

Adrenal Disease

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## ABSTRACTS

Effect of green tea rich in gamma-aminobutyric acid on blood pressure of Dahl salt-sensitive rats.

Abe Y, Umemura S, Sugimoto K, et al.

*Am J Hypertens.* 1995 Jan; 8(1):74-9.

gamma-Aminobutyric acid (GABA) is known to be involved in the regulation of blood pressure by modulating the neurotransmitter release in the central and peripheral sympathetic nervous systems. This study investigated the antihypertensive effect of green tea rich in GABA (GABA-rich tea) in young and old Dahl salt-sensitive (S) rats. GABA-rich tea was made by fermenting fresh green tea leaves under nitrogen gas. In experiment 1, 21 11-month-old rats, fed a 4% NaCl diet for 3 weeks, were given water (group W), an ordinary tea solution (group T), or a GABA-rich tea solution (group G) for 4 weeks. The average GABA intake was 4.0 mg/rat per day. After 4 weeks of the treatment, blood pressure was significantly decreased in group G (176 +/- 4; P < .01) compared with group W (207 +/- 9) or group T (193 +/- 5 mm Hg). Plasma GABA levels were more elevated in group G (111 +/- 54) than in group W (not detectable) or group T (14 +/- 8 ng/mL; P < .01 v G). In experiment 2, 21 5-week-old rats, fed a 4% NaCl diet, were divided into groups W, T, and G. The average GABA intake was 1.8 mg/rat per day. Body weight or chow and beverage consumption did not differ significantly among the three groups. After 4 weeks of the treatment, although blood pressure was comparable in groups W and T (165 +/- 3 v 164 +/- 5 mm Hg, mean +/- SE), it was significantly lower in group G (142 +/- 3 mm Hg) than in the other groups (P < .01). (ABSTRACT TRUNCATED AT 250 WORDS)

Decreased levels of dehydroepiandrosterone sulphate in severe critical illness: a sign of exhausted adrenal reserve?

Beishuizen A, Thijs LG, Vermes I.

*Crit Care.* 2002 Oct; 6(5):434-8.

INTRODUCTION: Dehydroepiandrosterone (DHEA) and its sulphate (DHEAS) are pleiotropic adrenal hormones with immunostimulating and antiglucocorticoid effects. The present study was conducted to evaluate the time course of DHEAS levels in critically ill patients and to study their association with the hypothalamic-pituitary-adrenal axis. MATERIALS AND METHOD: This was a prospective observational clinical and laboratory study, including 30 patients with septic shock, eight patients with multiple trauma, and 40 age- and sex-matched control patients. We took serial measurements of blood concentrations of DHEAS, cortisol, tumour necrosis factor-alpha and IL-6, and of adrenocorticotrophic hormone immunoreactivity over 14 days or until discharge/death. RESULTS: On admission, DHEAS was extremely low in septic shock (1.2 +/- 0.8 mol/l) in comparison with multiple trauma patients (2.4 +/- 0.5 micromol/l; P < 0.05) and control patients (4.2 +/- 1.8; P < 0.01). DHEAS had a significant (P < 0.01) negative correlation with age, IL-6 and Acute Physiology and Chronic Health Evaluation II scores in both patient groups. Only during the acute phase did DHEAS negatively correlate with dopamine. Nonsurvivors of septic shock (n = "11") had lower DHEAS levels (0.4 +/- 0.3 micromol/l) than did survivors (1.7 +/- 1.1 micromol/l; P < 0.01). The time course of DHEAS exhibited a persistent depletion during follow up, whereas cortisol levels were increased at all time points. CONCLUSION: We identified extremely low DHEAS levels in septic shock and, to a lesser degree, in multiple trauma patients as compared with those of age- and sex-matched control patients. There appeared to be a dissociation between DHEAS (decreased) and cortisol (increased) levels, which changed only slightly over time. Nonsurvivors of sepsis and patients with relative adrenal insufficiency had the lowest DHEAS values, suggesting that DHEAS might be a prognostic marker and a sign of exhausted adrenal reserve in critical illness

The influence of phosphatidylserine supplementation on mood and heart rate when faced with an acute stressor.

Benton D, Donohoe RT, Sillance B, et al.

*Nutr Neurosci.* 2001; 4(3):169-78.

