

DISEASE PREVENTION

Page 6

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Table of [Contents](#) 

-
- > Nutrition and newly emerging viral diseases: an overview.
 - > Pathogenesis and treatment of liver fibrosis in alcoholics: 1996 update.
 - > Adenocarcinomas of the esophagus and gastric cardia: the role of diet.
 - > Vitamin C, neutrophil function, and upper respiratory tract infection risk in distance runners: the missing link.
 - > Equine degenerative myeloencephalopathy.
 - > Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study.
 - > Functional effects of food components and the gastrointestinal system: chicory fructooligosaccharides.
 - > [Coronary heart disease--a free radical associated disease? What is the value of antioxidant substances?]
 - > Antioxidant flavonols and ischemic heart disease in a Welsh population of men: the Caerphilly Study.
 - > [Vitamin E as a possible aid in the control of disease problems on pig farms: a field test]
 - > Antioxidants and dementia.
 - > [Is supplemental vitamin E for prevention of coronary heart disease ov value?]
 - > The 'diet heart' hypothesis in secondary prevention of coronary heart disease.
 - > Tea and health: a historical perspective.
 - > [Prevalence and risk factors in the population of Graz (Austrian Stroke Prevention Study)]

- > Beta-2-agonists have antioxidant function in vitro. 2. The effect of beta-2-agonists on oxidant-mediated cytotoxicity and on superoxide anion generated by human polymorphonuclear leukocytes.
- > Antioxidant vitamins and cardiovascular disease: current perspectives and future directions [editorial]
- > Protective effects of silymarin against photocarcinogenesis in a mouse skin model.
- > Which changes in diet prevent coronary heart disease? A review of clinical trials of dietary fats and antioxidants.
- > Antioxidants in the prevention of atherosclerosis.
- > [Cardio-protective effect of red wine as reflected in the literature]
- > Tea and heart disease [letter]
- > Cancer risk factors for selecting cohorts for large-scale chemoprevention trials.
- > Protection against induction of mouse skin papillomas with low and high risk of conversion to malignancy by green tea polyphenols.
- > Efficacy of a dentifrice and oral rinse containing sanguinaria extract in conjunction with initial periodontal therapy.
- > The impact of zinc supplementation on *Schistosoma mansoni* reinfection rate and intensities: a randomized, controlled trial among rural Zimbabwean schoolchildren.
- > Methylenetetrahydrofolate reductase polymorphism, dietary interactions, and risk of colorectal cancer.
- > Nutrition in women. Assessment and counseling.
- > Hypertension and borderline isolated systolic hypertension increase risks of cardiovascular disease and mortality in male physicians.
- > Bronchial reactivity and dietary antioxidants.
- > Effects of bisamil on coronary-occlusion-reperfusion injury and free-radical-induced reactions.
- > Whole-grain consumption and chronic disease: protective mechanisms.
- > Dietary manipulation of plasma carotenoid concentrations of squirrel monkeys (*Saimiri sciureus*).
- > Mechanisms of spontaneous human cancers.
- > Molecular epidemiology in environmental carcinogenesis.
- > Vitamin C intake and susceptibility to the common cold.

> [Alcohol and free radicals: from basic research to clinical prospects]

> Melatonin reduces mortality from Aleutian disease in mink (*Mustela vison*).

> Exercise causes blood glutathione oxidation in chronic obstructive pulmonary disease: prevention by O₂ therapy.

Nutrition and newly emerging viral diseases: an overview.

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J Nutr (United States) May 1997, 127 (5 Suppl) p948S-950S

Infectious diseases are on the increase worldwide. When discussing interactions of nutrition and infection, nutritionists have traditionally considered only the effects of diet on the host. Recent data, however, indicate that, at least for an RNA virus, host nutrition can influence the genetic make-up of the pathogen and thereby alter its virulence. This symposium was organized to alert the nutrition community to this discovery and its possible implications for the investigation of nutrition-infection interrelationships. Topics covered in the symposium include the following: the public health threat of emerging viral diseases; the rapid evolution of viral RNA genomes; oxidants and antioxidants in viral diseases-disease mechanisms and metabolic regulation; and increased virulence of coxsackievirus B3 due to vitamin E or selenium deficiency. If the findings with coxsackievirus are more broadly applicable to other RNA viruses, the results could be of great public health significance because RNA viruses constitute the majority of all plant, animal and human viruses. (18 Refs.)

Pathogenesis and treatment of liver fibrosis in alcoholics: 1996 update.

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Section of Liver Disease, Bronx VA Medical Center, Mount Sinai School of Medicine, New York, N.Y., USA.

Dig Dis (Switzerland) Jan-Apr 1997, 15 (1-2) p42-66

Fibrosis is a common end stage for most chronic liver diseases. It results from an imbalance between collagen production and degradation. One promising approach for prevention and treatment is the stimulation of collagenolytic processes. In nonhuman primates it was found that polyenylphosphatidylcholine (PPC), extracted from soybeans, protects against alcohol-induced fibrosis and cirrhosis and prevents the associated hepatic phosphatidylcholine (PC) depletion by increasing 18:2-containing PC species; it also attenuates the transformation of lipocytes into collagen-producing transitional cells. Furthermore, it increases collagen breakdown, as shown in cultured lipocytes enriched with pure dilinoleoyl PC (18:2-18:2 PC), the main PC species present in the extract, which may be the active ingredient. Since PC appears to promote the breakdown of collagen, there is reasonable hope that this treatment may affect not only the progression of the disease, but may also reverse preexisting fibrosis, as demonstrated for CCl₄-induced cirrhosis in the rat. Therefore, PPC may be useful for the management of fibrosis of alcoholic and nonalcoholic etiologies as well. S-Adenosylmethionine opposes CCl₄-induced fibrosis and can affect some of the consequences of the ethanol-induced oxidative stress in experimental animals and in man. Anti-inflammatory medications (corticosteroids, colchicine) are also being used and agents that interfere with collagen synthesis, such as inhibitors of prolyl-4-hydroxylase and antioxidants, are being tested. (175 Refs.)

Adenocarcinomas of the esophagus and gastric cardia: the role of diet.

Zhang ZF; Kurtz RC; Yu GP; Sun M; Gargon N; Karpch M Jr; Fein JS; Harlap S

Department of Epidemiology and Biostatistics, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.

The incidence of adenocarcinomas of the esophagus and gastric cardia (ACEGC) has been increasing for the past 10-15 years in the United States. The reason for this increase is unknown. This hospital-based case-control study was conducted to assess the effects of dietary and nutritional factors on the risk of ACEGC. A total of 95 incident cases with pathological diagnosis and 132 cancer-free controls were included in the study. Patients were recruited at Memorial Sloan-Kettering Cancer Center from 1 November 1992 to 1 November 1994. Epidemiologic data were collected by a modified National Cancer Institute Health Habits History Questionnaire. Nutritional and dietary factors were analyzed using a logistic regression model. Increased risk of ACEGC was significantly related to higher intake of dietary calories and fat after controlling for several potential confounding factors. Decreased risk of ACEGC was significantly associated with high ingestion of dietary fiber, lutein, niacin, vitamin B6, iron, and zinc. Higher intakes of vitamin A, beta-carotene, vitamin E, folate, phosphorus, and potassium were associated with a decreased risk of the disease, but these were not statistically significant. The study suggests that ACEGC can be preventable through dietary interventions.

