

Exercise Enhancement and Risk Precautions

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ABSTRACTS

The effect of ephedrine/caffeine mixture on energy expenditure and body composition in obese women.

Astrup A, Buemann B, Christensen NJ, et al.

Metabolism. 1992 Jul; 41(7):686-8.

Treatment with beta 2-agonists promotes fat loss and muscle growth in numerous species, but human studies are lacking. We studied the effect of a compound with beta 2-agonistic properties (ephedrine 20 mg/caffeine 200 mg [E + C]). Fourteen obese women were treated with a 4.2-MJ/d diet and either E + C or placebo (P) three times per day for 8 weeks in a double-blind study. Weight-loss was not different in the groups, but the E + C group lost 4.5 kg more body fat and 2.8 kg less fat-free mass (FFM). The decrease in 24-hour energy expenditure (EE) seen in the P group was 10% at day 1 and 13% at day 56, but was only 7% and 8% in the treated group (P = .044). The higher EE in the E +C group was entirely covered by fat oxidation. These findings provide evidence that promotion of fat loss and preservation of FFM during weight reduction may also be achieved pharmacologically in humans

Pharmacology of thermogenic drugs.

Astrup A, Toubro S, Christensen NJ, et al.

Am J Clin Nutr. 1992 Jan; 55(1 Suppl):246S-8S.

Thermogenic combinations of ephedrine with caffeine and newer selective beta 3-agonists are being assessed for the treatment of obesity. The actions of beta-agonists may be multifaceted, with acute stimulation of thermogenic mechanisms in various tissues. During chronic treatment recruitment of brown fat may occur and hypertrophy of skeletal muscle may occur and simultaneously increase lean body tissue and reduce fat mass by stimulation of lipolysis and energy expenditure. The weight-reducing effect of an ephedrine-caffeine combination was superior to placebo treatment during 24 wk of energy restriction in obese women, whereas caffeine and ephedrine separately had no effect. In a second study it was found that ephedrine-caffeine compared with placebo preserved fat-free mass and enhanced fat loss, which could be accounted for both by anorexia (75%) and by increased thermogenesis (25%). The ephedrine-caffeine compound seems useful for the treatment of obesity and may serve as reference in the clinical assessment of new beta-agonists

Hippocampal brain-derived neurotrophic factor gene regulation by exercise and the medial septum.

Berchtold NC, Kesslak JP, Cotman CW.

J Neurosci Res. 2002 Jun 1; 68(5):511-21.

Brain-derived neurotrophic factor (BDNF) enhances synaptic plasticity and neuron function. We have reported that voluntary exercise increases BDNF mRNA levels in the hippocampus; however, mechanisms underlying this regulation have not been defined. We hypothesized that medial septal cholinergic and/or gamma amino butyric acid (GABA)ergic neurons, which provide a major input to the hippocampus, may regulate the baseline gene expression and exercise-dependent gene upregulation of this neurotrophin. Focal lesions were produced by medial septal infusion of the saporin-linked immunotoxins 192-IgG-saporin or OX7-saporin. 192-IgG-saporin produced a selective and complete loss of medial septal cholinergic neurons with no accompanying GABA loss. Baseline BDNF mRNA was reduced in the hippocampus of sedentary animals, but exercise-induced gene upregulation was not impaired, despite complete loss of septo-hippocampal cholinergic afferents. OX7-saporin produced a graded lesion of the medial septum characterized by predominant GABA neuron loss with less reduction in the number of cholinergic cells. OX7-saporin lesion reduced baseline hippocampal BDNF mRNA and attenuated exercise-induced gene upregulation, in a dose-dependent manner. These results suggest that combined loss of septal GABAergic and cholinergic input to the hippocampus may be important for exercise-dependent BDNF gene regulation, while cholinergic activity on its own is not sufficient. These results are discussed in relation to their implications for aging and Alzheimer's disease

Health promotion by encouraged use of stairs.

Blamey A, Mutrie N, Aitchison T.

BMJ. 1995 Jul 29; 311(7000):289-90.

Herbal ephedra/caffeine for weight loss: a 6-month randomized safety and efficacy trial.

Boozer CN, Daly PA, Homel P, et al.

Int J Obes Relat Metab Disord. 2002 May; 26(5):593-604.

OBJECTIVE: To examine long-term safety and efficacy for weight loss of an herbal Ma Huang and Kola nut supplement (90/192 mg/day ephedrine alkaloids/caffeine). **DESIGN:** Six-month randomized, double-blind placebo controlled trial. **SUBJECTS:** A total of 167 subjects (body mass index (BMI) 31.8 \pm 4.1 kg/m²) randomized to placebo (n=84) or herbal treatment (n=83) at two outpatient weight control research units. **MEASUREMENTS:** Primary outcome measurements were changes in blood pressure, heart function and body weight. Secondary variables included body composition and metabolic changes. **RESULTS:** By last observation carried forward analysis, herbal vs placebo treatment decreased body weight (-5.3 \pm 5.0 vs. -2.6 \pm 3.2 kg, P<0.001), body fat (-4.3 \pm 3.3 vs. -2.7 \pm 2.8 kg, P=0.020) and LDL-cholesterol (-8 \pm 20 vs. 0 \pm 17 mg/dl, P=0.013), and increased HDL-cholesterol (+2.7 \pm 5.7 vs. -0.3 \pm 6.7 mg/dl, P=0.004). Herbal treatment produced small changes in blood pressure variables (+3 to -5 mm Hg, P< or =0.05), and increased heart rate (4 \pm 9 vs. -3 \pm 9 bpm, P<0.001), but cardiac arrhythmias were not increased (P>0.05). By self-report, dry mouth (P<0.01), heartburn (P<0.05), and insomnia (P<0.01) were increased and diarrhea decreased (P<0.05). Irritability, nausea, chest pain and palpitations did not differ, nor did numbers of subjects who withdrew. **CONCLUSIONS:** In this 6-month placebo-controlled trial, herbal ephedra/caffeine (90/192 mg/day) promoted body weight and body fat reduction and improved blood lipids without significant adverse events

An obligation for primary care physicians to prescribe physical activity to sedentary patients to reduce the risk of chronic health conditions.

Chakravarthy MV, Joyner MJ, Booth FW.