There have been previous reports that supplements of phosphatidylserine (PS) blunted the release of cortisol in response to exercise stress and that it improved mood. The present study extended these observations by considering whether PS

supplementation influenced subjective feelings of stress and the change in heart rate when a stressful mental arithmetic task was performed. In young adults, with neuroticism scores above rather than below the median, the taking of 300mg PS each day for a month was associated with feeling less stressed and having a better mood. The study for the first time reports an improvement in mood following PS supplementation in a sub-group of young healthy adults

A randomized controlled trial of high dose ascorbic acid for reduction of blood pressure, cortisol, and subjective responses to psychological stress.

Brody S, Preut R, Schommer K, et al.

*Psychopharmacology (Berl)*. 2002 Jan; 159(3):319-24.

**RATIONALE:** Physiological responses to stress are considered disruptive to health. High-dose ascorbic acid has reduced indices of stress in laboratory animals. **METHODS:** We conducted a randomized double-blind, placebo-controlled 14-day trial of sustained-release ascorbic acid (60 healthy young adults; 3 x1000 mg/day Cetebe) and placebo (60 healthy young adults) for reduction of blood pressure, cortisol, and subjective response to acute psychological stress (Trier Social Stress Test, TSST, consisting of public speaking and mental arithmetic). Six subjects from each group were excluded. **RESULTS:** Compared to the placebo group, the ascorbic acid group had less systolic blood pressure (an increase of 23 versus 31 mmHg), diastolic blood pressure, and subjective stress responses to the TSST; and also had faster salivary cortisol recovery (but not smaller overall cortisol response). Cortisol response to 1 microg ACTH, and reported side-effects during the trial did not differ between groups. Plasma ascorbic acid level at the end of the trial but not pre-trial was associated with reduced stress reactivity of systolic blood pressure, diastolic blood pressure, and subjective stress, and with greater salivary cortisol recovery. **CONCLUSIONS:** Treatment with high-dose sustained-release ascorbic acid palliates blood pressure, cortisol, and subjective response to acute psychological stress. These effects are not attributable to modification of adrenal responsiveness

The American Medical Association Encyclopedia of Medicine.

Clayman CB.

1989;

Gerovital H3 in the treatment of the depressed aging patient.

Cohen SDKS.

*Psychosomatics*. 1974; 15(1):15-9.

Acetylsalicylic acid inhibits the pituitary response to exercise-related stress in humans.

Di Luigi L, Guidetti L, Romanelli F, et al.

*Med Sci Sports Exerc*. 2001 Dec; 33(12):2029-35.

**PURPOSE:** Prostaglandins (PGs) modulate the activity of the hypothalamus-pituitary axis, and pituitary hormones are largely involved in the physiological responses to exercise. The purpose of this study was to analyze the effects of acetylsalicylic acid (ASA), an inhibitor of PGs synthesis, in the pituitary responses to physical stress in humans. **METHODS:** Adrenocorticotropin (ACTH), beta-endorphin, cortisol, growth hormone (GH), and prolactin (PRL) responses to exercise were evaluated after administration of either placebo or ASA. Blood samples for hormone evaluations before (-30, -15, and 0 pre) and after (0 post, +15, +30, +45, +60, and +90 min) a 30-min treadmill exercise (75% of  $\dot{V}O_2(\text{max})$ ) were taken from 12 male athletes during two exercise trials. One tablet of ASA (800 mg), or placebo, was administered two times daily for 3 d before and on the morning of each exercise-test. **RESULTS:** The results clearly show that, compared with placebo, ASA ingestion significantly blunted the increased serum ACTH, beta-endorphin, cortisol, and GH levels before exercise (anticipatory response) and was associated with reduced cortisol concentrations after exercise. Furthermore, although no differences in the GH response to exercise were shown, a significantly reduced total PRL response to stress condition was observed after ASA. **CONCLUSION:** ASA influences ACTH, beta-endorphin, cortisol, GH, and PRL responses to exercise-related stress in humans (preexercise activation/exercise-linked response). Even though it is not possible to exclude direct action for ASA, our data indirectly confirm a role of PGs in these responses. We have to further evaluate the nature of the preexercise endocrine activation and, because of the large use of anti-inflammatory drugs in athletes, whether the interaction between ASA and hormones might positively or negatively influence health status, performance, and/or recovery

Psychoneuroendocrinological contributions to the etiology of depression, posttraumatic stress disorder, and stress-related

bodily disorders: the role of the hypothalamus-pituitary-adrenal axis.

Ehlert U, Gaab J, Heinrichs M.