Vitamin C, neutrophil function, and upper respiratory tract infection risk in distance runners: the missing link.

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Exerc Immunol Rev (United States) 1997, 3 p32-5

Moderate submaximal exercise results in neutrophilia and enhanced phagocytic and oxidative capacity of neutrophils. It has been hypothesized, however, that during intensive exercise and periods of intensive training this pro-oxidative effect becomes suppressive. Vitamin C is widely recognized for its antioxidant function in extracellular fluid, and it has been shown to neutralize O₂⁻, HOCl, and .OH and to attenuate the suppression of phagocytic function. Clinical manifestation of reduced neutrophil function following participation in ultramarathon races has, however, not been observed. Although neutrophils constitute 50-60% of leukocytes and although they are the first line of defense to bacteriological invasion, post-race episodes of upper respiratory tract infection (URTI) are not correlated with a decrement in the function of this individual parameter of immune function. The efficacy of Vitamin C supplements in reducing the incidence of post-race URTI symptoms, therefore, cannot be fully explained at this stage. (99 Refs.)

Equine degenerative myeloencephalopathy.

Miller MM; Collatos C

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Vet Clin North Am Equine Pract (United States) Apr 1997, 13 (1) p43-52

EDM is a neurologic disease of young horses characterized by the insidious development of symmetric ataxia. Decreased or absent cutaneous trunci reflex or slap test responses are considered clinical signs that increase the index of suspicion for this disease. In addition, concurrent predisposing factors, such as familial history, inadequate access to green pasture, and possible exposure to wood preservatives or insecticides, provide further supporting evidence for a clinical diagnosis. Vitamin E deficiency and a hereditary predisposition currently are considered the most significant factors in the pathogenesis of this disease. Histopathologically the lesions of EDM are those of neuraxonal dystrophy, characterized by prominent axonal and dendritic swelling, mild glial proliferation, and neuronal depletion and atrophy with lipofuscin-like pigment accumulation. Animals predisposed to EDM or with a clinical diagnosis of EDM should receive oral alpha-tocopherol acetate supplementation. Improvement in clinical signs may be seen following long-term treatment, but in general, the prognosis for complete recovery is poor. (31 Refs.)

Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study.

Pietinen P; Ascherio A; Korhonen P; Hartman AM; Willett WC; Albanes D; Virtamo J

Department of Nutrition, National Public Health Institute, Helsinki, Finland.

Am J Epidemiol (United States) May 15 1997, 145 (10) p876-87

The relation of intakes of specific fatty acids and the risk of coronary heart disease was examined in a cohort of 21,930 smoking men aged 50-69 years who were initially free of diagnosed cardiovascular disease. All men participated in the Finnish Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study and completed a detailed and validated dietary questionnaire at baseline. After 6.1 years of follow-up from 1985-1988, the authors documented 1,399 major coronary events and 635 coronary deaths. After controlling for age, supplement group, several coronary risk factors, total energy, and fiber intake, the authors observed a significant positive association between the intake of trans-fatty acids and the risk of coronary death. For men in the top quintile of trans-fatty acid intake (median = 6.2 g/day), the multivariate relative risk of coronary death was 1.39 (95% confidence interval (CI) 1.09-1.78) (p for trend = 0.004) as compared with men in the lowest quintile of intake (median = 1.3 g/day). The intake of omega-3 fatty acids from fish was also directly related to the risk of coronary death in the multivariate model adjusting also for trans-saturated and cis-monounsaturated fatty acids (relative risk (RR) = 1.30, 95% CI 1.01-1.67) (p for trend = 0.06 for men in the highest quintile of intake compared with the lowest). There was no association between intakes of saturated or cis-monounsaturated fatty acids, linoleic or linolenic acid, or dietary cholesterol and the risk of coronary deaths. All the associations were similar but somewhat weaker for all major coronary events.

Functional effects of food components and the gastrointestinal system: chicory fructooligosaccharides.

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Nutr Rev (United States) Nov 1996, 54 (11 Pt 2) pS38-42

Functional food science, as recently proposed by ILSI Europe, opens new perspectives in nutrition and food sciences. The systematic investigation of the interactions between food components or food ingredients and genomic, biochemical, cellular, or physiological functions is a unique way to improve both our knowledge and the role of nutrition in maintaining good health and in preventing disease. However, such basic knowledge is insufficient to justify claims, unless it is confirmed through relevant nutrition studies aimed at demonstrating the same effect and its positive consequences in humans. In the first stage, this demonstration will in most cases justify functional (physiological) claims (e.g., bifidogenic effect for fructooligosaccharides, bulking effect for nondigestible carbohydrates, protection against oxidative stress for antioxidants) with no reference to any health benefit. A true health claim will require, in most cases, additional studies involving large populations and long-term trials. It is anticipated that the better we understand the mechanism of interactions between food components and specific biological functions, the more we will be able to demonstrate functional effects, and the easier it will be to accumulate convincing evidence in favor of health promotion or disease prevention. Because of both its direct contact with eaten foods and the diversity of its s a potential target for many functional effects. Until now, only a limited number of these effects have been investigated so as to justify functional claims. Improvement of glucose absorption (leading to physiological glycemia and insulinemia), modulation of GI transit time, fecal bulking, acidification of colonic content, and control of cholesterol bioavailability are all recognized effects of dietary fiber. Balanced colonic microflora and immunostimulation are attributed to the consumption of probiotics. Prebiotics selectively modify the colonic microbiota and modulate hepatic lipogenesis. According to the ILSI Europe strategy for the development of functional foods, all these effects are of interest. Their support by sound scientific arguments will be a necessary condition for their implementation in food science and nutrition for the benefit of human health. (20 Refs.)

[Coronary heart disease--a free radical associated disease? What is the value of antioxidant substances?]

Doll M

Med Monatsschr Pharm (Germany) Mar 1997, 20 (3) p66-70

No abstract.

Antioxidant flavonols and ischemic heart disease in a Welsh population of men: the Caerphilly Study.

Hertog MG; Sweetnam PM; Fehily AM; Elwood PC; Kromhout D

Department of Chronic Diseases and Environmental Epidemiology, National Institute of Public Health and the Environment, Bilthoven, Netherlands.

Am J Clin Nutr (United States) May 1997, 65 (5) p1489-94

Antioxidant flavonols and their major food source, black tea, have been associated with a lower risk of ischemic heart disease (IHD) and stroke in Dutch men. We investigated whether flavonol intake predicted a lower rate of IHD in 1900 Welsh men aged 45-59 y, who were followed up for 14 y. Flavonol intake, mainly from tea to which milk is customarily added, was not related to IHD incidence [relative risk (RR), highest compared with lowest quartile: 1.0; 95% CI: 0.6, 1.6; P for trend = 0.996; n = 186] but was weakly positively related to IHD mortality (RR: 1.6; 95% CI: 0.9, 2.9; P = 0.119; n = 131) and cancer mortality (RR: 1.3; 95% CI: 0.7, 2.3; P = 0.150; n = 104) and strongly related to total mortality (RR: 1.4; 95% CI: 1.0, 2.0; P = 0.014; n = 334). Men with the highest consumption of tea (> 1.2 L, or > 8 cups/d) had an RR of 2.4 (95% CI: 1.5, 3.9) of dying in the follow-up period compared with men consuming < 300 mL/d (< 2 cups/d). We conclude that intake of antioxidant flavonols is not inversely associated with IHD risk in the United Kingdom. Possibly, flavonols from tea to which milk is added are not absorbed; experimental evidence suggests that adding milk to tea abolishes the plasma antioxidant-raising capacity of tea. The apparent association between tea consumption and increased mortality in this population merits further investigation.