Mayo Clin Proc. 2002 Feb; 77(2):165-73.

Physical inactivity increases the risk of many chronic disorders. Numerous studies have convincingly demonstrated that undertaking and maintaining moderate levels of physical activity (eg, brisk walking 3 hours a week) greatly reduces the incidence of developing many chronic health conditions, most notably type 2 diabetes mellitus, obesity, cardiovascular disease, and many types of cancers. However, the underlying mechanistic details of how physical activity confers such protective effects are not well understood and consequently constitute an active area of research. Although changing an individual's ingrained behavior is commonly perceived to be difficult, encouraging evidence suggests that intensive and repeated counseling by health care professionals can cause patients to become more physically active. Therefore, counseling patients to undertake physical activity to prevent chronic health conditions becomes a primary prevention modality. This article summarizes the vast epidemiologic and biochemical evidence supporting the many beneficial health implications of undertaking moderate physical activity and provides a rationale for incorporating physical activity counseling as part of routine practice in the primary care setting

Exercise and mineral status of athletes: calcium, magnesium, phosphorus, and iron.

Clarkson PM, Haymes EM.

Med Sci Sports Exerc. 1995 Jun; 27(6):831-43.

Calcium, magnesium, phosphorus, and iron are important to a wide variety of body functions, such as mineralization of bones, serving as cofactors to many enzyme systems, sustaining muscle and nerve excitation, and, in the case of iron, maintaining the oxygen carrying capacity of the blood. Many female athletes consume less calcium than the recommended dietary allowance (RDA). This is of concern because of the need to achieve peak bone mass during adolescence and the possible relationship of poor calcium intake to stress fractures. Athletes appear to have adequate magnesium and phosphorus status. However, those athletes who are on calorie-restricted diets may not be ingesting sufficient quantities of magnesium and possibly phosphorus. Limited data have suggested that magnesium status is indirectly related to strength improvement as well as the incidence of muscle cramps. Acute ingestion of phosphorus (phosphate loading) has been shown to improve aerobic capacity. Iron depletion is common in female athletes but similar to the general population. Iron supplements are of health benefit, but of questionable performance benefit, to those who are iron depleted and nonanemic. To maintain optimal status of these minerals, it is

recommended that nutrient rich foods be ingested including dairy products and foods high in heme iron

Biomarkers of oxidative stress after controlled human exposure to ozone.

Corradi M, Alinovi R, Goldoni M, et al.

Toxicol Lett. 2002 Aug 5; 134(1-3):219-25.

This study was aimed at evaluating whether controlled short-term exposure to ozone (O₃) induces changes in biomarkers of lung inflammation and oxidative stress in exhaled breath condensate (EBC) and blood of healthy subjects. Twenty-two volunteers were exposed to 0.1 ppm of O₃ for 2 h while performing moderate intermittent exercise. EBC and blood were collected before, immediately after and 18 h after exposure. Changes in biomarkers were measured both in EBC and blood, without significant alterations of lung function tests. Changes in EBC, but not in blood, were mainly accounted for by a subgroup of 'susceptible' individuals bearing the wild genotype for NAD(P)H:quinone oxidoreductase (NQO1) and the null genotype for glutathione-S-transferase M1 (GSTM1). Thus, a single 2-h exposure to 0.1 ppm of O₃ induces changes in biomarkers of inflammation and oxidative stress. Polymorphic NQO1 and GSTM1 act as modifier of the lung response to O₃

Exercise: a behavioral intervention to enhance brain health and plasticity.

Cotman CW, Berchtold NC.

Trends Neurosci. 2002 Jun; 25(6):295-301.

Extensive research on humans suggests that exercise could have benefits for overall health and cognitive function, particularly in later life. Recent studies using animal models have been directed towards understanding the neurobiological bases of these benefits. It is now clear that voluntary exercise can increase levels of brain-derived neurotrophic factor (BDNF) and other growth factors, stimulate neurogenesis, increase resistance to brain insult and improve learning and mental performance. Recently, high-density oligonucleotide microarray analysis has demonstrated that, in addition to increasing levels of BDNF, exercise mobilizes gene expression profiles that would be predicted to benefit brain plasticity processes. Thus, exercise could provide a simple means to maintain brain function and promote brain plasticity

Acute creatine supplementation and performance during a field test simulating match play in elite female soccer players.

Cox G, Mujika I, Tumilty D, et al.

Int J Sport Nutr Exerc Metab. 2002 Mar; 12(1):33-46.

This study investigated the effects of acute creatine (Cr) supplementation on the performance of elite female soccer players undertaking an exercise protocol simulating match play. On two occasions, 7 days apart, 12 players performed 5 x 11-min exercise testing blocks interspersed with 1 min of rest. Each block consisted of 11 all-out 20-m running sprints, 2 agility runs, and 1 precision ball-kicking drill, separated by recovery 20-m walks, jogs, and runs. After the initial testing session, subjects were assigned to either a CREATINE (5 g of Cr, 4 times per day for 6 days) or a PLACEBO group (same dosage of a glucose polymer) using a double-blind research design. Body mass (BM) increased (61.7 +/- 8.9 to 62.5 +/- 8.9 kg, p < .01) in the CREATINE group; however, no change was observed in the PLACEBO group (63.4 +/- 2.9 kg to 63.7 +/- 2.5 kg). No overall change in 20-m sprint times and agility run times were observed, although the CREATINE group achieved faster post-supplementation times in sprints 11, 13, 14, 16, 21, 23, 25, 32, and 39 (p < .05), and agility runs 3, 5, and 8 (p < .05). The accuracy of shooting was unaffected in both groups. In conclusion, acute Cr supplementation improved performance of some repeated sprint and agility tasks simulating soccer match play, despite an increase in BM

Overtraining increases the susceptibility to infection.

Fitzgerald L.

Int J Sports Med. 1991 Jun; 12 Suppl 1:S5-S8.

