade 1 or 2 CIN were randomly assigned either 10 mg of folic acid or a placebo daily for 6 months. Clinical status, human papillomavirus type 16 infection and blood folate levels were monitored at 2 month intervals. After 6-months no significant differences were observed between supplemented and unsupplemented subjects regarding dysplasia status, biopsy results, or prevalence of human papillomavirus type 16 infection. Folate deficiency may be involved as a cocarcinogen during the initiation of cervical dysplasia, but folic acid supplements do not alter the course of established disease.

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A medium chain triglyceride-based diet in patients with HIV and chronic diarrhea reduces diarrhea and malabsorption: a prospective, controlled trial.

Wanke CA, Pleskow D, Degirolami PC, et al.
Nutrition 1996;12:766-771

Our objective was to determine whether a medium-chained triglyceride (MCT)-based diet, compared to a long-chain triglyceride (LCT)-based diet, conveys a beneficial effect on diarrhea and fat malabsorption in human immunodeficiency virus (HIV)-infected individuals with chronic diarrhea and weight loss. A secondary objective was to evaluate the pathogens associated with the diarrhea and to evaluate whether the etiologic agent was a determinant of response to the nutritional intervention. Prospective, randomized double-blind comparative trial was conducted in 24 adult patients with HIV, diarrhea of greater than 4-wk duration, fat malabsorption, and loss of 10-20% of ideal body weight, these patients were recruited from our outpatient infectious disease clinic. Evaluations of diarrheal pathogens were made by complete stool examination, upper and lower endoscopy with quantitative culture, and biopsy. Body composition determinations, and measurements of fat, carbohydrate, and vitamin absorption pre- and postintervention. Patients were randomly assigned to one of two complete nutritional products with either medium- or long-chain triglyceride fat exclusively for 12 d followed by treatment of infectious pathogens. Ten patients were found to have Microsporidium and 9 patients had no identifiable pathogen. All patients responded to intervention with both nutritional products overall with 45% fewer stools, decreased stool fat and weight, and a significant increase in urine nitrogen. The group that received the MCT product demonstrated significantly decreased stool number (mean 4 to 2.5), stool fat (mean 14 to 5.4 g), and stool weight (mean 428 to 262 g) compared with baseline ($P < 0.01$ for all). Patients with both species of microsporidia and with pathogen negative diarrhea had good response. We found that HIV patients with diarrhea, regardless of etiology, and documented fat malabsorption may benefit symptomatically from a diet composed of an MCT-based liquid supplement.

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A polysaccharide fraction of Zizyphi fructus in augmenting natural killer activity by oral administration.

Yamaoka Y, Kawakita T, Kaneko M, Nomoto K. *Biol Pharm Bull* 1996;19: 936-939

Shosaiko-to (Xiao-chai-hu-tang, SHO), a Kampo medicine, was prepared by decocting a prescription of 7 kinds of crude drugs, namely Bupleuri Radix, Pinelliae Tuber, Scutellariae Radix, Zizyphi Fructus, Ginseng Radix, Glycyrrhizae Radix and Zingiberis Rhizoma. Previously, we reported that the effect of the orally administered SHO in augmenting natural killer (NK) activity in the peripheral blood was attributed to the acidic polysaccharide fraction. To characterize the active components in the crude materials in SHO, the effects of extracts and various fractions were investigated by oral administration. The extracts of Zizyphi Fructus, Zingiberis Rhizoma, Scutellariae Radix, Glycyrrhizae Radix and Pinelliae Tuber augmented NK activity by oral administration. The high weight molecular fraction of Zizyphi Fructus was the most effective in augmenting NK activity. Thus, we obtained an active polysaccharide fraction from the high weight molecular fraction of Zizyphi Fructus. This polysaccharide fraction with a high molecular weight of approximately 43,000 contained 54.7% carbohydrate, 61.8% uronic acid and 20.9% protein. The sugar moiety was composed of rhamnose, arabinose, xylose, fucose, mannose, galactose, glucose and galacturonic acid in molar ratios of 28:59:11:9:7:32:20:100.

Antioxidants in the treatment of schizophrenia (the correction of lipid peroxidation processes).

