

## ABSTRACTS

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## Ginkgo biloba

Ginkgo for memory enhancement: a randomized controlled trial.

**CONTEXT:** Several over-the-counter treatments are marketed as having the ability to improve memory, attention and related cognitive functions in as little as four weeks. These claims, however, are generally not supported by well-controlled clinical studies. **OBJECTIVE:** To evaluate whether ginkgo, an over-the-counter agent marketed as enhancing memory, improves memory in elderly adults as measured by objective neuropsychological tests and subjective ratings. **DESIGN:** Six-week randomized, double-blind, placebo-controlled, parallel-group trial. **SETTING AND PARTICIPANTS:** Community-dwelling volunteer men (n = 98) and women (n = 132) older than 60 years with Mini-Mental State Examination scores greater than 26 and in generally good health were recruited by a U.S. academic center via newspaper advertisements and enrolled over a 26-month period from July 1996 to September 1998.

**INTERVENTION:** Participants were randomly assigned to receive ginkgo, 40 mg three times per day (n = 115), or matching placebo (n = 115). **MAIN OUTCOME MEASURES:** Standardized neuropsychological tests of verbal and nonverbal learning and memory, attention and concentration, naming and expressive language, participant self-report on a memory questionnaire and care giver clinical global impression of change as completed by a companion. **RESULTS:** Two hundred three participants (88%) completed the protocol. Analysis of the modified intent-to-treat population (all 219 participants returning for evaluation) indicated that there were no significant differences between treatment groups on any outcome measure. Analysis of the fully evaluable population (the 203 who complied with treatment and returned for evaluation) also indicated no significant differences for any outcome measure. **CONCLUSIONS:** The results of this six-week study indicate that ginkgo did not facilitate performance on standard neuropsychological tests of learning, memory, attention and concentration or naming and verbal fluency in elderly adults without cognitive impairment. The ginkgo group also did not differ from the control group in terms of self-reported memory function or global rating by spouses, friends and relatives. These data suggest that when taken following the manufacturer's instructions, ginkgo provides no measurable benefit in memory or related cognitive function to adults with healthy cognitive function.

JAMA 2002 Aug 21;288(7):835-40

A placebo-controlled, double-blind, randomized trial of an extract of ginkgo biloba for dementia. North American EGb Study Group.

**CONTEXT:** EGb 761 is a particular extract of ginkgo biloba used in Europe to alleviate symptoms associated with numerous cognitive disorders. Its use in dementias is based on positive results from only a few controlled clinical trials, most of which did not include standard assessments of cognition and behavior. **OBJECTIVE:** To assess the efficacy and safety of EGb in Alzheimer's disease and multi-infarct dementia. **DESIGN:** A 52-week, randomized double-blind, placebo-controlled, parallel-group, multicenter study. **PATIENTS:** Mildly to severely demented outpatients with Alzheimer's disease or multi-infarct dementia, without other significant medical conditions. **INTERVENTION:** Patients assigned randomly to treatment with EGb (120 mg/d) or placebo. Safety, compliance, and drug dispensation were monitored every three months with complete outcome evaluation at 12, 26 and 52 weeks. **PRIMARY OUTCOME MEASURES:** Alzheimer's Disease Assessment Scale-Cognitive subscale (ADAS-Cog), Geriatric Evaluation by Relative's Rating Instrument (GERRI), and Clinical Global Impression of Change (CGIC). **RESULTS:** From 309 patients included in an intent-to-treat analysis, 202 provided evaluable data for the 52-week end point analysis. In the intent-to-treat analysis, the EGb group had an ADAS-Cog score 1.4 points better than the placebo group (P=.04) and a GERRI score 0.14 points better than the placebo group (P=.004). The same patterns were observed with the evaluable data set in which 27% of patients treated with EGb achieved at least a four-point improvement on the ADAS-Cog, compared with 14% taking placebo (P=.005); on the GERRI, 37% were considered improved with EGb, compared with 23% taking placebo (P=.003). No difference was seen in the CGIC. Regarding the safety profile of EGb, no significant differences compared with placebo were observed in the number of patients reporting adverse events or in the incidence and severity of these events. **CONCLUSIONS:** EGb was safe and appears capable of stabilizing and, in a substantial number of cases, improving the cognitive performance and the social functioning of demented patients for six months to one year. Although modest, the changes induced by EGb were objectively measured by the ADAS-Cog and were of sufficient magnitude to be recognized by the caregivers in the GERRI.

JAMA 1997 Oct 22-29;278(16):1327-32

Antioxidants and herbal extracts protect HT-4 neuronal cells against glutamate-induced cytotoxicity.

Antioxidant therapy has been shown to be beneficial in neurological disorders including Alzheimer's disease and cerebral ischemia. Glutamate-induced cytotoxicity in HT-4 neuronal cells has been previously demonstrated to be due to oxidative stress caused by depletion of cellular glutathione (GSH). The present study demonstrates that a wide variety of antioxidants inhibit glutamate-induced cytotoxicity in HT-4 neuronal cells. Low concentrations of alpha-tocopherol and its analogs were highly effective in protecting neuronal cells against cytotoxicity. Purified flavonoids and herbal extracts of ginkgo biloba (EGb 761) and French maritime pine bark (Pycnogenol) were also effective. We have previously shown that pro-glutathione agents can spare GSH and protect cells from glutamate insult in a C6 glial cell model. The protective effects of nonthiol-based antioxidants tested in the HT-4 line were not mediated via GSH level modulation. In contrast, protective effects of thiol-based pro-glutathione agents alpha-lipoic acid (LA) and N-acetyl cysteine (NAC) corresponded with a sparing effect on GSH levels in glutamate-treated HT-4 cells. Glutamate-induced cytotoxicity in HT-4 cells is a useful model system for testing compounds or mixtures for antioxidant activity.

Free Radic Res 2000 Feb;32(2):115-24

Mitochondria, oxidative stress and aging.

In the 1980's, Miquel and Fleming suggested that mitochondria play a key role in cellular aging. Mitochondria, and especially mitochondrial DNA (mtDNA), are major targets of free radical attack. At present, it is well established that mitochondrial deficits accumulate upon aging due to oxidative damage. Thus, oxidative lesions to mtDNA accumulate with age in human and rodent tissues. Furthermore, levels of oxidative damage to mtDNA are several times higher than those of nuclear DNA. Mitochondrial size increases whereas mitochondrial membrane potential decreases with age in brain and liver. Recently, we have shown that treatment with certain antioxidants, such as sulphur-containing antioxidants, vitamins C and E or the ginkgo biloba extract EGb 761, protects against the age-associated oxidative damage to mtDNA and oxidation of mitochondrial glutathione. Moreover, the extract EGb 761 also prevents changes in mitochondrial morphology and function associated with aging of the brain and liver. Thus, mitochondrial aging may be prevented by antioxidants. Furthermore, late onset administration of certain antioxidants is also able to prevent the impairment in physiological performance, particularly motor co-ordination, that occurs upon aging.