*Biol Psychol.* 2001 Jul; 57(1-3):141-52.

Following the assumption that stressors play an important part in the etiology and maintenance of psychiatric disorders, it is necessary to evaluate parameters reflecting stress-related physiological reactions. Results from these examinations may help to deepen the insight into the etiology of psychiatric disorders and to elucidate diagnostic uncertainties. One of the best-known stress-related endocrine reactions is the hormonal release of the hypothalamic-pituitary-adrenal (HPA) axis. Dysregulations of this axis are associated with several psychiatric disorders. Profound hyperactivity of the HPA-axis has been found in melancholic depression, alcoholism, and eating disorders. In contrast, posttraumatic stress disorder, stress-related bodily disorders like idiopathic pain syndromes, and chronic fatigue syndrome seem to be associated with diminished HPA activity (lowered activity of the adrenal gland). Hypotheses referring to (a) the psychophysiological meaning and (b) the development of these alterations are discussed

Oral dehydroepiandrosterone (DHEA) replacement therapy in women with Addison's disease.

Gebre-Medhin G, Husebye ES, Mallmin H, et al.

*Clin Endocrinol (Oxf).* 2000 Jun; 52(6):775-80.

**OBJECTIVE:** Patients with primary adrenocortical failure (Addison's disease) have abnormally low levels of DHEA and androgens relative to age. To define a suitable dose, the effect of oral dehydroepiandrosterone (DHEA) replacement therapy in women with Addison's disease (n = 9) was evaluated. **DESIGN AND MEASUREMENTS:** DHEA was administered as a daily oral dose of either 50 mg (n = 5) or 200 mg (n = 4). Blood sampling and measurements of insulin sensitivity (as measured with euglycemic insulin clamp technique) and body composition (as measured by dual energy X-ray absorptiometry) were performed before and during DHEA treatment and at a 3-month follow up. **RESULTS:** DHEA and DHEA(S) levels were restored to normal in those patients receiving 50 mg whereas DHEA(S) level was slightly above the normal reference value in those receiving 200 mg. Circulating levels of androgens (androstenedione, testosterone and testosterone/SHBG ratio) were normalized in all patients. A slight rise in IGF-1 levels was seen in both groups as was a decrease in the levels of low and high density lipoproteins. No effect on blood glucose levels or insulin sensitivity was seen and no change of body composition was observed. No serious side-effects were seen, but some of the patients experienced increased apocrine sweat secretion (n = 7), itchy scalp (n = 2) and acne (n = 7), all of which were reversed when DHEA was discontinued. **CONCLUSION:** A daily replacement dose of 50 mg of DHEA results in near physiological levels of DHEA, DHEA(S) androstenedione and testosterone in women with Addison's disease, without severe side-effects

The effects of procaine/haematoporphyrin on age-related decline: a double-blind trial.

Hall MR, Briggs RS, MacLennan WJ, et al.

*Age Ageing.* 1983 Nov; 12(4):302-8.

A randomized, double-blind study of procaine/haematoporphyrin (KH3) has been carried out over two years in a selected population of healthy elderly subjects. The period of study exceeds 500 patient years. The trial population was weighted to contain a larger proportion of subjects aged over 75 years than a standard population; those receiving active KH3 had similar characteristics on entry to those receiving placebo. Over the course of two years, KH3 was shown to be an active substance in that: (a) decrement in the consolidation of new learning was prevented in the treatment group (less than 1.0%, as against 38% in the placebo group); (b) the prevalence of incontinence increased significantly in the placebo group, but not in the active group (P less than 0.05); (c) there was a significant increase in grip strength in the active treatment group (+22%, P less than 0.01 v. placebo); (d) more adverse reactions were observed on treatment with KH3 (P less than 0.005)

Improvement in mood and fatigue after dehydroepiandrosterone replacement in Addison's disease in a randomized, double blind trial.

Hunt PJ, Gurnell EM, Huppert FA, et al.

*J Clin Endocrinol Metab.* 2000 Dec; 85(12):4650-6.

Dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS) are adrenal precursors of steroid biosynthesis and centrally acting neurosteroids. Glucocorticoid and mineralocorticoid deficiencies in Addison's disease require life-long hormone replacement, but

the associated failure of DHEA synthesis is not corrected. We conducted a randomized, double blind study in which 39 patients with Addison's disease received either 50 mg oral DHEA daily for 12 weeks, followed by a 4-week washout period, then 12 weeks of placebo, or vice versa. After DHEA treatment, levels of DHEAS and Delta(4)-androstenedione rose from subnormal to within the adult physiological range. Total testosterone increased from subnormal to low normal with a fall in serum sex hormone-binding globulin in females, but with no change in either parameter in males. In both sexes, psychological assessment showed significant enhancement of self-esteem with a tendency for improved overall well-being. Mood and fatigue also improved significantly, with benefit being evident in the evenings. No effects on cognitive or sexual function, body composition, lipids, or bone mineral density were observed. Our results indicate that DHEA replacement corrects this steroid deficiency effectively and improves some aspects of psychological function. Beneficial effects in males, independent of circulating testosterone levels, suggest that it may act directly on the central nervous system rather than by augmenting peripheral androgen biosynthesis. These positive effects, in the absence of significant adverse events, suggest a role for DHEA replacement therapy in the treatment of Addison's disease

Nutritional and botanical interventions to assist with the adaptation to stress.

Kelly GS.

*Altern Med Rev.* 1999 Aug; 4(4):249-65.

Prolonged stress, whether a result of mental/emotional upset or due to physical factors such as malnutrition, surgery, chemical exposure, excessive exercise, sleep deprivation, or a host of other environmental causes, results in predictable systemic effects. The systemic effects of stress include increased levels of stress hormones such as cortisol, a decline in certain aspects of immune system function such as natural killer cell cytotoxicity or secretory-IgA levels, and a disruption of gastrointestinal microflora balance. These systemic changes might be a substantial contributor to many of the stress-associated declines in health. Based on human and animal research, it appears a variety of nutritional and botanical substances - such as adaptogenic herbs, specific vitamins including ascorbic acid, vitamins B1 and B6, the coenzyme forms of vitamin B5 (pantethine) and B12 (methylcobalamin), the amino acid tyrosine, and other nutrients such as lipoic acid, phosphatidylserine, and plant sterol/sterolin combinations - may allow individuals to sustain an adaptive response and minimize some of the systemic effects of stress

Effects of L-theanine on the release of brain waves in human volunteers.

Kobayashi K.

*Nippon Noegik Kaishi.* 1998;(72):153-7.

Effects of phosphatidylserine on the neuroendocrine response to physical stress in humans.

Monteleone P, Beinat L, Tanzillo C, et al.

*Neuroendocrinology.* 1990 Sep; 52(3):243-8.

The activity of brain cortex-derived phosphatidylserine (BC-PS) on the neuroendocrine and neurovegetative responses to physical stress was tested in 8 healthy men who underwent three experiments with a bicycle ergometer. According to a double-blind design, before starting the exercise, each subject received intravenously, within 10 min, 50 or 75 mg of BC-PS or a volume-matched placebo diluted in 100 ml of saline. Blood samples were collected before and after the exercise for plasma epinephrine (E), norepinephrine (NE), dopamine (DA), adrenocorticotropin (ACTH), cortisol, growth hormone (GH), prolactin (PRL) and glucose determinations. Blood pressure and heart rate were also recorded. Physical stress induced a clear-cut increase in plasma E, NE, ACTH, cortisol, GH and PRL, whereas no significant change was observed in plasma DA and glucose. Pretreatment with both 50 and 75 mg BC-PS significantly blunted the ACTH and cortisol responses to physical stress

Serum levels of dehydroepiandrosterone sulfate in patients with asymptomatic cortisol producing adrenal adenoma: comparison with adrenal Cushing's syndrome and non-functional adrenal tumor.

Morio H, Terano T, Yamamoto K, et al.

*Endocr J.* 1996 Aug; 43(4):387-96.

The reported number of adrenal incidentalomas has been increasing because of wider application of imaging techniques. Patients with asymptomatic cortisol producing adrenal adenoma (ASCA) which secretes cortisol without clinical evidence of Cushing's syndrome has been more frequently observed than previously assumed, and they have a risk of adrenal insufficiency after adrenalectomy. Therefore patients with incidentalomas should be screened for cortisol overproduction. The aim of this study