Recent research studies and other evidence suggest that although moderate exercise is good for the immune system, the demanding training programs of many top athletes may suppress the immune system and thereby increase susceptibility to infections. A number of top athletes have suffered from unusual infections normally associated with immune deficiency, and immune abnormalities have been demonstrated in resting samples from top athletes. Studies from several exercise laboratories have shown that after a single exhausting exercise session there is temporary immune depression, with marked changes in numbers and functional capacities of lymphocytes. These changes, which last for up to several hours, are seen in athletes and

untrained individuals. In several studies in the United States, students who were very active in sports have been shown to be more susceptible to infections than their less active colleagues. Exercising hard during the incubation phase of an infection can increase the severity of the illness. This article examines the evidence, discusses possible mechanisms, and considers the implications

The safety and efficacy of pharmaceutical and herbal caffeine and ephedrine use as a weight loss agent.

Greenway FL.

Obes Rev. 2001 Aug; 2(3):199-211.

Since passage of the Dietary Supplement Health and Education Act of 1994, the sale of herbal dietary supplements containing caffeine and ephedrine for weight loss has become widespread in the United States. Reports of adverse events associated with the use of these non-prescription supplements have raised concerns in the United States regulatory community. Restricting the use of these products is now being considered. Such restriction should be based upon controlled clinical trials. This review of the literature in Medline relative to the use of caffeine and ephedrine in the treatment of obesity concludes that caffeine and ephedrine are effective in causing weight loss. Caffeine and ephedrine give equivalent weight loss to Diethylpropion and superior weight loss compared to dexfenfluramine. Caffeine and ephedrine have a long history of safe, non-prescription use. The adverse events accompanying acute dosing are mild and transient. Adverse events with caffeine and ephedrine reach and remain at placebo levels after 4-12 weeks of continuous treatment, but data from randomized trials up to 6 months only are available. Obesity is chronic, requires chronic treatment, its incidence is increasing and it has few effective treatments. The benefits of caffeine and ephedrine in treating obesity appear to outweigh the small associated risks. Restriction of dietary herbal supplements containing caffeine and ephedrine, often with other ingredients, should be based on controlled clinical trials of these products

Double-blind intervention trial on modulation of ozone effects on pulmonary function by antioxidant supplements.

Grievink L, Zijlstra AG, Ke X, et al.

Am J Epidemiol. 1999 Feb 15; 149(4):306-14.

The aim of this study was to investigate whether the acute effects of ozone on lung function could be modulated by antioxidant vitamin supplementation in a placebo-controlled study. Lung function was measured in Dutch bicyclists ($n = 38$) before and after each training session on a number of occasions ($n = 380$) during the summer of 1996. The vitamin group ($n = 20$) received 100 mg of vitamin E and 500 mg of vitamin C daily for 15 weeks. The average ozone concentration during exercise was 77 microg/m³ (range, 14-186 microg/m³). After exclusion of subjects with insufficient compliance from the analysis, a difference in ozone exposure of 100 microg/m³ decreased forced expiratory volume in 1 second (FEV₁) 95 ml (95% confidence interval (CI) -265 to -53) in the placebo group and 1 ml (95% CI -94 to 132) in the vitamin group; for forced vital capacity, the change was -125 ml (95% CI -384 to -36) in the placebo group and -42 ml (95% CI -130 to 35) in the vitamin group. The differences in ozone effect on lung function between the groups were statistically significant. The results suggest that supplementation with the antioxidant vitamins C and E confers partial protection against the acute effects of ozone on FEV₁ and forced vital capacity in cyclists

An acute clinical trial evaluating the cardiovascular effects of an herbal ephedra-caffeine weight loss product in healthy overweight adults.

Kalman D, Incledon T, Gaunaurd I, et al.

Int J Obes Relat Metab Disord. 2002 Oct; 26(10):1363-6.

OBJECTIVE: This study was undertaken to determine the acute effects of a commercial weight loss supplement containing herbal ephedrine and caffeine on cardiovascular function in healthy overweight adults. **DESIGN:** Randomized double blind clinical trial evaluating the cardiovascular effects of an ephedra-caffeine (Xenadrine(TM); XEN) based herbal product vs placebo (PLA). **SUBJECTS:** Twenty-seven healthy overweight adults (age 21-60 y; body mass index ≥ 25 kg/m²). **MEASUREMENTS:** Systolic and diastolic blood pressure, heart rate, serial electrocardiograms (EKG) and Doppler echocardiograms. **RESULTS:** A comparison of means between the groups indicated no statistically significant differences at the start of the study for the variables above. There were no serious adverse events. When examining the effects of XEN vs PLA on cardiovascular health/function, there were no significant effects observed in heart rate, systolic blood pressure, diastolic blood pressure, left ventricular ejection fraction, heart valve function or in cardiovascular physiology within the parameters measured. **CONCLUSION:** These findings indicate that, over a 14-day period, ingestion of the commercial weight loss supplement in a healthy overweight population did not produce any noticeable cardiovascular side effects

Docosahexaenoic and eicosapentaenoic acids inhibit in vitro human endothelial cell production of interleukin-6.

Khalfoun B, Thibault F, Watier H, et al.

Adv Exp Med Biol. 1997; 400B:589-97.

The interaction between lymphocytes, cytokines, and endothelial cells (EC) is a key step in the inflammatory process. Interleukin-6 (IL-6) a pleiotropic cytokine in its effects, seems to be an early indicator of acute systemic inflammation. In this study, we have examined the effects of polyunsaturated fatty acids (PUFAs) on the production of IL-6 by human unstimulated EC or EC stimulated with TNF-alpha (100 U/ml); IL-4 (100 U/ml); LPS (1 ug/ml); or allogeneic peripheral blood lymphocytes (PBL). Twenty-four hour culture supernatants of immunoreactive IL-6 were measured by Sandwich ELISA. We have shown that the production of IL-6 was potentiated when EC were stimulated with TNF-alpha; IL-4; LPS; or monocyte-depleted PBL in comparison to unstimulated EC. The addition of n-3 PUFAs in culture medium (100 ug/ml DHA or EPA) significantly reduces the production of IL-6 by unstimulated EC; or stimulated with TNF-alpha; IL-4 pg/ml; LPS or depleted PBL respectively for DHA and EPA, whereas the n-6 PUFAs (Arachidonic acid), even used at the highest concentration, was ineffective. This inhibitory effect is PUFA dose dependent but is more potent with EPA than DHA. Regardless of the mode of action, since IL-6 is known to be involved in hematopoiesis, in the regulation of the immune response and in the inflammatory reaction, these results suggest that n-3 PUFAs may play a role in suppressing inflammation. Further studies are needed to elucidate the mechanism involved and the choice between the two fatty acids for clinical and therapeutic purposes

Effects of creatine in a transgenic animal model of amyotrophic lateral sclerosis.