Free Radic Res 2000 Mar;32(3):189-98

Ginkgo biloba inhibits hydrogen peroxide-induced activation of nuclear factor kappa B in vascular endothelial cells.

The present study determined the effects of ginkgo biloba extract (GBE) on the activation of nuclear factor kappa B (NF-kappaB) and the level of hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) in bovine pulmonary artery endothelial cells (PAEC). H<sub>2</sub>O<sub>2</sub> showed a concentration-dependent activation of NF-kappaB. GBE demonstrated a concentration-dependent suppression of NF-kappaB activated by H<sub>2</sub>O<sub>2</sub>. GBE directly scavenged H<sub>2</sub>O<sub>2</sub> in a cell-free system; it also decreased H<sub>2</sub>O<sub>2</sub> levels in PAEC. These results suggest that the inhibitory effect of GBE on H<sub>2</sub>O<sub>2</sub>-induced NF-kappaB activation may be caused by its scavenging and suppression of H<sub>2</sub>O<sub>2</sub>. Our experiments demonstrate that GBE can inhibit NF-kappaB activation induced by H<sub>2</sub>O<sub>2</sub> and may thus be effective for the prevention or treatment of atherosclerosis and other disorders related to NF-kappaB activation.

Gen Pharmacol 1999 Nov;33(5):369-75

Vitamin K

Inhibition of human platelet aggregation by vitamin K.

The effect of several vitamin K (Vit K) analogues on the aggregation of human platelets was examined. The analogues were potent inhibitors of aggregation induced by ADP, thrombin, collagen and arachidonate but were less active against aggregation induced by the calcium ionophore A23187. Vit K3 also prevented platelet membrane phosphatide breakdown induced by collagen. These effects were not due to a direct inhibition of enzymes involved in the liberation of arachidonate or its subsequent transformation. The analogues exerted no effects on enzymes regulating intraplatelet cAMP. However, these effects could be overcome by increasing extracellular Ca<sup>++</sup> levels, indicating a possible interaction with Ca<sup>++</sup> regulation in platelets.

Thromb Res 1985 Jan 1;37(1):103-14

Vitamin K2 (menatetrenone) for bone loss in patients with cirrhosis of the liver.

**OBJECTIVE:** Bone loss frequently appears in the natural history of liver disease. The effects of therapy for osteoporosis associated with cirrhosis of the liver are still controversial. We evaluated the effects of vitamin K2 on osteopenia in women with cirrhosis.

**METHODS:** The subjects were 50 women with cirrhosis who had underlying hepatitis viral infections. Half of the patients were

randomly assigned to receive vitamin K2 (menatetrenone). The bone mineral density (BMD) of the lumbar vertebrae was measured by dual-energy X-ray absorptiometry at entry and at 1-yr intervals for 2 yr. RESULTS: The percentages of change from the initial BMD at 1 and 2 yr after initiation of the study were, respectively, +0.1 +/- 2.6% and -0.5 +/- 3.5% for the vitamin K2-treated group and -2.2 +/- 2.4% and -4.6 +/- 3.9% for the control group. The changes in BMD at each timepoint differed significantly between the control and treated groups ( $p = 0.008$  for 1 yr and  $p = 0.002$  for 2 yr). In the vitamin K2-treated group, the ratio of osteocalcin to undercarboxylated osteocalcin in those patients with increases in BMD after 1 yr of treatment was significantly lower than that in patients showing decreases in BMD ( $p = 0.017$ ). No adverse effects of vitamin K2 were noted. CONCLUSIONS: Vitamin K2 can prevent bone loss and may therefore be useful in the management of bone disease in women with cirrhosis of the liver.

Am J Gastroenterol 2002 Apr;97(4):978-81

Effects of vitamin K(2) on bone of ovariectomized rats and on a rat osteoblastic cell line.

The effects of vitamin K(2) on bone mineral density (BMD) and bone metabolic markers of ovariectomized rats, and those on mRNA expression of osteocalcin and IL-6 on a rat osteoblastic cell line, were investigated. BMD and bone metabolic markers were examined in ovariectomized rats after 2 months' treatment with vitamin K(2), and mRNA expression of osteocalcin and IL-6 were measured in the cell line after 24-hour treatment with vitamin K(2). Vitamin K(2) attenuated the decline in BMD after ovariectomy in the rats, and suppressed serum deoxypyridinoline levels of the ovariectomized rats. No effect on osteocalcin and IL-6 mRNA expression on the cell line was observed. In conclusion, vitamin K(2) has a bone-protective effect on ovariectomized rats.

Gynecol Obstet Invest 2002;53(3):144-8

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Maintenance of trabecular structure and bone volume by vitamin K(2) in mature rats with long-term tail suspension.

Bone volume loss is one of the major health problems during long-term spaceflight. We examined the effects of vitamin K(2) on bone abnormalities in tail-suspended mature male Sprague-Dawley rats (13 weeks old). In this model, increased bone resorption and sustained suppression of bone formation resulted in progressive bone loss in four weeks, which simulates bone changes in humans during spaceflight. A significant decrease in bone mineral density (BMD), as well as a decreased mineral apposition rate (MAR), increased the number of osteoclasts per bone perimeter (N.Oc/B.Pm), and increased osteoclast surface per bone surface (Oc.S/BS) in the suspended group was effectively prevented by vitamin K(2), given orally (menatetrenone, 22 mg/kg body weight). Microfocus computed tomography (CT) and node-strut analyses revealed that the volume and structure of trabecular bone were maintained near normal by the vitamin K(2) treatment. A recent report has suggested the abnormal metabolism or action of vitamin K in a microgravity environment, and our data therefore suggest that vitamin K(2) may be useful for the prevention of bone loss and for the maintenance of normal trabecular structure during spaceflight.

J Bone Miner Metab 2002;20(4):216-22

Vitamin K intake and hip fractures in women: a prospective study.