is to discover an easy screening test to uncover ASCA. We investigated the hormone profiles of 4 patients with ASCA in comparison with 11 patients with non-functional adrenal tumor and 10 patients with adrenal Cushing's syndrome. We also investigated the expression of dehydroepiandrosterone sulfotransferase (DHEA-ST) in surgically removed attached non-neoplastic adrenal tissues by immunostaining, which was considered to represent the degree of suppression of the hypothalamo-pituitary-adrenal axis. Serum dehydroepiandrosterone sulfate (DHEA-S) levels of all the patients with ASCA and adrenal Cushing's syndrome were lower than those of healthy subjects of corresponding age, but they were within the normal range in the patients with non-functional adrenal tumors. The serum DHEA-S level reflects the degree of suppression of the normal adrenal gland by cortisol hypersecretion from adrenal tumors. But the serum level of DHEA-S decreases with age, and because the normal range of serum DHEA-S is low in elderly subjects, we should be careful to evaluate the level of DHEA-S in elderly patients with adrenal Cushing's syndrome or ASCA. The immunohistochemical study showed DHEA-ST expression was noticeably suppressed in the adjacent adrenal cortex in ASCA and adrenal Cushing's syndrome. The decreased expression of DHEA-ST may reflect autonomous neoplastic cortisol secretion and subsequent ACTH suppression in ASCA and adrenal Cushing's syndrome. A single measurement of plasma ACTH or measurement of ACTH response to corticotropin-releasing hormone was not enough to screen for ASCA because of the wide variation among the cases. Dexamethasone suppression test is essential in identifying ASCA and also a single determination of serum DHEA-S is easy and may be useful for the screening of ASCA in adrenal incidentalomas in young and middle aged subjects, and is especially useful for outpatients

Encyclopedia of Natural Medicine.

Murray MT.

1997;

The Facts You Need to Know: Addison's Disease, Cushing's Syndrome, Congenital Adrenal Hyperplasia, and Hyperaldosteronism.

NADF.

1998

Tea catechin supplementation increases antioxidant capacity and prevents phospholipid hydroperoxidation in plasma of humans.

Nakagawa K, Ninomiya M, Okubo T, et al.

*J Agric Food Chem.* 1999 Oct; 47(10):3967-73.

The effect of green tea catechin supplementation on antioxidant capacity of human plasma was investigated. Eighteen healthy male volunteers who orally ingested green tea extract (254 mg of total catechins/subject) showed 267 pmol of epigallocatechin-3-gallate (EGCg) per milliliter of plasma at 60 min after administration. The plasma phosphatidylcholine hydroperoxide (PCOOH) levels attenuated from 73.7 pmol/mL in the control to 44.6 pmol/mL in catechin-treated subjects, being correlated inversely with the increase in plasma EGCg level. The results suggested that drinking green tea contributes to prevent cardiovascular disease by increasing plasma antioxidant capacity in humans

Effects of six months melatonin treatment on sleep quality and serum concentrations of estradiol, cortisol, dehydroepiandrosterone sulfate, and somatomedin C in elderly women.

Pawlikowski M, Kolomecka M, Wojtczak A, et al.

*Neuroendocrinol Lett.* 2002 Apr; 23 Suppl 1:17-9.

**OBJECTIVES:** The role of melatonin in aging is still under debate. Therefore, an open pilot study on the effects of melatonin administration on some sleep parameters, routine hematological and biochemical parameters, and concentrations of hormones was performed in elderly women. **SUBJECTS AND METHODS:** The study was performed on 14 women (volunteers), aged from 64 to 80 years (mean age 71+/-4.6 years). Melatonin (2 mg daily at 19:00 h) was administered during 6 months. Before and after melatonin treatment the peripheral venous blood samples were taken in the morning (approx. at 08:00 h) after the overnight fast. The total blood count, glucose, total cholesterol, LDL, HDL, and triglycerides were estimated by routine laboratory methods. The serum concentrations of the following hormones were determined: 17-beta-estradiol, dehydroepiandrosterone sulfate (DHEAS), cortisol, and somatomedin C (IGF-I). Additionally, before and after 6 months of melatonin therapy the investigated subjects answered to a questionnaire dealing with sleep parameters and self-estimation of general health status. **RESULTS:** In 35.7% of investigated subjects an improvement in general sleep quality and in such sleep parameters as sleep initiation, sleep latency, number of awakenings episodes, wake time after sleep onset, was observed. A significant decrease of estradiol concentrations

was observed after 6 months of the melatonin treatment in comparison to initial levels. IGF-I was found to be slightly but significantly increased after the 6 months melatonin therapy. Cortisol levels did not change significantly, during the melatonin treatment. DHEAS concentrations increased after melatonin therapy. Moreover, a tendency towards a higher DHEAS/cortisol ratio was found after 6 months of treatment. Melatonin treatment did not influence significantly either the parameters of total blood count or glucose and serum lipids levels. CONCLUSIONS: On the basis of this preliminary open study it seems that melatonin administration may be beneficial for elderly subjects

Vitamin C supplementation attenuates the increases in circulating cortisol, adrenaline and anti-inflammatory polypeptides following ultramarathon running.