[Vitamin E as a possible aid in the control of disease problems on pig farms: a field test]

Lamberts FJ
Dierenartsenpraktijk Bladel-Haperl.
Tijdschr Diergeneeskd (Netherlands) Apr 1 1997, 122 (7) p190-2

In two sow-herds problems with weaning-diarrhoea and *Streptococcus suis* meningitis were successfully controlled by strategic use of antibiotics during the post-weaning period. In an attempt to reduce the intake of antibiotics by farm animals, the vitamin E level in the post-weaning diet was increased from 20 IE/kg to 80 IE/kg, because vitamin E is thought to increase resistance. The effect on both farms was stunning, so a small field trial was started. In this trial the higher level of vitamin E had a statistically significant beneficial effect on weaning-diarrhoea. The author concludes that in some cases an increased level of vitamin E can have a positive effect on disease management on pig-farms and can lead to reduced use of antibiotics.

Antioxidants and dementia.

Lethem R; Orrell M
Department of Psychiatry, Whittington Hospital, London, UK.
Lancet (England) Apr 26 1997, 349 (9060) p1189-90

No abstract.

[Is supplemental vitamin E for prevention of coronary heart disease of value?]

Thiery J; Teupser D
Klinikum Grosshadern, Ludwig-Maximilians-Universitat, Munchen.
Internist (Berl) (Germany) Feb 1997, 38 (2) p168-76; discussion 176

No abstract.

The 'diet heart' hypothesis in secondary prevention of coronary heart disease.

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CERMEP CNRS UMR 1216, Lyon, France.
Eur Heart J (England) Jan 1997, 18 (1) p13-8

From this detailed analysis of the main dietary trials conducted over the last 30 years in the secondary prevention of coronary heart disease, it can be said that the older trials were conducted on low risk patients and used high fat diets (about 40% of energy as lipids), comprising low saturated fat and cholesterol intake but very high (15 to 20% of energy) polyunsaturated fat intake, particularly from the omega-6 fatty acid family. These experimental diets were designed to reduce blood cholesterol and failed to

improve prognosis. By contrast, recent trials were not primarily designed to reduce cholesterol, were conducted in medium- and high-risk patients and used low fat diets supplemented by omega-3 fatty acids from various sources. In two of these trials, the consumption of natural antioxidants, oligoelements and vegetable proteins was increased. Recurrence rate was reduced in the range of 30 to 70%. One conclusion from these well-conducted recent experiments on more than 3000 patients is that new and more specific dietary recommendations are clearly warranted in secondary prevention of coronary heart disease. They should be more specific and more clearly defined and therefore different from those generally provided in the U.S.A. and Europe at present. In a recent Consensus Panel statement, authors wrote less than one line to describe a cardioprotective diet in patients with coronary heart disease, summarized as < or = 30% fat, < 7% saturated fat, < 200 mg.day⁻¹ cholesterol. This is both too much (too restrictive to hope that white European and American patients will adhere in the long-term) and insufficient because dietary counselling cannot be restricted to three factors. Ulbricht and Southgate recently emphasized that the relationship between diet and coronary heart disease is more complex than the current cholesterol hypothesis. They identified at least seven major dietary factors, including fibres, although the evidence of an effect on coronary heart disease is weak. However, they did not mention vegetable and fish proteins which are rich in arginine and L-glutamine, major regulators of cardiovascular function. Thus, new dietary advice should include: reduce intake of total (not more than 30% of energy) and saturated (less than 10%) fats maintain intake at least minimally, of the essential omega-6 fatty acids augment consumption of oleic acid and moderately increase consumption of omega-3 fatty acids augment intake of natural antioxidants maintain sufficient intake of vegetable proteins As conceptualized in the 'Mediterranean' and 'Asian-vegetarian' types of diet, it is very important that a healthy diet should be thought of as a whole rather than as a recitation of good and bad components. Although these protective dietary modifications should probably all be used in each patient to obtain maximal efficacy, these scientifically quantitated principles should be adapted to the culture, ethnic origin and 'image of the world' of each patient in order to create an environment favourable to the perception of positive associations between various foods and healthy habits.

Tea and health: a historical perspective.

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Cancer Lett (Ireland) Mar 19 1997, 114 (1-2) p315-7

In many parts of the world, green tea and black tea are produced from the plant *Camellia sinensis*. Tea is one of the most widely consumed beverages, second only to water. It is one of the safest beverages since it is made with boiling, sterile water and has been popular for over 4000 years. Dogma has it that people knew it might have health promoting properties since it was frequently used as fluid supply for patients suffering from infectious diseases. However, detailed, focused research on the health benefits of tea is of recent vintage. Initially, such research was carried out in Japan and China and, because the local customs, this research involved green tea. Now, a number of other scientists in Europe and in the United States have conducted investigations on black tea, and in some laboratories exacting comparative studies were performed utilizing black and green tea. The major interest in tea and health stems from the high level of antioxidant tea polyphenols in green tea and black tea. The chemistry of the tea polyphenols has been worked out to some extent. Thus, their role in lowering the risk of heart disease and of a number of types of cancer begins to be understood. Most productive are multi-disciplinary approaches, considering data from epidemiology and field studies, and laboratory research in animal models for heart disease and cancers of various types, as well as through in vitro experiments.

[Prevalence and risk factors in the population of Graz (Austrian Stroke Prevention Study)]

Schmidt R; Reinhart B; Schumacher M; Hayn M; Schmidt H; Fazekas F; Niederkorn K; Horner S; Lechner H; Offenbacher H; Eber B; Weinrauch V; Auer-Grumbach P; Kleinert G; Roob G; Kostner GM; Esterbauer H

Universitätskliniken für Neurologie, Universität Graz.

Wien Med Wochenschr (Austria) 1997, 147 (2) p36-40

The Austrian Stroke Prevention Study recruited 1960 randomly selected subjects aged 50 to 75 years during a 3-year period of enrollment. The response rate of the study was 32.4%. A telephone interview with 200 randomly selected non-responders yielded no differences to responders regarding the frequency of major vascular risk factors known to the subjects. Besides demographics, the study assessed arterial hypertension, diabetes mellitus, cardiac disease, smoking, a complete lipid status including the apolipoprotein-E genotype, serum fibrinogen and antiscavenger antibodies as well as various natural antioxidants such as vitamins A, C, E and beta-carotene. Arterial hypertension, diabetes mellitus, cardiac disease and hypercholesterolemia > 200 mg/dl were strikingly common and occurred in 38%, 7.6%, 32% and 76%, respectively. Suboptimal plasma concentrations of vitamin A, E, and beta-carotene were noted in 77.2%, 56.1% and in 53.2% of study participants. The rate of treatment of major risk factors was 70% for arterial hypertension and diabetes mellitus, but only 37.1% and 6.3% for cardiac disease and hypercholesterolemia > 250 mg/dl. Diet was commonly used to treat diabetes but was almost neglected in the treatment of other vascular risk factors. These

data provide an orientation on the prevalence of risk factors and the use of primary preventive measures for stroke treatment in our community.