Kut'ko II, Frolov VM, Pustovoi IuG, et al. *Zh Nevropatol Psikhiatr Im S S Korsakova* 1996;96:32-34

It was established in the course of 185 schizophrenic patients' examination that intensification of lipid peroxidation (LP) took place in relapses of the disease. It was manifested either in increase of blood serum levels of both malonic dialdehyde and diene conjugates, or in decrease of erythrocytes' resistance to LP mediated hemolysis. Alterations in indices of either spontaneous or induced chemoluminescence were revealed too. LP indices were lower by the end of the treatment in hospital, but remained significantly higher than normal values. Application of antioxidants in combined treatment of schizophrenic patients promoted decrease of LP activity as well as improvement in mental state of patients. LP activity was high in the remission too. Determination of LP indices may have prognostic importance.

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Reduced intravenous glutathione in the treatment of early Parkinson's disease.

Sechi G, Deledda MG, Bua G, et al. *Prog Neuropsychopharmacol Biol Psychiatry* 1996;20: 1159-1170

1. Several studies have demonstrated a deficiency in reduced glutathione (GSH) in the nigra of patients with Parkinson's Disease (PD). In particular, the magnitude of reduction in GSH seems to parallel the severity of the disease. This finding may indicate a means by which the nigra cells could be therapeutically supported. 2. The authors studied the effects of GSH in nine patients with early, untreated PD. GSH was administered intravenous, 600 mg twice daily, for 30 days, in an open label fashion. Then, the drug was discontinued and a follow-up examination carried-out at 1-month interval for 2-4 months. Thereafter, the patients were treated with carbidopa-levodopa. 3. The clinical disability was assessed by using two different rating scale and the Webster Step-Second Test at baseline and at 1-month interval for 4-6 months. All patients improved significantly after GSH therapy, with a 42% decline in disability. Once GSH was stopped the therapeutic effect lasted for 2-4 months. 4. Our data indicate that in untreated PD patients GSH has symptomatic efficacy and possibly retards the progression of the disease.

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Adjuvant therapy with the pineal hormone melatonin in patients with lymph node relapse due to malignant melanoma.

Lissoni P, Brivio O, Brivio F, et al. *J Pineal Res* 1996;21:239-242

Several experimental studies have shown that melatonin has an oncostatic action, either by stimulating host antitumor immune defenses or by directly inhibiting the growth of some cancer histotypes, including melanoma. Our previous clinical studies demonstrated that melatonin may induce stabilization of the disease in untreatable metastatic solid tumor patients, and these results have been confirmed by others, at least in patients with metastatic melanoma. On the contrary, at present there are no data related to the possible efficacy of melatonin as an adjuvant endocrine therapy. This study was performed to investigate the impact of melatonin therapy on the disease-free survival (DFS) in melanoma patients surgically treated for regional node recurrence. The study included 30 node-relapsed melanoma patients, who were randomized to receive no treatment or adjuvant therapy of melatonin (20 mg/day orally in the evening) every day until disease progression. After a median follow up of 31 months, the percent of DFS was significantly higher in melatonin-treated individuals than in controls. The DFS curve was also significantly longer in melatonin group than in controls. No melatonin-related toxicity was observed. This preliminary study suggests that an adjuvant endocrine therapy with melatonin may be effective in preventing disease progression in node-relapsed melanoma patients.

Recurrent aphthous stomatitis and thiamine deficiency.

Haisraeli-Shalish M, Livneh A, Katz J, et al. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1996;82: 634-636

Recurrent aphthous stomatitis is a disease of unknown cause. To examine whether thiamine (vitamin B1) deficiency is associated with recurrent aphthous stomatitis, we studied vitamin B1 levels in 70 patients with recurrent aphthous stomatitis and in 50 members of a control group. The vitamin B1 level was determined as thiamine pyrophosphate effect on transketolase activity in red blood cell lysates. Low levels of vitamin B1 were detected in 49 patients but in only two members of the control group ($p < 0.0001$). These low levels were not associated with patient age, sex, or underlying disease causing recurrent aphthous stomatitis. Our finding suggests an association between thiamine deficiency and recurrent aphthous stomatitis.

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Lipid peroxidation and human sperm motility: protective role of vitamin E.