Peters EM, Anderson R, Nieman DC, et al.

*Int J Sports Med.* 2001 Oct; 22(7):537-43.

The effects of vitamin C supplementation on the alterations in the circulating concentrations of cortisol, adrenaline, interleukin-10 (IL-10) and interleukin-1 receptor antagonist (IL-1Ra) which accompany ultramarathon running were measured using immunochemiluminescence, radioimmunoassay and ELISA procedures. Forty-five participants in the 1999 Comrades 90 km marathon were divided into equal groups (n = 15) receiving 500 mg/day Vit C (VC-500), 1500 mg/day Vit C (VC-1500) or placebo (P) for 7 days before the race, on the day of the race, and for 2 days following completion. Runners recorded dietary intake before, during and after the race and provided 35 ml blood samples 15 - 18 hrs before the race, immediately post-race, 24 hrs post race and 48 hrs post-race. Twenty-nine runners (VC-1500, n = 12; VC-500, n = 10; P, n = 7) complied with all study requirements. All post-race concentrations were adjusted for plasma volume changes. Analyses of dietary intakes and blood glucose and anti-oxidant status on the day preceding the race and the day of the race did not reveal that carbohydrate intake or plasma vitamins E and A were significant confounders in the study. Mean pre-race concentrations of serum vitamin C in VC-500 and VC-1500 groups (128 +/- 31 and 153 +/- 34 micromol/l) were significantly higher than in the P group (83 +/- 39 micromol/l). Immediate post-race serum cortisol was significantly lower in the VC-1500 group (p < 0.05) than in P and VC-500 groups. When the data from VC-500 and P groups was combined (n = "17)," immediate post-race plasma adrenaline, IL-10 and IL-1Ra concentrations were also significantly lower (p < 0.05) in the VC-1500 group. The study demonstrates an attenuation, albeit transient, of both the adrenal stress hormone and anti-inflammatory polypeptide response to prolonged exercise in runners who supplemented with 1500 mg vitamin C per day when compared to < or = "500" mg per day

Attenuation of increase in circulating cortisol and enhancement of the acute phase protein response in vitamin C-supplemented ultramarathoners.

Peters EM, Anderson R, Theron AJ.

*Int J Sports Med.* 2001 Feb; 22(2):120-6.

Supplementary vitamin C (2 x 500 mg tablets daily) or a matched placebo was administered to 10 and 6 ultramarathon athletes respectively for 7 days prior to participation in a 90 kilometer running event, as well as on the day of the race and for 2 days after its completion. Circulating concentrations of vitamins A, C and E, as well as those of leukocytes and platelets, myeloperoxidase, C-reactive protein (CRP), interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF), cortisol, and creatine kinase were measured 16 hours before the race and at 30 min, 24 hours, and 48 hours after completion. Pre-race vitamin C concentrations in the supplemented group were unchanged after the race (118.2 +/- 15.9 and 115.9 +/- 11.9 micromol/l) while an increase was observed in the placebo group immediately post-race (85.8 +/- 11.9 to 107.4 +/- 18.8 micromol), with a return to pre-race values after 24 hours. Immediately on completion of the race transient elevations occurred in the concentrations of circulating neutrophils, monocytes and platelets, IL-6, cortisol, CRP, and creatine kinase in both groups. In the supplemented group the concentrations of CRP were significantly higher (p < 0.01) at each of the post-race time-points while those of cortisol were 30% lower immediately post-race. These observations provide evidence that supplementation with vitamin C may blunt the adaptive mobilization of this vitamin from the adrenals during exercise-induced oxidative stress and may be associated with an enhancement of the acute phase protein response and attenuation of the exercise-induced increase in serum cortisol

Licorice ingestion and blood pressure regulating hormones.

Schambelan M.

*Steroids.* 1994 Feb; 59(2):127-30.