Beta-2-agonists have antioxidant function in vitro. 2. The effect of beta-2-agonists on oxidant-mediated cytotoxicity and on superoxide anion generated by human polymorphonuclear leukocytes.

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Department of Internal Medicine, University Hospital Bergmannsheil, Bochum, Germany.
Respiration (Switzerland) 1997, 64 (1) p23-8

Therapeutic agents which may be able to enhance the antioxidant screen of the epithelial surface of the lung have the potential to influence the progression of lung inflammation. This study evaluates the efficacy of a variety of antiasthma drugs to reduce oxidant-mediated cytotoxicity and to inhibit superoxide anion generated by human polymorphonuclear leukocytes. We quantified in vitro the prevention of H₂O₂-mediated cytotoxicity (lactate dehydrogenase release assay) using the antiasthma drugs as follows: ipratropium bromide, salbutamol (salbutamol base), fenoterol (fenoterol hydrobromide), terbutaline (terbutaline sulfate), isoproterenol, prednisolone (prednisolone hydrogensuccinate), beclomethasone (17,21-beclomethasone dipropionate) and reduced glutathione. Furthermore, fenoterol and isoproterenol were evaluated ex vivo to reduce superoxide anion (O₂⁻) generated by freshly isolated polymorphonuclear cells (PMN) from smokers with chronic obstructive lung disease (n = 10). Using a concentration of 10(-4) M, reduction of cytotoxicity was quite different among beta(2)-agonists: fenoterol (97.8%) > isoproterenol (67.6%) > salbutamol (41.8%) > terbutaline (30.5%) > ipratropium bromide (18.1%). Corticosteroids and theophylline had no antioxidant effect. The cellular O₂⁻ production of freshly isolated PMN was significantly (p < 0.05, comparisons 0 vs. > or = 10(-7) M) reduced with fenoterol and isoproterenol at concentrations > or = 10(-7) M. Propranolol had no inhibitory effect on antioxidant properties of beta(2)-agonists. We hypothesize that the antioxidant function of beta(2)-agonists is related to the number and formation of se results demonstrate that beta(2)-agonists have in part a good intrinsic scavenger function on reactive oxygen species when used in micromolar concentrations. However, to achieve this effect supratherapeutic concentrations were necessary. Thus, the conceivable benefit of beta(2)-agonists in the treatment of high oxidant burden in vivo seems doubtful.

Antioxidant vitamins and cardiovascular disease: current perspectives and future directions [editorial]

Hennekens CH
Eur Heart J (England) Feb 1997, 18 (2) p177-9

No abstract.

Protective effects of silymarin against photocarcinogenesis in a mouse skin model.

Katiyar SK; Korman NJ; Mukhtar H; Agarwal R
Department of Dermatology, Case Western Reserve University, Cleveland, OH 44106, USA.
J Natl Cancer Inst (United States) Apr 16 1997, 89 (8) p556-66

BACKGROUND: Nonmelanoma skin cancer is the most common cancer among humans; solar UV is its major cause. Therefore, it is important to identify agents that can offer protection against this cancer. **PURPOSE:** We evaluated the protective effects of silymarin, a flavonoid compound isolated from the milk thistle plant, against UVB radiation-induced nonmelanoma skin cancer in mice and delineated the mechanism(s) of its action.

METHODS: For long-term studies, three different protocols of treatment were employed, each evaluating protection by silymarin at a different stage of carcinogenesis. Female SKH-1 hairless mice were subjected to 1) UVB-induced tumor initiation followed by phorbol ester-mediated tumor promotion, 2) 7,12-dimethylbenz[a]anthracene-induced tumor initiation followed by UVB-mediated tumor promotion, and 3) UVB-induced complete carcinogenesis. Forty mice were used in each protocol and were divided into control and treatment groups. Silymarin was applied topically at a dose of 9 mg per application before UVB exposure, and its effects on tumor incidence (% of mice with tumors), tumor multiplicity (number of tumors per mouse), and average tumor volume per mouse were evaluated. In short-term studies, the following parameters were measured: formation of sunburn and apoptotic

cells, skin edema, epidermal catalase and cyclooxygenase (COX) activities, and enzymatic activity and messenger RNA (mRNA) expression for ornithine decarboxylase (ODC), a frequently observed marker at tumor promotion stage. Fisher's exact test was used to evaluate differences in tumor incidence, two-sample Wilcoxon rank sum test was used for tumor multiplicity and tumor volume, and Student's t test was used for all other measurements. All statistical tests were two-sided.

RESULTS: In the protocol with UVB-induced tumor initiation, silymarin treatment reduced tumor incidence from 40% to 20% ($P = .30$), tumor multiplicity by 67% ($P = .10$), and tumor volume per mouse by 66% ($P = .14$). In the protocol with UVB-induced tumor promotion, silymarin treatment reduced tumor incidence from 100% to 60% ($P < .003$), tumor multiplicity by 78% ($P < .0001$), and tumor volume per mouse by 90% ($P < .003$). The effect of silymarin was much more profound in the protocol with UVB-induced complete carcinogenesis, where tumor incidence was reduced from 100% to 25% ($P < .0001$), tumor multiplicity by 92% ($P < .0001$), and tumor volume per mouse by 97% ($P < .0001$). In short-term experiments, silymarin application resulted in statistically significant inhibition in UVB-caused sunburn and apoptotic cell formation, skin edema, depletion of catalase activity, and induction of COX and ODC activities and ODC mRNA expression.

CONCLUSIONS AND IMPLICATION: Silymarin can provide substantial protection against different stages of UVB-induced carcinogenesis, possibly via its strong antioxidant properties. Clinical testing of its usefulness is warranted.

Which changes in diet prevent coronary heart disease? A review of clinical trials of dietary fats and antioxidants.

Oliver MF
National Heart & Lung Institute, Imperial College, London, UK.
Acta Cardiol (Belgium) 1996, 51 (6) p467-90

No abstract.

Antioxidants in the prevention of atherosclerosis.

Olsson AG; Yuan XM
Department of Internal Medicine, University Hospital, Linköping, Sweden.
Curr Opin Lipidol (United States) Dec 1996, 7 (6) p374-80

Four antioxidant treatment modalities against atherosclerosis and coronary heart disease are scrutinized: probucol, beta-carotene, alpha-tocopherol and anti-iron treatment. A pattern seems to have emerged in which some treatments look promising, but others are disappointing. Most published studies of antioxidation in atherosclerosis have been ad-hoc in that the primary endpoint of the study has not been a diagnosis related to atherosclerosis; this may be misleading. The most promising antioxidant seems to be alpha-tocopherol, supported by the results of the Cambridge Heart Antecreasing high density lipoprotein concentration and is therefore unlikely to influence atheroma in people. beta-Carotene has been repeatedly shown to be ineffective against coronary heart disease. Anti-iron treatment has not yet been tested in animal models or in man. More has to be learned of the role of antioxidation in atherosclerosis before the effectiveness of this treatment modality can be established. (45 Refs.)