Suleiman SA, Ali ME, Zaki ZM, et al. *J Androl* 1996;17:530-537

Asthenospermia is the main factor of male infertility among patients consulting the Asir Infertility Center in Abha, Saudi Arabia. Lipid peroxidation occurring in both the seminal plasma and spermatozoa was estimated by malondialdehyde (MDA) concentration. Spermatozoal MDA concentration was higher in men with decreased sperm motility. The MDA concentration in the seminal plasma exhibited no relationship with sperm concentration, sperm motility, the number of immotile spermatozoa, or even the absence of spermatozoa. The MDA concentration in sperm pellet suspensions of asthenospermic and oligoasthenospermic patients was almost twice that of the normospermic males. The MDA concentration in the sperm pellet suspension from normospermic or oligospermic patients was about 10% that in the seminal plasma. However, the MDA concentration in the sperm pellet suspension of asthenospermic or oligoasthenospermic patients was about 15% that in the seminal plasma. Treatment of asthenospermic patients with oral Vitamin E significantly decreased the MDA concentration in spermatozoa and improved sperm motility. Eleven out of the 52 treated patients (21%) impregnated their spouses; nine of the spouses successfully ended with normal term deliveries, whereas the other two aborted in the first trimester. No pregnancies were reported in the spouses of the placebo-treated patients.

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Differential stimulation of cortisol and dehydroepiandrosterone levels by food in obese and normal subjects: relation to body fat distribution.

Korbonits M, Trainer PJ, Nelson ML, et al. *Clin Endocrinol* 1996;45:699-706

BACKGROUND: It has been previously shown that food intake elevates circulating ACTH and cortisol levels, but no report has been published regarding the changes in circulating dehydroepiandrosterone (DHEA). DHEA was originally described as a weak androgen, but more recently it has been associated with a wide range of metabolic functions. In addition, previous studies have described a hyper-responsive hypothalamo-pituitary-adrenal axis in obese subjects in response to various stimuli, but the specific response to food has not been studied. SUBJECTS AND DESIGN: We studied the effect of food on the hypothalamo-pituitary-adrenal axis in 20 subjects of normal body mass index (BMI range 18-25) and also in a group of 12 obese subjects (BMI range 34-61). Levels of glucose, insulin, ACTH, cortisol and dehydroepiandrosterone were measured every 20 minutes. RESULTS: A small rise in DHEA accompanies the rise in circulating ACTH and cortisol in response to food in both lean and obese subjects, but DHEA rose independently of cortisol and ACTH on the fasting day. In the obese subjects, food induced a significantly greater change in serum cortisol (peak cortisol rise (mean +/- SEM); normal-weight group, 169 +/- 14%; obese group, 294 +/- 23%) and in the cortisol/DHEA ratio (area under the curve; normal-weight group, 202 +/- 15%; obese group, 292 +/- 29%) than in the normal-weight subjects. This difference was particularly notable in those with central-type obesity (waist/hip ratio > 0.80). A group of the normal, jean female subjects showed no cortisol rise after food intake. CONCLUSION: Our results suggest that DHEA may vary independently of circulating cortisol, and that the cortisol response to food is enhanced in obese subjects, particularly in those with central obesity. We speculate that there may be a caused connection between the cortisol response to food in normal subjects, and the subsequent distribution of fat if such subjects overeat sufficiently to become obese.

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Abstracts

Recently Published Abstracts

Influence of high dietary selenium intake on the thyroid hormone level in human serum.

Bratter P, Negretti de Bratter VE. *J Trace Elem Med Biol* 1996;10:163-166

Effects of high dietary selenium supply (range 170-980 micrograms per day) on the metabolism of thyroid hormones were studied in serum of mothers living in seleniferous areas of Venezuela. Free thyroxine (FT4), free triiodothyronine (FT3) and human thyroid stimulating hormone (hTSH) were found to be within the normal range but a significant inverse correlation was found between the FT3 and selenium. It was hypothesized that the activity of hepatic selenoenzyme type I iodothyronine 5'-deiodinase, which catalyzes the production of T3 from T4, becomes depressed at high levels of dietary intake of selenium. The effect is discussed with respect to the safe level of dietary selenium intake, which was estimated to be below 500 micrograms per day.

Effectiveness of glycyrrhizin for oral lichen planus in patients with chronic HCV infection.

Da Nagao Y, Sata M, Suzuki H, et al. *J Gastroenterol* 1996;31:691-695

Oral lichen planus (OLP), an intractable inflammatory disease characterized by a band-like lymphocytic invasion under the oral mucosa, is frequently associated with hepatitis C virus (HCV) infection. We investigated the effects of glycyrrhizin, which is used to treat chronic liver dysfunction, in nine patients with OLP who were positive for HCV antibody and HCV RNA. A control group, eight patients with OLP who were also positive for HCV antibody and HCV RNA, was given only dental cleaning. Glycyrrhizin (GL) was given intravenously, at a dose of 40 ml (0.2% solution) daily, for 4 consecutive weeks. Six (66.7%) of the nine patients given GL improved clinically (P = 0.0141 vs non-GL group), suggesting that GL is useful in treating OLP.

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