Klivenyi PFRJMRBTBMBKAMAOAMGWMK-DRBMF.

Nat Med. 1999; 5(3):347-50.

The effects of insulin, glucose and diabetes on prostaglandin production by rat kidney glomeruli and cultured glomerular mesangial cells.

Kreisberg JI, Patel PY.

Prostaglandins Leukot Med. 1983 Aug; 11(4):431-42.

Glomeruli isolated from streptozotocin-diabetic rats produced significantly greater amounts of immunoreactive prostaglandin (PG)E₂, PGF₂ alpha, and prostacyclin (PGI₂) measured as the stable metabolite 6-keto-PGF₁ alpha than control glomeruli. These data led to studies to determine whether the vasoactive glomerular mesangial cell exhibited alterations in arachidonic acid metabolism in diabetes. Therefore, we isolated and cultured under identical conditions, mesangial cells from normal and streptozotocin-diabetic rats. Normal mesangial cells produced predominantly PGE₂ (57-72%) with PGE₂ greater than PGF₂ alpha greater than PGI₂ after stimulation of acylhydrolase with melittin. Mesangial cells from diabetic rats produced predominantly PGI₂ (55-73%) with PGI₂ greater than PGE₂ greater than PGF₂ alpha. A similar prostaglandin profile was obtained when arginine vasopressin (AVP) was used to stimulate acylhydrolase activity. In addition, diabetic mesangial cells synthesized greater amounts of prostaglandins than normal mesangial cells cultured for the same number of passages. When cultured under high-glucose conditions (in tissue culture medium with a final glucose concentration of 550 mg/dl) to mimic the diabetic state in vitro, normal mesangial cells produced proportionately greater amounts of PGE₂, PGF₂ alpha and PGI₂; no alteration to predominantly PGI₂ production was observed. Insulin addition to the high-glucose condition tended to attenuate prostaglandin production. Diabetic mesangial cells likewise produced more prostaglandins when cultured under high-glucose conditions; however, the increases were not proportional among the 3 prostaglandins examined. PGE₂ production increased to a greater degree than PGI₂. With insulin present in the high-glucose condition, there was a disproportional attenuation of all prostaglandins produced, with PGI₂ decreasing more than PGE₂. Thus, the streptozotocin-induced diabetic state resulted in an alteration in mesangial cell arachidonic acid metabolism

[Physical activity to delay the effects of aging on mobility].

Lacour JR, Kostka T, Bonnefoy M.

Presse Med. 2002 Jul 27; 31(25):1185-92.

SARCOPENIA: Aging is accompanied by the progressive reduction in cardio-pulmonary capacity and muscular strength. These two phenomena are partly related to the decrease in muscle mass, or sarcopenia. CARDIO-PULMONARY CAPACITY: Measured by maximum oxygen consumption (VO₂max), it demonstrates the individual's capacity for movement. It is also the principle marker of mortality due to cardiovascular events. VO₂max decreases by around 0.8% each year, in close correlation

with the evolution in muscle mass. These phenomena are partly related to reduced physical activity and, particularly, intense activity greater than 6 MET. Regular practice of moderately intense physical activity can maintain VO₂max at a level 20 to 35% superior to that of the mean level in the same age range, and is associated with increased autonomic nervous system activity. **DECREASED MUSCULAR STRENGTH:** Sarcopenia and the proportional decrease in fast-twitch muscle fibers are related to a reduction in physical activity. The decrease in muscular strength is a handicapping factor and increases the risk of falls. Two sessions of training per week can increase by more than 30% the strength of the muscles concerned, by increasing the muscle volume and the maximum frequency of emission of motoneuron influx. The production of somatotropin, insulin-like growth factor-1 and testosterone can also be increased. High-resistance exercises are themselves sufficient to increase bone density. In the light of these advantages, the practice of workouts in endurance and strength should be encouraged

Effects of creatine supplementation on exercise performance and muscular strength in amyotrophic lateral sclerosis: preliminary results.

Mazzini L, Balzarini C, Colombo R, et al.

J Neurol Sci. 2001 Oct 15; 191(1-2):139-44.

Creatine supplementation in humans has been reported to enhance power and strength both in normal subjects and in patients with various neuromuscular diseases. The purpose of this study was to examine the effects of supplementation on exercise performance and maximal voluntary isometric muscular contraction (MVIC) in Amyotrophic Lateral Sclerosis (ALS) patients. We report the results obtained in 28 patients with probable/definite ALS. In each patient we acquired the dynamometric measurement of MVIC in 10 muscle groups of upper and lower limbs and a measure of fatigue by means of an high-intensity intermittent protocol in elbow flexors and knee extensors muscles. All patients completed the protocols at the baseline and after supplementation of 20 g per day for 7 days and after supplementation of 3 g per day for 3 and 6 months. MVIC increased after 7 days of supplementation in 20 patients (70%) in knee extensors and in 15 (53%) of them also in elbow flexors. A statistically significant difference between pre and post-treatment mean values of MVIC was found both in elbow flexors ($P < 0.05$) and knee extensors ($p < 0.04$). The analysis of the slopes of fatigue test showed a statistically significant improvement after 7 days of supplementation in 11 patients (39%) in elbow flexors and in 9 patients (32%) also in knee extensors muscles. During the 6-month follow-up period all the examined parameters showed a linear progressive decline. In conclusion, our preliminary results have demonstrated that supplementation temporarily increases maximal isometric power in ALS patients so it may be of potential benefit in situations such as high intensity activity and it can be proposed as a symptomatic treatment

Oral supplementation with whey proteins increases plasma glutathione levels of HIV-infected patients.

Micke P, Beeh KM, Schlaak JF, et al.

Eur J Clin Invest. 2001 Feb; 31(2):171-8.