**BACKGROUND:** Vitamin K mediates the gamma-carboxylation of glutamyl residues on several bone proteins, notably osteocalcin. High serum concentrations of undercarboxylated osteocalcin and low serum concentrations of vitamin K are associated with lower bone mineral density and increased risk of hip fracture. However, data are limited on the effects of dietary vitamin K. **OBJECTIVE:** We investigated the hypothesis that high intakes of vitamin K are associated with a lower risk of hip fracture in women. **DESIGN:** We conducted a prospective analysis within the Nurses' Health Study cohort. Diet was assessed in 72,327 women aged 38 to 63 y with a food-frequency questionnaire in 1984 (baseline). During the subsequent 10 y of follow-up, 270 hip fractures resulting from low or moderate trauma were reported. **RESULTS:** Women in quintiles 2 to 5 of vitamin K intake had a significantly lower age-adjusted relative risk (RR: 0.70; 95% CI: 0.53, 0.93) of hip fracture than women in the lowest quintile (< 109 microg/d). Risk did not decrease between quintiles two and five and risk estimates were not altered when other risk factors for osteoporosis, including calcium and vitamin D intakes, were added to the models. Risk of hip fracture was also inversely associated with lettuce consumption (RR: 0.55; 95% CI: 0.40, 0.78) for one or more servings per day compared with one or fewer servings per week), the food that contributed the most to dietary vitamin K intakes. **CONCLUSIONS:** Low intakes of vitamin K may increase the risk of hip fracture in women. The data support the suggestion for a reassessment of the vitamin K requirements that are based on bone health and blood coagulation.

Am J Clin Nutr 1999 Jan;69(1):74-9

Warfarin exposure and calcification of the arterial system in the rat.

There is evidence from knock-out mice that the extrahepatic vitamin K-dependent protein, matrix gla protein, is necessary to prevent arterial calcification. The aim of this study was to determine if a warfarin treatment regimen in rats, designed to cause extra-hepatic vitamin K deficiency, would also cause arterial calcification. Sprague-Dawley rats were treated from birth for five to 12 weeks with daily doses of warfarin and concurrent vitamin K1. This treatment causes an extrahepatic vitamin K deficiency without affecting the vitamin K-dependent blood clotting factors. At the end of treatment the rats were killed and the vascular system was examined for evidence of calcification. All treated animals showed extensive arterial calcification. The cerebral arteries and the veins and capillaries did not appear to be affected. It is likely that humans on long-term warfarin treatment have extrahepatic vitamin K deficiency and hence they are potentially at increased risk of developing arterial calcification.

Int J Exp Pathol 2000 Feb;81(1):51-6

High blood pressure and bone-mineral loss in elderly white women: a prospective study. Study of Osteoporotic Fractures Research Group.

**BACKGROUND:** High blood pressure is associated with abnormalities in calcium metabolism. Sustained calcium loss may lead to increased bone-mineral loss in people with high blood pressure. We investigated the prospective association between blood pressure and bone-mineral loss over time in elderly white women. **METHODS:** We studied 3,676 women who were initially assessed in 1988 to 90 (mean age 73 years [SD 4, range 66-91 years]; mean bodyweight 65.3 kg [11.5]; blood pressure 137/75 mm Hg [17/9]) who were not on thiazide diuretics. Mean follow-up was 3.5 years. Anthropometry, blood pressure and bone-mineral

density at the femoral neck were measured at baseline and bone densitometry was repeated after 3.5 years by dual-energy X-ray absorptiometry. FINDINGS: After adjustment for age, initial bone-mineral density, weight and weight change, smoking and regular use of hormone-replacement therapy, the rate of bone loss at the femoral neck increased with blood pressure at baseline. In the quartiles of systolic blood pressure, yearly bone losses increased from 2.26 mg/cm<sup>2</sup> (95% CI 1.48-3.04) in the first quartile to 3.79 mg/cm<sup>2</sup> in the fourth quartile (3.13-4.45; test for heterogeneity, p=0.03; test for linear trend, p=0.01), equivalent to yearly changes of 0.34% (0.20-0.46) and 0.59% (0.49-0.69; test for heterogeneity, p=0.02; test for linear trend, p=0.005). There was no significant interaction with age. The exclusion of women on antihypertensive drugs did not alter the results. For diastolic blood pressure, there was an association with bone loss in women younger than 75 years. INTERPRETATION: Higher blood pressure in elderly white women is associated with increased bone loss at the femoral neck. This association may reflect greater calcium losses associated with high blood pressure, which may contribute to the risk of hip fractures.

Lancet 1999 Sep 18;354(9183):971-5

Vertebral fractures and mortality in older women: a prospective study. Study of Osteoporotic Fractures Research Group.

BACKGROUND: Osteoporotic fractures, including clinically detected vertebral fractures, are associated with increased mortality. However, only one-third of vertebral fractures are diagnosed. It is unknown whether vertebral fractures, whether clinically apparent or not, are associated with greater mortality. OBJECTIVES: To test the hypothesis that women with prevalent vertebral fractures have greater mortality than those without fractures and to describe causes of death associated with vertebral fractures. DESIGN: Prospective cohort study with mean follow-up of 8.3 years. SETTING: Four clinical centers in the United States. PARTICIPANTS: A total of 9,575 women aged 65 years or older and enrolled in the Study of Osteoporotic Fractures. MEASUREMENTS: Vertebral fractures by radiographic morphometry; calcaneal bone mineral density; demographic, medical history and lifestyle variables; blood pressure; and anthropometric measures. In a subset of 606 participants, thoracic curvature was measured during a second clinic visit. MAIN OUTCOME MEASURES: Hazard ratios for mortality and cause-specific mortality. RESULTS: At baseline, 1,915 women (20.0%) were diagnosed as having vertebral fractures. Compared with women who did not have a vertebral fracture, women with one or more fractures had a 1.23-fold greater age-adjusted mortality rate (95% confidence interval, 1.10-1.37). Mortality rose with greater numbers of vertebral fractures, from 19 per 1000 woman-years in women with no fractures to 44 per 1000 woman-years in those with five or more fractures (P for trend, <.001). In particular, vertebral fractures were related to the risk of subsequent cancer (hazard ratio, 1.4 95% confidence interval, 1.1-1.7) and pulmonary death (hazard ratio, 2.1 95% confidence interval, 1.4-3.0). In the subset of women who underwent thoracic curvature measurements, severe kyphosis was also related to pulmonary deaths (hazard ratio, 2.6;95% confidence interval, 1.3-5.1). CONCLUSION: Women with radiographic evidence of vertebral fractures have an increased mortality rate, particularly from pulmonary disease and cancer.

Arch Intern Med 1999 Jun 14;159(11):1215-20

Whey protein

The bovine protein alpha-lactalbumin increases the plasma ratio of tryptophan to the other large neutral amino acids, and in vulnerable subjects raises brain serotonin activity, reduces cortisol concentration, and improves mood under stress.