[Cardio-protective effect of red wine as reflected in the literature]

Lugasi A; Blazovics A; Dworschk E; Feher J
Orszagos Elelmezes- es Taplalkozastudományi Intezet, Budapest.
Orv Hetil (Hungary) Mar 16 1997, 138 (11) p673-8

Many scientific studies have been searching for the reason of so-called Paradox, the anomaly which means that in several parts of France and other Mediterranean countries the morbidity and mortality of coronary heart diseases in absolute value and in consideration of its rate to other manner of death is significantly lower than that is in other developed countries, despite of the high consumption of fat and saturated fatty acids. The reason of this cardioprotective effect might be among others the typical Mediterranean diet and the regularly consumption of red wine. This conception may be proved since the polyphenolic compounds present in red wine in concentration of 1800-3000 mg/l are antioxidants, free radical scavengers and inhibit the lipid peroxidation processes in vitro and in vivo, as well. Beside dietary antioxidants such as tocopherols, ascorbic acid and carotenoids, the

polyphenolic compounds of plant origin exert favourable effects on cardioprotective mechanisms. Phenolic compounds of red wine (flavonoids and non-flavonoid components) inhibit the oxidation of low-density lipoproteins, the eicosanoid synthesis and platelet aggregation and promote the formation of endothel-dependent relaxation factor (nitrogen oxide). According to scientific results of the last decade it seems to be proved that moderate consumption of red wine - 2-3 unit/day for healthy men, and 1-2 unit/day for healthy women (1 unit = 12 g alcohol) -, cannot be criticised either medically nor socially and have a beneficial effect on human; Male

Tea and heart disease [letter]

Walsh GP
Lancet (England) Mar 8 1997, 349 (9053) p735

No abstract.

Cancer risk factors for selecting cohorts for large-scale chemoprevention trials.

Greenwald P
Division of Cancer Prevention and Control, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20892, USA.
J Cell Biochem Suppl (United States) 1996, 25 p29-36

Many anticipate that application of findings in molecular genetics will help to achieve greater precision in defining high-risk populations that may benefit from chemopreventive interventions. We must recognize, however, that genetic susceptibility, environmental factors, and complex gene-environment interactions are all likely to be risk determinants for most cancers. Cohort studies of twins and cancer indicate that having "identical" genes is generally not a very accurate predictor of cancer incidence. Data from twin studies support the suggestion that environmental factors such as tobacco use significantly influence cancer risk. The complexities of the genetic contribution to disease risk are exemplified by the development of Duchenne muscular dystrophy in only one of monozygotic twin girls, hypothesized to be the result of X chromosome inactivation, with the distribution patterns of the X chromosome being skewed to the female X in the manifesting twin and to the male X in the normal twin. Evidence from transgenic and genetic-environmental studies in animals support the possibility of genetic-environmental interactions. Calorie restriction modifies tumor expression in p53 knockout mice; a high-fat, low-calcium, low-vitamin D diet increases prepolyp hyperplasia formation in Apc-mutated mice; and calorie restriction early in life influences development of obesity in the genetically obese Zucker rat (fah environmental modulation of gene expression suggests that chemoprevention has the potential to reduce risk for both environmentally and genetically determined cancers. In view of the growing research efforts in chemoprevention, the NCI has developed a Prevention Trials Decision Network (PTDN) to formalize the evaluation and approval process for large-scale chemoprevention trials. The PTDN addresses large trial prioritization and the associated issues of minority recruitment and retention; identification and validation of biomarkers as intermediate endpoints for cancer; and chemopreventive agent selection and development. A comprehensive database is being established to support the PTDN's decision-making process and will help to determine which agents investigated in preclinical and early phase clinical trials should move to large-scale testing. Cohorts for large-scale chemoprevention trials include individuals who are determined to be at high risk as a result of genetic predisposition, carcinogenic exposure, or the presence of biomarkers indicative of increased risk. Current large-scale trials in well-defined, high-risk populations include the Breast Cancer Prevention Trial (tamoxifen), the Prostate Cancer Prevention Trial (finasteride), and the N-(4-hydroxyphenyl) retinamide (4-HPR) breast cancer prevention study being conducted in Milan. Biomarker studies will provide valuable information for refining the design and facilitating the implementation of future large-scale trials. For example, potential biomarkers are being assessed at biopsy in women with ductal carcinoma in situ (DCIS). The women are then randomized to either placebo, tamoxifen, 4-HPR, or tamoxifen plus 4-HPR for 2-4 weeks, at which time surgery is performed and the biomarkers reassessed to determine biomarker modulation by the interventions. For prostate cancer, modulation of prostatic intraepithelial neoplasia (PIN) by 4-HPR and difluoromethylornithine is being investigated; similar studies are being planned for oltipraz, dehydroepiandrosterone, and vitamin E plus selenomethionine. The validation of biomarkers as surrogate endpoints for cancer incidence in high-risk cohorts will allow more agents to be evaluated in shorter studies that use fewer subjects to achieve the desired statistical power. (37 Refs.)

Protection against induction of mouse skin papillomas with low and high risk of conversion to malignancy by green tea polyphenols.

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Carcinogenesis (England) Mar 1997, 18 (3) p497-502

We earlier showed that a polyphenolic fraction isolated from green tea (GTP) affords protection against tumor promotion and tumor progression in SENCAR mouse skin. The present study was designed to further evaluate the protective effect of GTP against the induction and subsequent progression of papillomas to squamous cell carcinomas (SCCs) in experimental protocols where papillomas were developed with a low or high probability of their malignant conversion. Topical application of GTP (6 mg/animal) 30 min prior to that of 12-O-tetradecanoylphorbol-13-acetate (TPA) either once a week for 5 weeks (high risk TPA protocol) or once a week for 20 weeks (low risk TPA protocol) or mezerein (MEZ) twice a week for 20 weeks (high risk MEZ protocol) in 7,12-dimethylbenz[a]anthracene (DMBA)-initiated mouse skin resulted in significant protection against skin tumor promotion in terms of tumor incidence (32-60%), multiplicity (49-63%) and tumor volume/mouse (73-90%) at the termination of the experiment at 20 weeks. In three separate malignant progression experiments when papilloma yield in DMBA-initiated and TPA or MEZ promoted low and high risk protocols was stabilized at 20 weeks, animals were divided into two subgroups. These animals were either topically treated twice weekly with acetone (0.2 ml/animal, spontaneous malignant conversion group) or with GTP (6 mg/animal in 0.2 ml acetone) for an additional period of 31 weeks. During these treatment regimens, all suspected carcinomas were recorded and each one was verified histopathologically either at the time when tumor-bearing mouse died/moribund or at the termination of the experiment at 51 weeks. GTP resulted in significant protection against the malignant conversion of papillomas to SCC in all the protocols employed. At the termination of the experiment at 51 weeks, these protective effects were evident in terms of mice with carcinomas (35-41%), carcinomas per mouse (47-55%) and percent malignant conversion of papillomas to carcinomas (47-58%). The kinetics of malignant conversion suggest that a subset of papillomas formed in the early phase of tumor promotion in all the protocols had a higher probability of malignant conversion into SCCs because all the positive control groups (acetone treated) produced nearly the same number of carcinomas (33-38 in a group of 20 animals) at the end of the progression period. In the GTP-treated group of animals the number of carcinomas formed was less (14-20 in a group of 20 animals), which shows the ability of GTP to protect against the malignant conversion of papillomas of higher probability irrespective of the risk involved, GTP may be highly useful in affording protection against skin cancer risk.