HIV infection is characterized by an enhanced oxidant burden and a systemic deficiency of the tripeptide glutathione (GSH), a major antioxidant. The semi-essential amino acid cysteine is the main source of the free sulfhydryl group of GSH and limits its synthesis. Therefore, different strategies to supplement cysteine supply have been suggested to increase glutathione levels in HIV-infected individuals. The aim of this study was to evaluate the effect of oral supplementation with two different cysteine-rich whey protein formulas on plasma GSH levels and parameters of oxidative stress and immune status in HIV-infected patients. In a prospective double blind clinical trial, 30 patients (25 male, 5 female; mean age (+/- SD) 42 +/- 9.8 years) with stable HIV infection (221 +/- 102 CD4 + lymphocytes L-1) were randomized to a supplemental diet with a daily dose of 45 g whey proteins of either Protectamin (Fresenius Kabi, Bad Hamburg, Germany) or Immunocal (Immunotec, Vandreuil, Canada) for two weeks. Plasma concentrations of total, reduced and oxidized GSH, superoxide anion (O₂⁻) release by blood mononuclear cells, plasma levels of TNF-alpha and interleukins 2 and 12 were quantified with standard methods at baseline and after therapy. Pre-therapy, plasma GSH levels (Protectamin: 1.92 +/- 0.6 microM; Immunocal: 1.98 +/- 0.9 microM) were less than normal (2.64 +/- 0.7 microM, $P = 0.03$). Following two weeks of oral supplementation with whey proteins, plasma GSH levels increased in the Protectamin group by 44 +/- 56% (2.79 +/- 1.2 microM, $P = 0.004$) while the difference in the Immunocal group did not reach significance (+ 24.5 +/- 59%, 2.51 +/- 1.48 microM, $P = 0.43$). Spontaneous O₂⁻ release by blood mononuclear cells was stable (20.1 +/- 14.2 vs. 22.6 +/- 16.1 nmol h⁻¹ 10⁶ cells, $P = 0.52$) whereas PMA-induced O₂⁻ release decreased in the Protectamin group (53.7 +/- 19 vs. 39.8 +/- 18 nmol h⁻¹ 10⁶ cells, $P = 0.04$). Plasma concentrations of TNF-alpha and interleukins 2 and 12 ($P > 0.08$, all comparisons) as well as routine clinical parameters remained unchanged. Therapy was well tolerated. In glutathione-deficient patients with advanced HIV-infection, short-term oral supplementation with whey proteins increases plasma glutathione levels. A long-term clinical trial is clearly warranted to see if this "biochemical efficacy" of whey proteins translates into a more favourable course of the disease

Prevalence of healthcare providers asking older adults about their physical activity levels?

MMWR.

Morb Mortal Wkly Rep. 1998; 51(19):412-4.

Compromised concentrations of ascorbate in fluid lining the respiratory tract in human subjects after exposure to ozone.

Mudway IS, Krishna MT, Frew AJ, et al.

Occup Environ Med. 1999 Jul; 56(7):473-81.

OBJECTIVES: Ozone (O₃) imposes an oxidative burden on the lung in two ways. Firstly, directly as a consequence of its oxidising character during exposure, and secondly, indirectly by engendering inflammation. In this study the second pathway was considered by ascertaining the impact of O₃ on the redox state of the fluid lining the respiratory tract 6 hours after challenge. **METHODS:** Nine subjects were exposed in a double blind crossover control trial to air and 200 ppb O₃ for 2 hours with an intermittent exercise and rest protocol. Blood samples were obtained and lung function (forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁)) assessed before, immediately after, and 6 hours after exposure. Bronchoalveolar lavage (BAL) was performed 6 hours after challenge. Inflammation was assessed in BAL fluid (total and differential cell counts, plus myeloperoxidase concentrations), and plasma and BAL fluid redox state were determined by measuring concentrations of antioxidants and markers of oxidative damage. **RESULTS:** Neutrophil numbers in BAL fluid increased 2.2-fold ($p = 0.07$) 6 hours after exposure and this was accompanied by increased myeloperoxidase concentrations in BAL fluid ($p = 0.08$). On the other hand, BAL fluid macrophage and lymphocyte numbers decreased 2.5-fold ($p = 0.08$) and 3.1-fold ($p = 0.08$), respectively at this time. Of the antioxidants examined, only ascorbate in BAL fluid was affected by O₃, falling in all subjects relative to air values (0.1 (0.0-0.3) v 0.3 (0.2-1.2) $\mu\text{mol/l}$ ($p = 0.008$)). A marginal decrease in plasma ascorbate was also detected at this time ($p < 0.05$). Although the decrease in macrophage numbers seemed to be causally related to the increase in neutrophils ($R = -0.79$), myeloperoxidase concentrations ($R = -0.93$) and ascorbate concentrations ($R = 0.6$), no clear associations were apparent between ascorbate changes and neutrophils or myeloperoxidase concentration after O₃. **CONCLUSIONS:** Ascorbate in the fluid lining the respiratory tract is depleted as a consequence of O₃ exposure at 6 hours after exposure. This was contemporaneous with, although not quantitatively related to the increase in neutrophil numbers and myeloperoxidase concentrations. Decreased macrophage numbers 6 hours after O₃ related to the degree of neutrophilic inflammation with populations conserved where ascorbate concentration in the fluid lining the respiratory tract were high after exposure. These results imply that ascorbate has a critical protective role against inflammatory oxidative stress induced by O₃

Physical activity increases mRNA for brain-derived neurotrophic factor and nerve growth factor in rat brain.

Neeper SA, Gomez-Pinilla F, Choi J, et al.

Brain Res. 1996 Jul 8; 726(1-2):49-56.

Brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) support the viability and function of many types of neurons, and are likely mediators of activity-dependent changes in the CNS. We examined BDNF and NGF mRNA levels in several brain areas of adult male rats following 0, 2, 4, or 7 nights with ad libitum access to running wheels. BDNF mRNA was significantly increased in several brain areas, most notably in the hippocampus and caudal 1/3 of cerebral cortex following 2, 4, and 7 nights with exercise. Significant elevations in BDNF mRNA were localized in Ammon's horn areas 1 (CA1) and 4 (CA4) of the hippocampus, and layers II-III of the caudal neocortex and retrosplenial cortex. NGF mRNA was also significantly elevated in the hippocampus and caudal 1/3 of the cortex, affecting primarily the dentate gyrus granular layer (DG) and CA4 of the hippocampus and layers II-III in caudal neocortex

Promoting and prescribing exercise for the elderly.