BACKGROUND: Increased brain serotonin may improve the ability to cope with stress, whereas a decline in serotonin activity is involved in depressive mood. The uptake of the serotonin precursor, tryptophan, into the brain is dependent on nutrients that influence the cerebral availability of tryptophan via a change in the ratio of plasma tryptophan to the sum of the other large neutral amino acids (Trp-LNAA ratio). Therefore, a diet-induced increase in tryptophan availability may increase brain serotonin synthesis and improve coping and mood, particularly in stress-vulnerable subjects. OBJECTIVE: We tested whether alpha-lactalbumin, a whey protein with a high tryptophan content, may increase the plasma Trp-LNAA ratio and reduce depressive mood and cortisol concentrations in stress-vulnerable subjects under acute stress. DESIGN: Twenty-nine highly stress-vulnerable subjects and 29 relatively stress-invulnerable subjects participated in a double-blind, placebo-controlled study. Subjects were exposed to experimental stress after the intake of a diet enriched with either alpha-lactalbumin or sodium-caseinate. Diet-induced changes in the plasma Trp-LNAA ratio and prolactin were measured. Changes in mood, pulse rate, skin conductance, and cortisol concentrations were assessed before and after the stressor. RESULTS: The plasma Trp-LNAA ratio was 48% higher after the alpha-lactalbumin diet than after the casein diet (P = 0.0001). In stress-vulnerable subjects this was accompanied by higher prolactin concentrations (P = 0.001), a decrease in cortisol (P = 0.036), and reduced depressive feelings (P = 0.007) under stress. CONCLUSIONS: Consumption of a dietary protein enriched in tryptophan increased the plasma Trp-LNAA ratio and, in stress-vulnerable subjects, improved coping ability, probably through alterations in brain serotonin.

Am J Clin Nutr 2000 Jun;71(6):1536-44

Whey protein rich in alpha-lactalbumin increases the ratio of plasma tryptophan to the sum of the other large neutral amino acids and improves cognitive performance in stress-vulnerable subjects.

BACKGROUND: Cognitive performance often declines under chronic stress exposure. The negative effect of chronic stress on

performance may be mediated by reduced brain serotonin function. The uptake of the serotonin precursor tryptophan into the brain depends on nutrients that influence the availability of tryptophan by changing the ratio of plasma tryptophan to the sum of the other large neutral amino acids (Trp-LNAA ratio). In addition, a diet-induced increase in tryptophan may increase brain serotonergic activity levels and improve cognitive performance, particularly in high stress-vulnerable subjects. OBJECTIVE: We tested whether alpha-lactalbumin, a whey protein with a high tryptophan content, would increase the plasma Trp-LNAA ratio and improve cognitive performance in high stress- vulnerable subjects. DESIGN: Twenty-three high stress-vulnerable subjects and 29 low stress-vulnerable subjects participated in a double-blind, placebo-controlled, crossover study. All subjects conducted a memory-scanning task after the intake of a diet enriched with either alpha-lactalbumin (alpha-lactalbumin diet) or sodium caseinate (control diet). Blood samples were taken to measure the effect of dietary manipulation on the plasma Trp-LNAA ratio. RESULTS: A significantly greater increase in the plasma Trp-LNAA ratio after consumption of the alpha-lactalbumin diet than after the control diet ( $P = 0.0001$ ) was observed; memory scanning improved significantly only in the high stress-vulnerable subjects ( $P = 0.019$ ). CONCLUSION: Because an increase in the plasma Trp-LNAA ratio is considered to be an indirect indication of increased brain serotonin function, the results suggest that dietary protein rich in alpha-lactalbumin improves cognitive performance in stress-vulnerable subjects via increased brain tryptophan and serotonin activities.

Am J Clin Nutr 2002 Jun;75(6):1051-6

A pre-exercise alpha-lactalbumin-enriched whey

protein meal preserves lipid oxidation and decreases adiposity in rats.

The composition of the pre-exercise food intake is known to affect substrate utilization during exercise and thus can affect long-term changes in body weight and composition. These parameters were measured in male rats exercised two h daily over five wk, either in the fasting state or 1 h after they ingested a meal enriched with glucose (Glc), whole milk protein (WMP), or alpha-lactalbumin-enriched whey protein (CPalphaL). Compared with fasting, the Glc meal increased glucose oxidation and decreased lipid oxidation during and after exercise. In contrast, the WMP and CPalphaL meals preserved lipid oxidation and increased protein oxidation, the CPalphaL meal increasing protein oxidation more than the WMP meal. At the end of the study, body weight was larger in the WMP-, Glc-, and CPalphaL-fed rats than in the fasted ones. This resulted from an increased fat mass in the WMP and Glc rats and to an increased lean body mass, particularly muscles, in the CPalphaL rats. We conclude that the potential of the CPalphaL meal to preserve lipid oxidation and to rapidly deliver amino acids for use during exercise improved the efficiency of exercise training to decrease adiposity.

Am J Physiol Endocrinol Metab 2002 Sep;283(3):E565-72

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Irritable bowel syndrome

Enteric-coated peppermint-oil capsules in the treatment of irritable bowel syndrome: a prospective, randomized trial.

To determine the efficacy and tolerability of an enteric-coated peppermint-oil formulation (Colpermin), we conducted a prospective, randomized, double-blind, placebo-controlled clinical study in 110 outpatients (66 men/44 women; 18 to 70 years of age) with symptoms of irritable bowel syndrome. Patients took one capsule (Colpermin or placebo) three to four times daily, 15-30 min before meals, for one month. Fifty-two patients on Colpermin and 49 on placebo completed the study. Forty-one patients on Colpermin (79%) experienced an alleviation of the severity of abdominal pain (29 were pain-free); 43 (83%) had less abdominal distension, 43 (83%) had reduced stool frequency, 38 (73%) had fewer borborygmi, and 41 (79%) less flatulence. Corresponding figures for the placebo group were: 21 patients (43%) with reduced pain (4 were pain-free), 14 (29%) with reduced distension, 16 (32%) with reduced stool frequency, 15 (31%) with fewer borborygmi, and 11 (22%) with less flatulence. Symptom improvements after Colpermin were significantly better than after placebo ( $P < 0.05$ ; Mann-Whitney U-test). One patient on Colpermin experienced heartburn (because of chewing the capsules) and one developed a mild transient skin rash. There were no significant changes in liver function test results. Thus, in this trial, Colpermin was effective and well tolerated.