Efficacy of a dentifrice and oral rinse containing sanguinaria extract in conjunction with initial periodontal therapy.

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Aust Dent J (Australia) Feb 1997, 42 (1) p47-51

In the treatment of periodontal disease initial therapy aims at reducing marginal inflammation so allowing assessment of residual disease and further treatment options. The aim of the present study was to determine whether the use of a dentifrice and oral rinse containing sanguinaria extract led to a more rapid resolution of gingival inflammation following initial therapy. Thirty-four subjects, randomly assigned to one of two treatment groups, took part in this randomized double-blind parallel study. All subjects received initial therapy including oral hygiene instruction and scaling and root planing as required. One group also received an active dentifrice and oral rinse containing sanguinaria extract (an antiplaque agent) and zinc chloride. The other group received a placebo dentifrice and oral rinse. The recorded at six sites per tooth at baseline, two weeks after initial therapy and six weeks after initial therapy. There was no significant difference between the groups for any of the parameters at the baseline examination. Two weeks following initial therapy both groups showed a statistically significant increase in the number of sites with PLI of 0 or 1 ($p < 0.0001$) and a statistically significant increase in the number of sites with a GI of 0 or 1 (that is, no bleeding on probing), ($p < 0.0001$). Also there was a statistically significant increase in the number of sites with probing depths ≤ 3 mm ($p < 0.0001$) compared with baseline. These changes were maintained through to six weeks post therapy. There was no significant advantage to the sanguinaria group. Results demonstrate that initial therapy in the form of oral hygiene instruction, scaling and root planing leads to a significant improvement in periodontal status which is maintained at least in the short term. Further, use of a dentifrice and oral rinse containing sanguinaria did not improve the efficacy of initial therapy.

The impact of zinc supplementation on Schistosoma mansoni reinfection rate and intensities: a randomized, controlled trial among rural Zimbabwean schoolchildren.

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Eur J Clin Nutr (England) Jan 1997, 51 (1) p33-7

OBJECTIVES: To assess the effect of zinc supplementation on susceptibility to *S. mansoni* reinfections among schoolchildren.

DESIGN: Randomized, double-blind, placebo-controlled trial.

SETTING AND SUBJECTS: 313 rural Zimbabwean schoolchildren (144 boys and 169 girls), 11-17 y).

INTERVENTIONS: Supplementation with zinc (or placebo on schooldays for 12 months. Due to drought, a food programme was in operation during the last eight months of the study.

OUTCOME MEASURES: *S. mansoni* and *S. haematobium* reinfection rates and intensities.

RESULTS: There was no difference in reinfection rates between the zinc and placebo groups (25 vs 29%, $P = 0.46$). However, the median intensity of *S. mansoni* reinfection, although low in both groups, was significantly lower in the zinc than in the placebo group (7 vs 13 eggs per gram of faeces, $P = 0.048$). No difference in either *S. haematobium* reinfection rates or intensities were seen.

CONCLUSIONS: Zinc supplementation reduced the intensity of *S. mansoni* reinfections. Although the intensities of reinfection were very low, the finding probably reflects a biological effect of zinc that could be of public health importance in settings with higher transmission.

Methylenetetrahydrofolate reductase polymorphism, dietary interactions, and risk of colorectal cancer.

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Cancer Res (United States) Mar 15 1997, 57 (6) p1098-102

Folate derivatives are important in experimental colorectal carcinogenesis; low folate intake, particularly with substantial alcohol intake, is associated with increased risk. The enzyme 5,10-methylenetetrahydrofolate reductase (MTHFR) catalyzes the conversion of 5,10-methylenetetrahydrofolate, required for purine and thymidine syntheses, to 5-methyltetrahydrofolate, the primary circulatory form of folate necessary for methionine synthesis. A common mutation (677C-->T) in MTHFR reduces enzyme activity, leading to lower levels of 5-methyltetrahydrofolate. To evaluate the role of folate metabolism in human carcinogenesis, we examined the associations of MTHFR mutation, plasma folate levels, and their interaction with risk of colon cancer. We also examined the interaction between genotype and alcohol intake. We used a nested case-control design within the Physicians were ages 40-84 at baseline when alcohol intake was ascertained and blood samples were drawn. During 12 years of follow-up, we identified 202 colorectal cancer cases and matched them to 326 cancer-free controls by age and smoking status. We genotyped for the MTHFR polymorphism and measured plasma folate levels. Men with the homozygous mutation (15% in controls) had half the risk of colorectal cancer [odds ratio (OR), 0.49; 95% confidence interval (CI), 0.27-0.87] compared with the homozygous normal or heterozygous genotypes. Overall, we observed a marginal significant increased risk of colorectal cancer (OR, 1.78; 95% CI, 0.93-3.42) among those whose plasma folate levels indicated deficiency (<3 ng/ml) compared with men with adequate folate levels. Among men with adequate folate levels, we observed a 3-fold decrease in risk (OR, 0.32; 95% CI, 0.15-0.68) among men with the homozygous mutation compared with those with the homozygous normal or heterozygous genotypes. However, the protection due to the mutation was absent in men with folate deficiency. In men with the homozygous normal genotype who drank little or no alcohol as reference, those with the homozygous mutation who drank little or no alcohol had an 8-fold decrease in risk (OR, 0.12; 95% CI, 0.03-0.57), and for moderate drinkers, a 2-fold decrease in risk (OR, 0.42; 95% CI, 0.15-1.20); no decrease in risk was seen in those drinking 1 or more drinks/day. Our findings provide support for an important role of folate metabolism in colon carcinogenesis. In particular, these results suggest that the 677C-->T mutation in MTHFR reduces colon cancer risk, perhaps by increasing 5,10-methylenetetrahydrofolate levels for DNA synthesis, but that low folate intake or high alcohol consumption may negate some of the protective effect.

Nutrition in women. Assessment and counseling.

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Prim Care (United States) Mar 1997, 24 (1) p37-51

Nutritional aspects of health care for women are receiving special attention in the lay and research press. Primary care physicians must have accurate knowledge of general nutrition to counsel patients accordingly. This article addresses a practical approach to nutritional assessment and counseling. Current data on specific nutrients and disease are evaluated. Attention is given to antioxidant vitamins and disease as well as calcium, vitamin D, and osteoporosis. (59 Refs.)

Hypertension and borderline isolated systolic hypertension increase risks of cardiovascular disease and mortality in male physicians.

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Circulation (United States) Mar 4 1997, 95 (5) p1132-7

BACKGROUND: The objective of this study was to examine whether definite hypertension and borderline isolated systolic hypertension predict subsequent cardiovascular disease and mortality.