Nied RJ, Franklin B.

Am Fam Physician. 2002 Feb 1; 65(3):419-26.

Regular exercise provides a myriad of health benefits in older adults, including improvements in blood pressure, diabetes, lipid profile, osteoarthritis, osteoporosis, and neurocognitive function. Regular physical activity is also associated with decreased mortality and age-related morbidity in older adults. Despite this, up to 75 percent of older Americans are insufficiently active to achieve these health benefits. Few contraindications to exercise exist and almost all older persons can benefit from additional physical activity. The exercise prescription consists of three components: aerobic exercise, strength training, and balance and flexibility. Physicians play a key role in motivating older patients and advising them regarding their physical limitations and/or comorbidities. Motivating patients to begin exercise is best achieved by focusing on individual patient goals, concerns, and barriers to exercise. Strategies include the "stages of change" model, individualized behavioral therapy, and an active lifestyle. To increase long-term compliance, the exercise prescription should be straightforward, fun, and geared toward a patient's individual health needs, beliefs, and goals

Exercise and immune function. Recent developments.

Nieman DC, Pedersen BK.

Sports Med. 1999 Feb; 27(2):73-80.

Comparison of immune function in athletes and nonathletes reveals that the adaptive immune system is largely unaffected by athletic endeavour. The innate immune system appears to respond differentially to the chronic stress of intensive exercise, with natural killer cell activity tending to be enhanced while neutrophil function is suppressed. However, even when significant changes in the level and functional activity of immune parameters have been observed in athletes, investigators have had little success in linking these to a higher incidence of infection and illness. Many components of the immune system exhibit change after prolonged heavy exertion. During this 'open window' of altered immunity (which may last between 3 and 72 hours, depending on the parameter measured), viruses and bacteria may gain a foothold, increasing the risk of subclinical and clinical infection. However, no serious attempt has been made by investigators to demonstrate that athletes showing the most extreme post-exercise immunosuppression are those that contract an infection during the ensuing 1 to 2 weeks. This link must be established before the 'open window' theory can be wholly accepted. The influence of nutritional supplements, primarily zinc, vitamin C, glutamine and carbohydrate, on the acute immune response to prolonged exercise has been measured in endurance athletes. Vitamin C and glutamine have received much attention, but the data thus far are inconclusive. The most impressive results have been reported in the carbohydrate supplementation studies. Carbohydrate beverage ingestion has been associated with higher plasma glucose levels, an attenuated cortisol and growth hormone response, fewer perturbations in blood immune cell counts, lower granulocyte and monocyte phagocytosis and oxidative burst activity, and a diminished pro- and anti-inflammatory cytokine response. It remains to be shown whether carbohydrate supplementation diminishes the frequency of infections in the recovery period after strenuous exercise. Studies on the influence of moderate exercise training on host protection and immune function have shown that near-daily brisk walking compared with inactivity reduced the number of sickness days by half over a 12- to 15-week period without change in resting immune function. Positive effects on immunosurveillance and host protection that come with moderate exercise training are probably related to a summation effect from acute positive changes that occur during each exercise bout. No convincing data exist that moderate exercise training is linked with improved T helper cell counts in patients with HIV, or enhanced immunity in elderly participants

Role of red meat and arachidonic acid in protein kinase C activation in rat colonic mucosa.

Pajari AM, Hakkanen P, Duan RD, et al.

Nutr Cancer. 1998; 32(2):86-94.

Two studies were conducted to investigate the role of meat and arachidonic acid in colonic signal transduction, particularly protein kinase C (PKC) activation. In Study 1, 26 male Wistar rats were fed a casein- or a beef-based diet for four weeks. PKC activity was measured from the proximal and distal colonic mucosa and diacylglycerol concentration from fecal samples. The beef diet significantly increased membrane PKC activity in the proximal and distal colon and cytosolic PKC in the distal colon. No differences were found in fecal diacylglycerol concentration for the rats maintained on the two diets. In Study 2, 57 male Wistar rats were divided into three dietary treatment groups: a control group, a group supplemented with arachidonic acid at 8 mg/day (an amount equivalent to that available from the beef diet in Study 1), and a group supplemented with fish oil at 166 mg/day. After a four-week supplementation period, 6 rats per group were used for colonic phospholipid fatty acid analysis and 13 rats per group were used for analysis of colonic prostaglandin E2 concentration, sphingomyelinase, and PKC activities. Supplementation of dietary arachidonic acid resulted in incorporation of arachidonic acid into colonic phosphatidylcholine, which was associated with an increase in mucosal prostaglandin E2 concentration compared with the fish oil group. However, arachidonate supplementation had no effect on sphingomyelinase or PKC activities. These data indicate that meat significantly increases colonic PKC activity, but this effect is probably not due to the arachidonic acid content of meat

Effect of creatine loading on long-term sprint exercise performance and metabolism.

Preen D, Dawson B, Goodman C, et al.

Med Sci Sports Exerc. 2001 May; 33(5):814-21.

PURPOSE: This study examined whether creatine (Cr) supplementation could enhance long-term repeated-sprint exercise performance of approximately 80 min in duration. **METHODS:** Fourteen active, but not well-trained, male subjects initially performed 10 sets of either 5 or 6 x 6 s maximal bike sprints, with varying recoveries (24, 54, or 84 s between sprints) over a period of 80 min. Work done (kJ) and peak power (W) were recorded for each sprint, and venous blood was collected preexercise and on four occasions during the exercise challenge. Muscle biopsies (vastus lateralis) were obtained preexercise as well as 0 min and 3 min postexercise. Subjects were then administered either 20 g.d⁻¹ Cr.H₂O (N = 7) or placebo (N = 7) for

5 d. Urine samples were collected for each 24 h of the supplementation period. Subjects were then retested using the same procedures as in test 1. RESULTS: Total work done increased significantly ($P < 0.05$) from 251.7 +/- 18.4 kJ presupplementation to 266.9 +/- 19.3 kJ (6% increase) after Cr ingestion. No change was observed for the placebo group (254.0 +/- 10.4 kJ to 252.3 +/- 9.3 kJ). Work done also improved significantly ($P < 0.05$) during 6 x 6 s sets with 54-s and 84-s recoveries and approached significance ($P = 0.052$) in 5 x 6 s sets with 24-s recovery in the Cr condition. Peak power was significantly increased ($P < 0.05$) in all types of exercise sets after Cr loading. No differences were observed for any performance variables in the placebo group. Resting muscle Cr and PCr concentrations were significantly elevated ($P < 0.05$) after 5 d of Cr supplementation (Cr: 48.9%; PCr: 12.5%). Phosphocreatine levels were also significantly higher ($P < 0.05$) immediately and 3 min after the completion of exercise in the Cr condition. CONCLUSION: The results of this study indicate that Cr ingestion (20 g.day⁻¹ x 5 d) improved exercise performance during 80 min of repeated-sprint exercise, possibly due to an increased TCr store and improved PCr replenishment rate

Effects of oral creatine supplementation on high intensity, intermittent exercise performance in competitive squash players.