J Gastroenterol 1997 Dec;32(6):765-8

Stress management for irritable bowel syndrome: a controlled trial.

Thirty-five patients with irritable bowel syndrome were randomized to receive treatment in a stress management programme or conventional therapy which included the antispasmodic Colpermin. The stress management programme involved a median of six 40-min sessions with a physiotherapist during which patients were helped to understand the nature of their symptoms, their relationship to stress and were taught relaxation exercises. Two-thirds of those in the stress management programme found the programme effective in relieving symptoms and experienced fewer attacks of less severity. This benefit was maintained for at least 12 months. Few of those given conventional management had any benefit. A stress management programme would appear to be of value for patients with irritable bowel syndrome.

Digestion 1991;50(1):36-42

Delayed release peppermint oil capsules (Colpermin) for the spastic colon syndrome: a pharmacokinetic study.

Excretion of menthol (as glucuronide) from orally ingested peppermint oil contained in Colpermin was compared with oil contained in two soft gelatine capsules. Total 24 h urinary excretion of menthol was similar in the two formulations in healthy volunteers, but peak menthol excretion levels were lower and excretion delayed with Colpermin. Menthol excretion was reduced in ileostomy patients who took Colpermin and moderate amounts of unmetabolized menthol were recovered from the ileostomy effluent. This is consistent with Colpermin being a delayed-release form of peppermint oil.

Br J Clin Pharmacol 1984 Oct;18(4):638-40

High-fiber diet supplementation in patients with irritable bowel syndrome (IBS): a multicenter, randomized, open trial comparison between wheat bran diet and partially hydrolyzed guar gum (PHGG).

High-fiber diet supplementation is commonly used in IBS, although it poses several management problems. Partially hydrolyzed guar gum (PHGG) has shown beneficial effects in animal and human studies, but its potential role in IBS symptom relief has not been evaluated yet. We investigated PHGG in IBS patients and compared it to a wheat bran diet. Abdominal pain, bowel habits and subjective overall rating were longitudinally evaluated in 188 adult IBS patients (139 women and 49 men) for 12 weeks. Patients were classified as having diarrhea-predominant, constipation-predominant or changeable bowel habits and were randomly assigned to groups receiving fiber (30 g/day of wheat bran) or PHGG (5 g/day). After four weeks, patients were allowed to switch group, depending on their subjective evaluation of their symptoms. Significantly more patients switched from fiber to PHGG (49.9%) than from PHGG to fiber (10.9%) at four weeks. Per protocol analysis showed that both fiber and PHGG were effective in improving pain and bowel habits, but no difference was found between the two groups. Conversely, intention-to-treat analysis showed a significantly greater success in the PHGG group (60%) than in the fiber group (40%). Moreover, significantly more patients in the PHGG group reported a greater subjective improvement than those in the Fiber group. In conclusion, improvements in core IBS symptoms

(abdominal pain and bowel habits) were observed with both bran and PHGG, but the latter was better tolerated and preferred by patients, revealing a higher probability of success than bran and a lower probability of patients abandoning the prescribed regimen, suggesting that it can increase the benefits deriving from fiber intake in IBS, making it a valid option to consider for high-fiber diet supplementation.

Dig Dis Sci 2002 Aug;47(8):1697-704

Enteric-coated, pH-dependent peppermint oil capsules for the treatment of irritable bowel syndrome in children.

In a randomized, double-blind controlled trial, 42 children with irritable bowel syndrome (IBS) were given pH-dependent, enteric-coated peppermint oil capsules or placebo. After two weeks, 75% of those receiving peppermint oil had reduced severity of pain associated with IBS. Peppermint oil may be used as a therapeutic agent during the symptomatic phase of IBS.

J Pediatr 2001 Jan;138(1):125-8

Peppermint oil for irritable bowel syndrome: a critical review and metaanalysis.

**OBJECTIVE:** Peppermint oil is the major constituent of several over-the-counter remedies for symptoms of irritable bowel syndrome (IBS). As the etiology of IBS is not known and treatment is symptomatic, there is a ready market for such products. However, evidence to support their use is sparse. The aim of this study was to review the clinical trials of extracts of peppermint (*Mentha X piperita* L.) as a symptomatic treatment for IBS. **METHODS:** Computerized literature searches were performed to identify all randomized controlled trials of peppermint oil for IBS. Databases included Medline, Embase, Biosis, CISCOM, and the Cochrane Library. There were no restrictions on the language of publication. Data were extracted in a standardized, predefined fashion, independently by both authors. Five double blind, randomized, controlled trials were entered into a metaanalysis. **RESULTS:** Eight randomized, controlled trials were located. Collectively they indicate that peppermint oil could be efficacious for symptom relief in IBS. A metaanalysis of five placebo-controlled, double blind trials seems to support this notion. In view of the methodological flaws associated with most studies, no definitive judgment about efficacy can be given. **CONCLUSION:** The role of peppermint oil in the symptomatic treatment of IBS has so far not been established beyond reasonable doubt. Well designed and carefully executed studies are needed to clarify the issue.

Am J Gastroenterol 1998 Jul;93(7):1131-5

Peppermint oil-caraway oil fixed combination in non-ulcer dyspepsia--comparison of the effects of enteric preparations.

Two hundred twenty three patients with non-ulcer dyspepsia (dysmotility type dyspepsia or essential/idiopathic dyspepsia, also in combination with irritable bowel syndrome) were included in a prospective, randomized, reference- and double-blind controlled multicentre trial to compare two different preparations of a fixed combination of peppermint oil and caraway oil. The aim of the trial was to evaluate the equivalence of the efficacy and tolerability of these two preparations. The test formulation consisted of the drug combination in an enteric coated capsule containing 90 mg peppermint oil and 50 mg caraway oil, while an enteric soluble formulation containing 36 mg peppermint oil and 20 mg caraway oil was used as the reference. The main target item defined was the "difference in pain intensity between the beginning and the end of therapy," measured by the patient on a visual analogue scale (0 = no pain, 10 = extremely strong pain). In 213 patients (n = 108 on the test preparation, n = 105 on the reference preparation) with mean pain intensity baseline measurements of 6.1 points in the test preparation group and 5.9 points in the reference group a statistically significant decline in pain intensity was observed in the two groups (-3.6 resP. -3.3 points; p < 0.001; two-sided one-sample t-test). Equivalent efficacy of both preparations was demonstrated (p < 0.001; one-sided t-test for equivalence). With respect to concomitant variables, the results in both groups were also similar. Regarding "pain frequency," the efficacy of the test preparation was significantly better (p = 0.04; two-sided t-test for difference). Both preparations were well tolerated. Despite the higher dose, the adverse event "eructation with peppermint taste" was less frequent in the group treated with the test formulation, due to the enteric coated capsule preparation.