Nearly half a century ago Revers reported that administration of a paste prepared from succus liquiritiae, a dried watery extract of the roots of *Glycyrrhiza glabra*, resulted in a reduction in abdominal symptoms as well as radiographic evidence of healing in patients suffering from gastric ulcer. Subsequent studies demonstrated that this preparation could prevent the formation of gastric ulcers in experimental animals and confirmed the salutary effects in patients, but found that approximately 20% of

patients so treated developed facial and dependent edema, often accompanied by headache, shortness of breath, stiffness, and pain in the upper abdomen. Although these symptoms suggested an allergic reaction, they were not accompanied by eosinophilia or relieved by antihistamines. These untoward effects usually subsided with a reduction of dose, although in some patients treatment had to be discontinued entirely. Given this profile of side effects, enthusiasm for licorice as a remedy for peptic ulcer disease soon faded. However, the popularity of licorice flavoring in candy and in other products such as chewing tobacco persists to this day, as do the problems in electrolyte and blood pressure homeostasis that can occasionally occur in individuals ingesting large quantities of licorice-containing products. Although the pattern of the renal response suggested that the active ingredients in licorice were acting directly on the mineralocorticoid receptors in the kidney, an even more fascinating explanation for the toxic effects of licorice has emerged in the past decade. (ABSTRACT TRUNCATED AT 250 WORDS)

Decreased melatonin concentration in Cushing's syndrome.

Soszynski P, Stowinska-Srzednicka J, Kasperlik-Zatuska A, et al.

*Horm Metab Res.* 1989 Dec; 21(12):673-4.

To determine the effect of hypercortisolaemia on the melatonin circadian secretion 12 patients with pituitary or adrenal dependent Cushing's syndrome and 5 healthy controls were studied. The melatonin circadian rhythm of secretion, observed in the control group, was abolished in the patients with hypercortisolaemia. Mean nocturnal melatonin levels and the integrated 24-hour secretion were significantly lower in the patients studied than those of the controls. Thus, in patients with Cushing's syndrome the melatonin levels are decreased and the circadian rhythm of this hormone is abolished

[Adrenal cortex functional activity in pantothenate deficiency and the administration of the vitamin or its derivatives].

Tarasov I, Sheibak VM, Moiseenok AG.

*Vopr Pitan.* 1985 Jul;(4):51-4.

Study of the corticosteroid content in the adrenals and blood of rats under pantothenate deficiency has demonstrated a decrease in adrenocortical function. A single administration of pantothenate in a dose of 3.3 mg/kg reduced the influence of hypovitaminosis on the adrenals. The pantothenate derivatives (pantethine, 4'-phosphopantothenate and CoA in particular) injected to intact animals in a single dose equimolar to 3.3 mg/kg calcium pantothenate per kg bw had a marked steroidogenous effect

Hypothalamic-pituitary-adrenal axis, neuroendocrine factors and stress.

Tsigos C, Chrousos GP.

*J Psychosom Res.* 2002 Oct; 53(4):865-71.

The stress system coordinates the adaptive responses of the organism to stressors of any kind.(1). The main components of the stress system are the corticotropin-releasing hormone (CRH) and locus ceruleus-norepinephrine (LC/NE)-autonomic systems and their peripheral effectors, the pituitary-adrenal axis, and the limbs of the autonomic system. Activation of the stress system leads to behavioral and peripheral changes that improve the ability of the organism to adjust homeostasis and increase its chances for survival. The CRH and LC/NE systems stimulate arousal and attention, as well as the mesocorticolimbic dopaminergic system, which is involved in anticipatory and reward phenomena, and the hypothalamic beta-endorphin system, which suppresses pain sensation and, hence, increases analgesia. CRH inhibits appetite and activates thermogenesis via the catecholaminergic system. Also, reciprocal interactions exist between the amygdala and the hippocampus and the stress system, which stimulates these elements and is regulated by them. CRH plays an important role in inhibiting GnRH secretion during stress, while, via somatostatin, it also inhibits GH, TRH and TSH secretion, suppressing, thus, the reproductive, growth and thyroid functions. Interestingly, all three of these functions receive and depend on positive catecholaminergic input. The end-hormones of the hypothalamic-pituitary-adrenal (HPA) axis, glucocorticoids, on the other hand, have multiple roles. They simultaneously inhibit the CRH, LC/NE and beta-endorphin systems and stimulate the mesocorticolimbic dopaminergic system and the CRH peptidergic central nucleus of the amygdala. In addition, they directly inhibit pituitary gonadotropin, GH and TSH secretion, render the target tissues of sex steroids and growth factors resistant to these substances and suppress the 5' deiodinase, which converts the relatively inactive tetraiodothyronine (T(4)) to triiodothyronine (T(3)), contributing further to the suppression of reproductive, growth and thyroid functions. They also have direct as well as insulin-mediated effects on adipose tissue, ultimately promoting visceral adiposity, insulin resistance, dyslipidemia and hypertension (metabolic syndrome X) and direct effects on the bone, causing "low turnover" osteoporosis. Central CRH, via glucocorticoids and catecholamines, inhibits the inflammatory reaction, while directly secreted by peripheral nerves CRH stimulates local inflammation (immune CRH). CRH antagonists may be useful in human pathologic states, such as melancholic depression and chronic anxiety, associated with chronic hyperactivity of the stress system, along with predictable behavioral, neuroendocrine, metabolic and immune changes,