METHODS AND RESULTS: This was a prospective cohort study with a mean follow-up of 11.7 years. The subjects were a group of 18,682 apparently healthy US men, aged 40 to 84 years, participating in the Physicians' Health Study, a randomized trial of low-dose aspirin and beta-carotene. The main outcome measures were total cardiovascular disease, myocardial infarction, stroke, cardiovascular death, with substantially increased risks of total cardiovascular disease (relative risk [RR] 1.92; 95% confidence interval [CI], 1.70 to 2.18), myocardial infarction (RR, 1.78; 95% CI, 1.49 to 2.13), stroke (RR, 2.19; 95% CI, 1.78 to 2.69), and cardiovascular death (RR, 2.10; 95% CI, 1.68 to 2.63). Borderline isolated systolic hypertension was associated with significantly increased risks of cardiovascular disease (RR, 1.32; 95% CI, 1.09 to 1.59), stroke (RR, 1.42; 95% CI, 1.04 to 1.93), and cardiovascular death (RR, 1.56; 95% CI, 1.13 to 2.15), as well as a possible but non-significant increased risk of myocardial infarction (RR, 1.26; 95% CI, 0.95 to 1.67). Hypertension and borderline isolated systolic hypertension were associated with significantly increased risks of 41% and 22%, respectively, for all-cause mortality.

CONCLUSIONS: Hypertension as well as borderline isolated systolic hypertension are associated with elevated risks of cardiovascular diseases, especially stroke and cardiovascular death. Hypertension is associated with an increased risk of myocardial infarction, and borderline isolated systolic hypertension predicts a possible but more modest increase in risk. These data add to the existing evidence that hypertension is a major cardiovascular risk factor and extend the findings to borderline isolated systolic hypertension.

Bronchial reactivity and dietary antioxidants.

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Thorax (England) Feb 1997, 52 (2) p166-70

BACKGROUND: It has been postulated that dietary antioxidants may influence the expression of allergic diseases and asthma. To test this hypothesis a case-control study was performed, nested in a cross sectional study of a random sample of adults, to investigate the relationship between allergic disease and dietary antioxidants.

METHODS: The study was performed in rural general practices in Grampian, Scotland. A validated dietary questionnaire was used to measure food intake of cases, defined, firstly, as people with seasonal allergic-type symptoms and, secondly, those with bronchial hyperreactivity confirmed by methacholine challenge, and of controls without allergic symptoms or bronchial reactivity.

RESULTS: Cases with seasonal symptoms did not differ from controls except with respect to the presence of atopy and an increased risk of symptoms associated with the lowest intake of zinc. The lowest intakes of vitamin C and manganese were associated with more than fivefold increased risks of bronchial reactivity. Decreasing intakes of magnesium were also significantly associated with an increased risk of hyperreactivity.

CONCLUSIONS: This study provides evidence that diet may have a modulatory effect on bronchial reactivity, and is consistent with the hypothesis that the observed reduction in antioxidant intake in the British diet over the last 25 years has been a factor in the increase in the prevalence of asthma over this period.

Effects of bisamil on coronary-occlusion-reperfusion injury and free-radical-induced reactions.

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Pharmacol Res (England) Jun 1996, 33 (6) p327-36

Isamil-an antiarrhythmic compound under clinical investigation-influences the reperfusion-induced arrhythmias and biochemical parameters characterizing occlusion-reperfusion-induced free-radical reactions. The left descending coronary artery (LAD) was occluded for 60 min in anaesthetized dogs followed by one hour of reperfusion. Blood samples were taken at different times of the occlusion and reperfusion for the determination of plasma concentration of malondialdehyde (MDA), reduced (GSH) and oxidized glutathione (GSSG); furthermore of the activity of catalase and superoxide dismutase (SOD). Free-radical generating capacity of polymorph neutrophil granulocytes (PMN) was also measured. At the end of the experiments heart tissue samples were excised from the injured areas and from the intact part of the left ventricular muscle. In tissues samples the concentrations of MDA and GSH and the activity of SOD were determined. Bisamil was given as an i.v. bolus injection at a dose of 2 mg kg⁻¹ several minutes prior to the end of LAD-occlusion; then the administration was repeated in the 30th minute of reperfusion. In the control group (10 dogs) ventricular fibrillation (VF) occurred in seven cases which resulted in death in three. In the bisamil-treated group, however, VF was seen in three cases and no death was recorded. Bisamil inhibited the elevation of the plasma concentration of MDA and GSSG during the reperfusion and abolished the decrease in the plasma concentration of GSH during the occlusion and reperfusion. The activity of SOD and catalase in plasma was much better preserved in the bisamil-treated group than in the controls. Bisamil significantly inhibited the increase of the superoxide-radical generating capacity of PMNs during the reperfusion. The data obtained from myocardial tissue samples supported the cardioprotective effect of bisamil. The biochemical investigation of ischemic-reperfused myocardium showed that bisamil promoted preservation of SOD-activity and of tissue glutathione. Results of this study clearly showed that bisamil has a significant effect on ischemiareperfusion injury. Besides its inhibitory effects on ischaemia-reperfusion induced arrhythmias it has a special benefit in influencing free-radical mediated damage leading to better preservation of membranes and to limitations of irreversible cell injuries.

Whole-grain consumption and chronic disease: protective mechanisms.

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Nutr Cancer (United States) 1997, 27 (1) p14-21

Dietary guidance recommends consumption of whole grains to reduce the risk of chronic diseases including cancer and cardiovascular disease. Epidemiologic studies support the belief that whole grains are protective against cancers, especially gastrointestinal cancers such as gastric and colonic, and cardiovascular disease. Components in whole grains that may be protective are diverse and include compounds that affect the gut environment, i.e., dietary fiber, resistant starch, and other undigestible compounds in whole grains, compounds that function as antioxidants such as trace minerals and phenolic compounds, and compounds that are phytoestrogens with potential hormonal effects. Many of the protective compounds in whole grains are also in fruits and vegetables, but some plant compounds are more concentrated in whole grains, such as phenolic compounds including ferulic and caffeic acid. Other potential mechanistic effects of whole grains include binding of carcinogens and modulation of glycemic index. Clearly, the range of protective substances in whole grains is impressive, and advice to consume additional whole grains is justifiable. (73 Refs.)

Dietary manipulation of plasma carotenoid concentrations of squirrel monkeys (*Saimiri sciureus*).

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J Nutr (United States) Jan 1997, 127 (1) p122-9

Primate retinas accumulate the dihydroxy xanthophylls, lutein and zeaxanthin, from the diet via the plasma. Control of plasma concentrations of these carotenoids may be useful for prevention of retinal disease by manipulating carotenoid content of the retina. We have measured the plasma response of male squirrel monkeys to changes in the carotenoid content of a nonpurified diet. We have also supplemented the diet with zeaxanthin and beta-carotene. Plasma responses to dietary changes were rapid. Within one week, most of the change in plasma concentrations had already occurred. Within two weeks of increasing zeaxanthin intake, plasma zeaxanthin concentrations were at a new, relatively stable level. beta-carotene concentrations in the plasma were low while the monkeys were consuming a standard laboratory diet, and were only slightly increased by supplementation. Plasma

lutein concentrations were unaffected by zeaxanthin supplementation. Our results suggest that it should be possible to manipulate plasma concentrations of each of the retinal carotenoids with little impact on the plasma concentrations of the other. This will facilitate exploration of the rates of accumulation of lutein and zeaxanthin in the retina, as well as exploration of the possibility of bioconversion from one xanthophyll to another.

Mechanisms of spontaneous human cancers.