Pharmazie 1999 Mar;54(3):210-5

Hormones

Are autoimmune thyroid dysfunction and depression related?

The objective of this study was to examine the relationship between autoimmune thyroid disease and depression in perimenopausal women. Thyroid function [TSH, free T4, and thyroid peroxidase antibodies (TPO-Ab)] and depression (using the Edinburgh Depression Scale) were assessed cross-sectionally together with other determinants of depression. The subjects were 583 randomly selected perimenopausal women (aged 47 to 54 yr) from a community cohort of 6,846 women. The main outcome measures were the occurrence of thyroid dysfunction (abnormal free T4 and/or TSH or elevated levels of TPO-Ab) and the

concomitant presence of depression according to the Edinburgh Depression Scale. Neither biochemical thyroid dysfunction nor menopausal status was related to depression. Apart from several psycho-social determinants (the occurrence of a major life event, a previous episode of depression, or financial problems), an elevated level of TPO-Ab ( $> \text{ or } = 100 \text{ U/mL}$ ) was significantly associated with depression (odds ratio, 3.0, 95% confidence interval, 1.3-6.8). We conclude that women with elevated TPO-Ab levels are especially vulnerable to depression, whereas postmenopausal status does not increase the risk of depression.

J Clin Endocrinol Metab 1998 Sep;83(9):3194-7

High serum cholesterol levels in persons with 'high-normal' TSH levels: should one extend the definition of subclinical hypothyroidism?

**OBJECTIVE:** The association between established hypothyroidism and high cholesterol levels is well known. The aim of the present study was to investigate the effect of thyroxine (T4) administration on cholesterol levels in hypercholesterolemic subjects with TSH levels within the normal range ('high-normal' TSH compared with 'low-normal' TSH). **DESIGN AND METHODS:** We determined TSH levels in 110 consecutive patients referred for hypercholesterolemia (serum cholesterol  $>7.5 \text{ mmol/l}$ ). Those with 'high-normal' TSH (2.0-4.0 microU/ml) as well as those with 'low-normal' TSH (0.40-1.99 microU/ml) were randomly assigned to receive either 25 or 50 microg T4 daily for two months. Thus, groups A and B (low-normal TSH) received 25 and 50 microg T4 respectively and groups C and D (high-normal TSH) received 25 and 50 microg T4 respectively. Serum T4, tri-iodothyronine (T3), TSH, free thyroxine index, resin T3 uptake and thyroid autoantibodies (ThAab) as well as total cholesterol, high and low density lipoprotein cholesterol (HDL, LDL), and triglycerides were determined before and at the end of the two-month treatment period. **RESULTS:** TSH levels were reduced in all groups. The most striking effect was observed in group D (TSH levels before:  $2.77 \pm 0.55$ , after:  $1.41 \pm 0.85$  microU/ml,  $P < 0.01$ ). Subjects in groups C and D had a higher probability of having positive ThAabs. A significant reduction in total cholesterol ( $P < 0.01$ ) and LDL ( $P < 0.01$ ) was observed after treatment only in group D. In those subjects in group D who were ThAab negative, there was no significant effect of thyroxine on cholesterol levels. **CONCLUSIONS:** Subjects with high-normal TSH levels combined with ThAabs may, in fact, have subclinical hypothyroidism presenting with elevated cholesterol levels. It is possible that these patients might benefit from thyroxine administration.

Eur J Endocrinol 1998 Feb;138(2):141-5

Low headache prevalence amongst women with high TSH values.

The aim of this large cross-sectional population-based study was to examine a possible positive or negative association between thyroid dysfunction and headache. Between 1995 and 1997, all 92,566 adults in Nord-Trøndelag County in Norway were invited to participate in a health survey. A total of 51,383 (56%) responded to a headache questionnaire, whereof thyroid-stimulating hormone (TSH) was measured in 28,058 individuals. These included 15,465 women and 8,019 men above 40 years of age, 1,767 randomly selected individuals between 20 and 40 years of age, and 2,807 (97%) with thyroid dysfunction. Associations between thyroid dysfunction and headache were assessed in multivariate analyses, estimating prevalence odds ratios (OR) with 95% confidence intervals (CIs). High TSH values were associated with low prevalence of headache. This was most evident amongst women with no history of thyroid dysfunction. Amongst these, headache was less probable (OR=0.5, 95% CI 0.3-0.7) if TSH  $> \text{ or } = 10 \text{ mU/l}$  than in women with normal TSH (0.2-4 mU/l). In all age groups between 40 and 80 years, TSH was lower amongst headache sufferers, especially migraineurs, than in those without headache complaints.

Eur J Neurol 2001 Nov;8(6):693-9

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## ABSTRACTS

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Daily migraine with visual aura associated with an occipital arteriovenous malformation.

A 51-year-old woman with daily attacks of migraine with visual aura is described. The aura always occurred on the right and the headache always on the left side of the head, suggesting a structural lesion in the left occipital lobe. The lesion appeared to be an arteriovenous malformation of which almost full obliteration resulted in a decrease in frequency of the aura and in intensity of the headache. Subsequent treatment of borderline hypothyroidism with levothyroxine brought about a dramatic improvement in frequency of both the aura and the headache. The case is discussed in the light of our present understanding of the pathogenesis of the migraine attack.

Headache 2001 Feb;41(2):193-7

Hypertension in thyroid disorders.

Hypertension is more common in hypothyroidic patients than in euthyroid controls in older age groups. Treatment of the thyroid deficiency alone lowers blood pressure in most patients. Hemodynamically, cardiac output is reduced and total peripheral resistance is elevated. The latter probably is secondary to an increase of sympathetic nervous tone and a relative increase in alpha-adrenergic response. In hyperthyroidism, elevation of diastolic blood pressure is uncommon. Systolic hypertension is more common in younger age groups. Treatment of the hyperthyroidism alone lowers systolic blood pressure in most patients. An increase in cardiac output and a decrease in total peripheral resistance accompany the hyperthyroidism. Potentiation of catecholamine action by an excess of thyroid hormone has been invoked as an explanation, because thyroid hormone excess is accompanied by increased beta-adrenergic receptors in some tissue, including heart.

Endocrinol Metab Clin North Am 1994 Jun;23(2):379-86

Levels of thyroid hormones and thyrotropic hormone in serum of women with perimenopausal arterial hypertension.