based on the interrelations outlined above. Conversely, potentiators of CRH secretion/action may be useful to treat atypical depression, postpartum depression and the fibromyalgia/chronic fatigue syndromes, all characterized by low HPA axis and LC/NE activity, fatigue, depressive symptomatology, hyperalgesia and increased immune/inflammatory responses to stimuli

Unusual association of thyroiditis, Addison's disease, ovarian failure and celiac disease in a young woman.

Valentino R, Savastano S, Tommaselli AP, et al.

*J Endocrinol Invest.* 1999 May; 22(5):390-4.

The coexistence of autoimmune endocrine diseases, particularly autoimmune thyroid disease and celiac disease (CD), has recently been reported. We here present a 23-year-old woman with a diagnosis of hypothyroidism due to Hashimoto's thyroiditis, autoimmune Addison's disease, and karyotypically normal spontaneous premature ovarian failure. Considering the close association between autoimmune diseases and CD, we decided to search for IgA anti-endomysium antibodies (EmA) in the serum. The positivity of EmA and the presence of total villous atrophy at jejunal biopsy allowed the diagnosis of CD. On a gluten-free diet the patient showed a marked clinical improvement accompanied, over a 3-month period, by a progressive decrease in the need for thyroid and adrenal replacement therapies. After 6 months, serum EmA became negative and after 12 months a new jejunal biopsy showed complete mucosal recovery. After 18 months on gluten-free diet, the anti-thyroid antibodies titre decreased significantly, and we could discontinue thyroid substitutive therapy. This case emphasizes the association between autoimmune polyglandular disease and CD; the precocious identification of these cases is clinically relevant not only for the high risk of complications (e.g. lymphoma) inherent to untreated CD, but also because CD is one of the causes for the failure of substitute hormonal therapy in patients with autoimmune thyroid disease

The relationship of serum DHEA-S and cortisol levels to measures of immune function in human immunodeficiency virus-related illness.

Wisniewski TL, Hilton CW, Morse EV, et al.

*Am J Med Sci.* 1993 Feb; 305(2):79-83.

Human immunodeficiency virus (HIV) is a major cause of immunoincompetence. Whether the virus, itself, accounts for all the deficiency remains in question. Steroids can also influence immune function; glucocorticoids cause immunoincompetence while dehydroepiandrosterone (DHEA) enhances immune function. Changes in the levels of such hormones during the course of HIV illness might result in significant changes in immune competence. The purpose of this study is to investigate whether dehydroepiandrosterone-sulphate (DHEA-S) or cortisol levels correlate with absolute CD4 lymphocyte levels. Plasma for cortisol and DHEA-S was drawn from 98 adults with HIV. Of these, 67 had simultaneous CD4 levels. Cortisol levels were 12.4 +/- 4.6 micrograms/dl, DHEA-S 262 +/- 142 micrograms/dl, and CD4 levels were 308 +/- 217/mm<sup>3</sup> (mean +/- SD). Correlational analysis revealed a significant relationship between DHEA-S and CD4 levels ( $r = 0.30$ ;  $p = 0.01$ ) but not between CD4 levels and cortisol ( $r = 0.11$ ;  $p = 0.36$ ) or cortisol/DHEA-S ratios ( $r = 0.17$ ;  $p = 0.16$ ). When analyzed by clinical subgroups, significant differences were also found with a decrease in DHEA-S levels seen in persons with more advanced illness. The data exhibit a positive relationship between the immune status of patients with HIV-related illness and DHEA, leading to the hypothesis that DHEA deficiency may worsen immune status

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