Romer LM, Barrington JP, Jeukendrup AE.

Int J Sports Med. 2001 Nov; 22(8):546-52.

The purpose of this study was to determine the effects of oral creatine supplementation on high intensity, intermittent exercise performance in competitive squash players. Nine squash players (mean +/- SEM VO₂max = 61.9 +/- 2.1 ml x kg⁻¹ x min⁻¹); body mass = 73 +/- 3 kg) performed an on-court "ghosting" routine that involved 10 sets of 2 repetitions of simulated positional play, each set interspersed with 30 s passive recovery. A double blind, crossover design was utilised whereby experimental and control groups supplemented 4 times daily for 5 d with 0.075 g x kg⁻¹ body mass of creatine monohydrate and maltodextrine, respectively, and a 4 wk washout period separated the crossover of treatments. The experimental group improved mean set sprint time by 3.2 +/- 0.8% over and above the changes noted for the control group ($P = 0.004$ and 95% CI = 1.4 to 5.1%). Sets 2 to 10 were completed in a significantly shorter time following creatine supplementation compared to the placebo condition ($P < 0.05$). In conclusion, these data support existing evidence that creatine supplementation improves high intensity, intermittent exercise performance. In addition, the present study provides new evidence that oral creatine supplementation improves exercise performance in competitive squash players

Impact of physical activity and sport on the immune system.

Shepard RJ, Shek PN.

Rev Environ Health. 1996 Jul; 11(3):133-47.

This review describes how exercise and physical training affect the immune system. Although many immune functions are stimulated by moderate physical activity, more vigorous effort and periods of heavy training suppress various immune response parameters. Experimental studies from our own laboratories and elsewhere illustrate that cellular infiltration of the active muscle is accompanied by phagocyte activation, suppressed NK-cell function, impaired lymphocyte proliferation, decreased in-vitro immunoglobulin production, pro-inflammatory eicosanoid release, cytokine cascade activation, and altered expression of cytokine receptors. Examples cover deliberate heavy training; single bouts of fatiguing, submaximal work; repeated bouts of exercise; and ultra-long distance athletic events. In young adults, age, environment, and light physical training do not change immune-response parameters. Parallels between immune impairment after vigorous exercise and reactions to surgical sepsis are noted. Vigorous exercise probably induces subclinical muscle injury and an associated inflammatory response. Heavy exercise may be a useful experimental model for developing more effective treatments for sepsis. For protection average athletes may take the anti-oxidant vitamins C and E and non-steroidal inflammatory drugs, if the muscles show signs of an inflammatory reaction. Top-level athletes have received immunoglobulin preparations

Enhancement of muscular performance by a coformulation of propionyl-L-carnitine, coenzyme Q10, nicotinamide, riboflavin and pantothenic acid in the rat.

Vargiu R, Licheri D, Carcassi AM, et al.

Physiol Behav. 2002 Jun 1; 76(2):257-63.

A coformulation of essential factors, i.e. propionyl-L-carnitine (PLC), coenzyme Q10 (CoQ10), nicotinamide (NAM), riboflavin and pantothenic acid, was administered orally to Wistar rats for 7 weeks and its efficacy was tested through in vivo and in vitro techniques in improving motor functions of striated, cardiac and smooth musculature of the rat. In vivo experiments showed that long-term supplementation significantly improved horizontal locomotor activity by about 19% in male and 26% in female rats. Maximum values of shortening velocity, work and power were significantly increased ($P < 0.05$) in papillary muscle isolated from treated rats. A positive inotropic effect was also observed on colonic smooth muscle strips upon treatment. Work was the most

affected parameter and it increased by 160% in smooth muscle from treated animals. The present results indicate that supplementation with the combination of the above mentioned substances elicits positive functional changes on motor performance of skeletal, cardiac and smooth muscle of the rat

Exercise, immunity and aging.

Venjatraman JT, Fernandes G.

Aging (Milano). 1997 Feb; 9(1-2):42-56.

In general population, many protective immune responses are impaired in old age, leading to an increased risk of infection. However, recent studies in SENIEUR subjects (healthy centenarians who are examples of successful aging) suggest that complex remodeling and reshaping of the immune system occurs with aging. An appropriate regular regimen of endurance exercise might help elderly to lead a quality of life by preserving immune function. However, very little is known regarding the interaction between exercise, aging and the immune system. Given that a number of age-related changes occur in many physiological systems which are known to alter the immune function both at rest and during exercise, it would be of value to learn the extent to which both acute and chronic exercise influence immune function in the elderly. The immune system response to exercise is multifaceted, depending on the nature of exercise. Significant interaction between the neuroendocrine and immune systems, and the role of lifestyle factors in immune function are known to occur. In theory, moderate exercise should help to reverse the adverse effects of aging upon the immune system by increasing the production of endocrine hormones which may contribute to less accumulation of autoreactive immune cells by enhancing the programmed cell death. Active elderly subjects demonstrated a significantly greater proliferative response to phytohemagglutinins (PHA) and to pokeweed mitogen (PWM), and higher rates of interleukin-2 (IL-2), interferon-gamma (IFN-gamma) and interleukin-4 (IL-4) production. A moderate training program can enhance the resting natural killer (NK) cell function of healthy elderly people, potentially increasing resistance to both viral infections and preventing the formation of malignant cells. Recent studies have suggested that endurance training in later life is associated with a lesser age-related decline in certain aspects of circulating T cell function and related cytokine production. It is important that the dose of physical activity needed to optimize immune function be defined more clearly at various points during the aging process both in females and males in order to optimize the immune function and to prevent any rise in adverse effects of exercise on the elderly population

Physiological responses to short-term exercise in the heat after creatine loading.