Test carried out in 96 women aged between 43 to 55 years ( $50.46 \pm 4.7$ ), who did not take any drugs during the last three months. The women were divided into two groups: premenopausal and early postmenopausal. Each group was subdivided according to blood pressure: with normal pressure and with arterial hypertension. The concentration of T4, T3 and TSH were measured using a radioimmunologic method. The saturation of carrier proteins was established with the T3/test, the result of which was used to divide T4 and T3 and to obtain FT4I and FT3I respectively. It was found that women with arterial hypertension have significantly higher ( $p < 0.001$ ) TSH concentration. The concentration of T3 and FT3I were significantly higher ( $p < 0.01$ ) in women with arterial hypertension in the postmenopausal period.

Ginekol Pol 1992;63(3):130-3

Thyroid disease and female reproduction.

**OBJECTIVE:** To review the menstrual function and fertility in thyroid disease, mainly in hyperthyroidism and hypothyroidism. Also, to register the consequences of  $(^{131}\text{I})$  therapy, which is used widely in the treatment of Graves' disease and thyroid cancer, on subsequent pregnancies and on fertility in these patients. **DESIGN:** A MEDLINE computer search was used to identify relevant studies. The type of menstrual disturbances and the status of fertility were recorded from all the studies found. Also, the fertility and genetic hazard of female patients with Graves' disease and thyroid cancer who were treated with  $(^{131}\text{I})$  were registered. **RESULT (S):** Both hyperthyroidism and hypothyroidism may result in menstrual disturbances. Menstrual abnormalities are less common now than in previous series. In a recent study, we found that only 21.5% of 214 thyrotoxic patients had some type of menstrual disturbance, compared to 50% to 60% in some older series. The most common manifestations are hypomenorrhea and oligomenorrhea. According to the results of endometrial biopsies, most thyrotoxic women remain ovulatory. Moreover, the genetic hazard incidence to radioiodine therapy in Graves' disease and thyroid carcinoma is very small; exposure to  $(^{131}\text{I})$  does not cause reduced fecundity, and the risk of loss of fertility is not a contraindication for its use in these patients. In hypothyroidism, the frequency of menstrual irregularities has very recently been reported to be 23.4% among 171 hypothyroid patients studied. This is much less than that reported in previous studies, which showed that 50% to 70% of hypothyroid female patients had menstrual abnormalities. The most common manifestation is oligomenorrhea. Severe hypothyroidism is commonly associated with failure of ovulation. Ovulation and conception can occur in mild hypothyroidism. These pregnancies are, however, often associated with abortions, stillbirths or prematurity. The latter may be of greater clinical importance in infertile women with unexplained infertility.

CONCLUSION(S): These new data, mainly concerning menstrual abnormalities in hyperthyroidism and hypothyroidism, are inconsistent with what is generally believed and written in the classic thyroid textbooks and indicate that such opinions should be revised.

Fertil Steril 2000 Dec;74(6):1063-70

Screening for hypothyroidism in infertile women.

OBJECTIVE: To determine the frequency of an elevated thyroid-stimulating hormone (TSH) level in 704 patients seeking treatment for infertility. STUDY DESIGN: Sera from 704 women evaluated for infertility were assayed for TSH levels using radioimmunoassay (normal, 0.45-4.09 mIU/mL). All women had at least one year of infertility. Women with a known history of thyroid disease were excluded from the review. RESULTS: Sixteen of 704 patients (2.3%) had elevated TSH levels and were treated with levothyroxine to normalize TSH. None of these women had overt clinical signs or symptoms of hypothyroidism. Of these women, 11 of 16, or 69%, had ovulatory dysfunction, and 7 (64%) later became pregnant while on thyroid replacement. Five of 704 (0.7%) women with infertility who presented without a history of ovulatory dysfunction had elevated TSH levels, and none became pregnant with treatment. CONCLUSION: The prevalence of elevated TSH in 704 women with at least one year of infertility was 2.3%. The majority of women diagnosed with hypothyroidism (11 of 16, or 69%) had ovulatory dysfunction. With treatment for hypothyroidism, successful pregnancies resulted in 7 of 11 (64%) of patients. Women with infertility and ovulatory dysfunction should be screened for hypothyroidism. Screening for hypothyroidism as part of a routine infertility workup in women with normal ovulatory function will yield few abnormal tests.

J Reprod Med 1999 May;44(5):455-7

Breast cancer

Nutrition and survival after the diagnosis of breast cancer: a review of the evidence.

PURPOSE: To review and summarize evidence from clinical and epidemiologic studies that have examined the relationship between nutritional factors, survival and recurrence after the diagnosis of breast cancer. MATERIALS AND METHODS: Relevant clinical and epidemiologic studies were identified through a Medline search. References of identified reports also were used to identify additional published articles for critical review. RESULTS: Several nutritional factors modify the progression of disease and prognosis after the diagnosis of breast cancer. Overweight or obesity is associated with poorer prognosis in the majority of the studies that have examined this relationship. Treatment-related weight gain also may influence disease-free survival, reduce quality of life and increase risk for comorbid conditions. Five of 12 studies that examined the relationship between dietary fat and survival found an inverse association, which was not evident on energy adjustment in most of these studies. The majority of the studies that examined intakes of vegetables or nutrients provided by vegetables and fruit found an inverse relationship with survival. Alcohol intake was not associated with survival in the majority of the studies that examined this relationship. CONCLUSION: Much remains to be learned about the role of nutritional factors in survival after the diagnosis of breast cancer. Healthy weight control with an emphasis on exercise to preserve or increase lean muscle mass and a diet that includes nutrient-rich vegetables can be recommended. Diets that have adequate vegetables, fruit, whole grains and low-fat dairy foods and that are low in saturated fat may help to lower overall disease risk in this population.

J Clin Oncol 2002 Aug 1;20(15):3302-16

Exercise counseling and programming preferences of cancer survivors.

PURPOSE: Exercise has emerged as an important quality-of-life intervention for cancer survivors, but exercise motivation is a challenge. The purpose of this study was to provide a comprehensive assessment of the exercise preferences of cancer survivors. DESCRIPTION OF STUDY: A mailed, self-administered survey was completed by 307 survivors of prostate, breast, colorectal or lung cancer. The survey contained questions on demographic and medical variables, past exercise and various exercise counseling and programming preferences. RESULTS: For exercise counseling, 84% of participants said they preferred or maybe preferred to receive exercise counseling at some point during their cancer experience. Moreover, 85% preferred to receive exercise counseling face to face, and 77% preferred to receive it from an exercise specialist affiliated with a cancer center. For exercise programming, 98% preferred recreational exercises, 81% preferred walking, 57% preferred unsupervised exercise (57%), and 56% preferred moderate-intensity exercise. In addition, 48% preferred to exercise in the morning, 44% preferred to exercise alone, 40% preferred to exercise at home and 32% preferred to start their exercise program before treatment. Chi-square analyses revealed that a small number of exercise preferences were moderated by demographic, medical and exercise variables. CLINICAL IMPLICATIONS: The results of this study indicate that cancer survivors have unique and varied exercise counseling and programming preferences. Fifty-six percent of cancer survivors preferred to exercise at moderate intensity rather than at high intensity. Moderate-intensity exercise has been shown previously to be relatively safe even for cancer survivors who are advanced in age. The key to success for inactive cancer survivors may be to provide reassurance that exercise is a safe and beneficial modality for cancer survivors and to prescribe an exercise program that builds their confidence by slowly increasing the level of exercise intensity.

Effects of weight control and physical activity in cancer prevention: role of endogenous hormone metabolism.

Excess body weight and/or lack of physical activity are increasingly recognized as major risk factors for cancer of the colon, breast, endometrium and prostate. This paper reviews the effects of excess body weight and physical inactivity on endogenous hormone metabolism (insulin, the IGF-I/IGFBP system and sex steroids) and of endocrine alterations with risk of cancer of the endometrium, breast, prostate and colon.

Ann N Y Acad Sci 2002 Jun;963:268-81

Effect of exercise on the rat mammary gland: implications for carcinogenesis.

Physical activity has been associated with decreased risk for developing breast cancer yet to date, the mechanism remains unknown. The purpose of this investigation was to evaluate the effects of moderate exercise training on the normal mammary gland in an attempt to identify alterations or differences that might be associated with tumor inhibition. A total of 170 female Sprague-Dawley rats were randomized to baseline (n=10), exercise (EX; n=80) or sham-exercise groups (SHAM; n=80). Treadmill training (20-25 m min<sup>-1</sup>, 15% grade, 30 min day<sup>-1</sup>, 5 days week<sup>-1</sup>) was started at 28 days of age (DOA). Animals were killed at 28, 42, 56, 70 and 84 DOA. Mammary glands were evaluated by histology and immunohistochemistry. Terminal end buds (TEB), structures susceptible to carcinogenesis were counted. Sexual maturation, estradiol and progesterone, and organ and muscle weights were also evaluated. No differences in growth, sexual maturation or steroid hormones were observed in response to training. No difference in the number of TEBs was observed at any timepoint between EX and SHAM. Proliferation was significantly increased at 56 DOA and tended to be increased at 42 and 70 DOA in the EX animals whereas cell death was significantly increased at 70 DOA and tended to be increased at 84 DOA in the EX animals. These data suggest no difference in the number of carcinogen-susceptible structures as a result of moderate exercise. The changes in cell proliferation and apoptosis with exercise training suggest altered cell turnover that will necessitate future study particularly with relevance to carcinogenesis.

Acta Physiol Scand 2002 Jun;175(2):147-56

Social stress and state-to-state differences in smoking and smoking related mortality in the United States.

This paper reports on the relationship between the stressfulness of the social environment, smoking and mortality rates for malignant neoplasms of the respiratory system and chronic obstructive pulmonary disease (COPD). A macro-social approach was employed with the 50 states of the United States serving as the units of analysis....The results show that populations that experience higher levels of stressful events smoke more heavily and eventually experience higher mortality from lung cancer and COPD. These relationships are robust: they are replicated for different time periods, for different measures of the independent and dependent variables, and with different analytic methods.

Soc Sci Med 1994 Jan;38(2):373-81

Influence of war circumstances on tumor morphological characteristics in patients with breast cancer.

The influence of war circumstances on tumor morphological characteristics in patients with breast cancer has not been studied up to now. The aim of this study is to investigate if war circumstances have influenced breast cancer incidence. The study covered both the patients in which during a period of observation a breast cancer was diagnosed as well as those who died of the same disease in the same period. Three sources of data were used: 1) The archives of the Oncology and Radiotherapy Center of the University Hospital "Split" (UHS): hospital data of 768 patients were reviewed. The war sample consisted of 380 patients aged 59.4+/-12.1 (31 to 86) (including 5 males), whereas the pre-war sample was made up of 388 patients aged 58.4+/-12.7 (19 to 88) (including three males); 2) Register of death of the Pathology Department of UHS with 162 analyzed persons whose deaths were caused by breast cancer in the six-year period between 1988 and 1993. The list of 162 dead patients included 79 people who died from breast cancer diagnosed in that period (1988 to 1993) and another 83 people that had been diagnosed before that period; 3) The biopsy register of the Pathology Department of UHS with 851 breast biopsies performed between 1988 and 1993. Breast cancer is predominantly a female illness (99.1%). The war circumstances influenced the of T, N and M rate. (TNM system refers to the stages of cancer.) The rate of N2, N3, M1 were conspicuously higher in the war period. There were significantly more malignant histological diagnoses found in new patients and also significantly more patients died due to breast cancer. Stress and other war circumstances undoubtedly have a negative impact on the numerous markers of breast cancer, which we have proved in this study.

Coll Antropol 2002 Jun;26(1):99-106

Glycemic index: overview of implications in health and disease.

The glycemic index concept is an extension of the fiber hypothesis, suggesting that fiber consumption reduces the rate of nutrient influx from the gut. The glycemic index has particular relevance to those chronic Western diseases associated with central obesity and insulin resistance. Early studies showed that starchy carbohydrate foods have very different effects on postprandial blood glucose and insulin responses in healthy and diabetic subjects, depending on the rate of digestion. A range of factors associated with food consumption was later shown to alter the rate of glucose absorption and subsequent glycemia and insulinemia. At this stage, systematic documentation of the differences that exist among carbohydrate foods was considered essential. The resulting glycemic index classification of foods provided a numeric physiologic classification of relevant carbohydrate foods in the prevention and treatment of diseases such as diabetes. Since then, low-glycemic-index diets have been shown to lower urinary C-peptide excretion in healthy subjects, improve glycemic control in diabetic subjects, and reduce serum lipids in hyperlipidemic subjects. Furthermore, consumption of low-glycemic index diets has been associated with higher HDL-cholesterol concentrations and, in large cohort studies, with decreased risk of developing diabetes and cardiovascular disease. Case-control studies have also shown positive associations between dietary glycemic index and the risk of colon and breast cancers. Despite inconsistencies in the data, sufficient, positive findings have emerged to suggest that the dietary glycemic index is of potential importance in the treatment and prevention of chronic diseases.

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