Volek JS, Mazzetti SA, Farquhar WB, et al.

Med Sci Sports Exerc. 2001 Jul; 33(7):1101-8.

PURPOSE: This investigation was designed to examine the influence of creatine (Cr) supplementation on acute cardiovascular, renal, temperature, and fluid-regulatory hormonal responses to exercise for 35 min in the heat. **METHODS:** Twenty healthy men were matched and then randomly assigned to consume 0.3 g.kg⁻¹ Cr monohydrate (N = 10) or placebo (N = 10) for 7 d in a double-blind fashion. Before and after supplementation, both groups cycled for 30 min at 60-70% VO₂(peak) immediately followed by three 10-s sprints in an environmental chamber at 37 degrees C and 80% relative humidity. **RESULTS:** Body mass was significantly increased (0.75 kg) in Cr subjects. Heart rate, blood pressure, and sweat rate responses to exercise were not significantly different between groups. There were no differences in rectal temperature responses in either group. Sodium, potassium, and creatinine excretion rates obtained from 24-h and exercise urine collection periods were not significantly altered in either group. Serum creatinine was elevated in the Cr group but within normal ranges. There were significant exercise-induced increases in cortisol, aldosterone, renin, angiotensin I and II, atrial peptide, and arginine vasopressin. The aldosterone response was slightly greater in the Cr (263%) compared with placebo (224%) group. Peak power was greater in the Cr group during all three 10-s sprints after supplementation and unchanged in the placebo group. There were no reports of adverse symptoms, including muscle cramping during supplementation or exercise. **CONCLUSION:** Cr supplementation augments repeated sprint cycle performance in the heat without altering thermoregulatory responses

Some new aspects of creatine kinase (CK): compartmentation, structure, function and regulation for cellular and mitochondrial bioenergetics and physiology.

Wallimann T, Dolder M, Schlattner U, et al.

Biofactors. 1998; 8(3-4):229-34.

Creatine kinase (CK) isoenzymes, specifically located at places of energy demand and energy production, are linked by a phosphocreatine/creatine (PCr/Cr) circuit, found in cells with intermittently high energy demands. Cytosolic CKs, in close conjunction with Ca²⁺-pumps, play a crucial role for the energetics of Ca²⁺-homeostasis. Mitochondrial Mi-CK, a cuboidal-shaped octamer with a central channel, binds and crosslinks mitochondrial membranes and forms a functionally coupled

microcompartment with porin and adenine nucleotide translocase for vectorial export of PCr into the cytosol. The CK system is regulated by AMP-activated protein kinase via PCr/Cr and ATP/AMP ratios. Mi-CK stabilizes and cross-links cristae- or inner/outer membranes to form parallel membrane stacks and, if overexpressed due to creatine depletion or cellular energy stress, forms those crystalline intramitochondrial inclusions seen in some mitochondrial cytopathy patients. Mi-CK is a prime target for free radical damage by peroxynitrite. Mi-CK octamers, together with CK substrates have a marked stabilizing and protective effect against mitochondrial permeability transition pore opening, thus providing a rationale for creatine supplementation of patients with neuromuscular and neurodegenerative diseases

Management of osteoporosis: is there a role for vitamin K?

Weber P.

Int J Vitam Nutr Res. 1997; 67(5):350-6.

Vitamin K is required for the biological activity of several coagulation factors, which is considered as the classical function of vitamin K. Recent research, however, suggests a role of vitamin K in bone metabolism. The metabolic role of vitamin K is to facilitate the carboxylation of glutamyl to gamma-carboxyglutamyl residues. Besides the hepatic tissue, in which the clotting factors are produced gamma-carboxyglutamyl-containing proteins are also abundantly available in bone tissue. Osteocalcin accounts for up to 80% of the total gamma-carboxyglutamyl content of mature bone. Human carboxylated osteocalcin contains 3 gamma-carboxyglutamyl residues which confer a highly specific affinity to the calcium ion of the hydroxyapatite molecule. Besides the gamma-carboxylation of osteocalcin vitamin K may also affect other parameters of bone metabolism, such as calcium hemostasis, and prostaglandin E2 and interleukin 6 production. Evidence from observational studies and first intervention trials indicate that vitamin K intakes much higher than the current recommendations improved biochemical markers of bone formation as well as bone density. In conclusion, the mechanistic data as well as the observational data and the results of the first controlled clinical trials in humans point to a beneficial effect of additional intakes of vitamin K in bone health

Effect of creatine supplementation on phosphocreatine resynthesis, inorganic phosphate accumulation and pH during intermittent maximal exercise.

Yquel RJ, Arsac LM, Thiadiere E, et al.

J Sports Sci. 2002 May; 20(5):427-37.

In this study, we examined the effect of creatine ingestion on muscle power output, muscle phosphocreatine resynthesis, inorganic phosphate and pH during repeated brief bouts of maximal exercise. Nine healthy males performed maximal plantar flexion before and after creatine ingestion (20 g x day⁻¹) for 6 days). The experimental protocol consisted of five 8 s bouts (bouts 1-5) interspersed with 30 s recovery, followed by bouts 6 (8 s) and 7 (16 s) separated by 1 and 2 min, respectively. Muscle phosphocreatine, inorganic phosphate and pH were estimated every 16 s by ³¹P magnetic resonance spectroscopy. After creatine ingestion, muscle power output increased by approximately 5% (P< 0.05) from bouts 3 to 7 and muscle phosphocreatine resynthesis increased (P< 0.05) during 10 min recovery. The higher phosphocreatine concentration observed after only 30 s of recovery was accompanied by lower inorganic phosphate accumulation and higher pH. Strong correlations were found between exercise power restoration and the corresponding pre-exercise phosphocreatine and inorganic phosphate concentrations and muscle pH after creatine ingestion. The better maintenance of muscle power output observed after creatine ingestion was attributed to a higher rate of phosphocreatine resynthesis, lower accumulation of inorganic phosphate and higher pH

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