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Environ Health Perspect (United States) May 1996, 104 Suppl 3 p633-7

Subfile: Is of much of human cancer remain obscure. The fraction that is spontaneous is unknown and cannot be calculated until all known external causes have been accounted for. This is not a feasible proposition. However, there is substantial evidence that about 80% of human cancer could be avoided by eliminating tobacco consumption; by dietary changes; by reducing infection with certain viruses, bacteria, and parasitic worms; and, in white populations, by avoiding sunburn. Alcohol, occupational and medical carcinogens, and certain patterns of reproductive behavior also contribute to the cancer burden. Cancers that cannot be attributed to these causes, and for which no other causes can be found, could be considered spontaneous and to arise from endogenous processes. Epidemiological evidence suggests that spontaneous and induced cancers share the same mechanism. Cancer is a genetic disorder of somatic cells. An accumulation of mutant genes that control the cell cycle, maintain genomic stability, and mediate apoptosis is central to carcinogenesis. Spontaneous mutation may cause spontaneous cancer. Endogenous causes of mutation include depurination and depyrimidation of DNA; proofreading and mismatch errors during DNA replication; deamination of 5-methylcytosine to produce C to T base pair substitutions; and damage to DNA and its replication imposed by products of metabolism (notably oxidative damage caused by oxygen free radicals). Deficiencies in cellular defense mechanisms may also provoke spontaneous mutation. These include defective DNA excision-repair; low levels of antioxidants, antioxidant enzymes, and nucleophiles that trap DNA-reactive electrophiles; and enzymes that conjugate nucleophiles with DNA-damaging electrophiles. Mechanisms underlying many of those cellular defenses are under genetic control. Thus, germ line mutations or polymorphisms of genes that govern them may also contribute to spontaneous cancer. (22 Refs.)

Molecular epidemiology in environmental carcinogenesis.

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Environ Health Perspect (United States) May 1996, 104 Suppl 3 p441-3

Molecular epidemiology has significant potential in preventing cancer and other diseases caused by environmental exposures (related to lifestyle, occupation, or ambient pollution). This approach attempts to prevent cancer by incorporating laboratory methods to document the molecular dose and preclinical effects of carcinogens, as well as factors that increases individual susceptibility to carcinogens. Recently we have carried out validation studies of biologic markers such as carcinogen--DNA and carcinogen--protein adducts, gene and chromosomal mutations, alterations in target oncogenes or tumor suppressor genes, polymorphisms in putative susceptibility genes (individual P450s, glutathione transferase M1), and serum levels of micronutrients. This research involves adults, infants, and children exposed to varying levels of carcinogens, as well as cancer cases and controls. On a group level, dose-response relationships have frequently been seen between various biomarkers and environmental exposures such as polycyclic aromatic hydrocarbons, cigarette smoke (active and passive), and ambient indoor and workplace air pollution. However, there is significant interindividual variation in biomarkers that appears to reflect a modulating effect on biomarkers (hence potential risk) by genetic and acquired susceptibility factors. Ongoing retrospective and nested case-control studies of lung and breast cancer are examining the association between biomarkers and cancer risk. Results of these studies are encouraging; they suggest that biomarkers, once validated, can be useful in identifying populations and individuals at risk in time to intervene effectively. (14 Refs.)

Vitamin C intake and susceptibility to the common cold.

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Br J Nutr (England) Jan 1997, 77 (1) p59-72

Although the role of vitamin C in common cold incidence had been studied extensively, the level of vitamin C intake has not been unequivocally shown to affect the incidence of colds. In the present study the six largest vitamin C supplementation (≥ 1 g/d) studies, including over 5000 episodes in all, have been analysed, and it is shown that common cold incidence is not reduced in the vitamin C-supplemented groups compared with the placebo groups (pooled rate ratio (RR) 0.99; 95% CI 0.93, 1.04). Consequently these six major studies give no evidence that high-dose vitamin C supplementation decreases common cold incidence in ordinary people. Nevertheless, the analysis was continued with the hypothesis that vitamin C intake may affect common cold susceptibility in specific groups of people. It was assumed that the potential effect of supplementation might be most conspicuous in subjects with low dietary vitamin C intake. The average vitamin C intake has been rather low in the UK and plasma vitamin C concentrations are in general lower in males than in females. In four studies with British females vitamin C supplementation had no marked effect on common cold incidence (pooled RR 0.95; 95% CI 0.86, 1.04). However, in four studies with British male schoolchildren and students a statistically highly significant reduction in common cold incidence was found in groups supplemented with vitamin C (pooled RR 0.70; 95% CI 0.60, 0.81). Thus, these studies with British males indicate that vitamin C intake has physiological effects on susceptibility to common cold infections, although the effect seems quantitatively meaningful only in limited groups of people and is not very large.

[Alcohol and free radicals: from basic research to clinical prospects]

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Ann Gastroenterol Hepatol (Paris) (France) May-Jun 1996, 32 (3) p128-33; discussion 133-4

Subfile: liver of rats following various conditions of ethanol administration. The ethanol-inducible cytochrome P450 2E1 plays a key role in its generation, favoured itself by an increase in the "redox-active" fraction of intracellular non-heme iron. Administration of ethanol elicits the generation of the 1-hydroxyethyl radical, which has been identified in vivo. Its reactivity contributes to alcohol-induced immunological disturbances. Liver inflammatory and fibrotic disorders can be reproduced in rats by long-term ethanol administration associated with a high fat diet. The severity of these disorders is correlated to the intensity of the oxidative stress. Some conditions of ethanol administration to rats also elicit an oxidative stress in the myocardium and central nervous system. Through its inhibitory effect on glutamine synthetase activity and resulting excitotoxicity it may contribute to neuronal death and possibly to dependence on alcohol. Disorders related to an oxidative stress were also reported in the serum and erythrocytes as well as in liver biopsies from alcoholic individuals. Their detection may be useful to follow the evolution of alcoholic liver diseases. Supplementation with antioxidants such as vitamin E may be considered in the prevention of severe cellular disorders in individuals consuming large amounts of alcoholic beverages. An increase in free radical production is likely playing a role in the induction of severe cellular damage linked to repeated withdrawals occurring as a result of heavy and sporadic ethanol intake. (41 Refs.)

Melatonin reduces mortality from Aleutian disease in mink (*Mustela vison*).

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J Pineal Res (Denmark) Nov 1996, 21 (4) p214-7

Aleutian disease (AD) results from a persistent parvoviral infection that results in marked hypergammaglobulinemia and immune complex mediated lesions of the kidney, liver, lungs and, arteries. Melatonin protected a strain and a demi/dark crossed strain of mink from AD. The biogenic amine also afforded protection against other non-diagnosed diseases naturally found on mink farms when it was available from a subcutaneously-placed reservoir. Some genetic strains of mink apparently differed in the resistance of mink to the virus and in the protective ability of melatonin. The demi strain was the most resistant followed by pastels, mahogany, darks, and those strains with the double recessive Aleutian gene. The protective action of melatonin appeared to result from melatonin's ability to scavenge free radicals, but it could also be due to the induction of antioxidant enzymes or to the modulation of immunity. Melatonin also protected mink against distemper.

Exercise causes blood glutathione oxidation in chronic obstructive pulmonary disease: prevention by O₂ therapy.

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J Appl Physiol (United States) Nov 1996, 81 (5) p2198-202

The aim of the present study was to determine whether glutathione oxidation occurs in chronic obstructive pulmonary disease (COPD) patients who perform exercise and whether this could be prevented. Blood glutathione red-ox ratio [oxidized-to-reduced glutathione (GSSG/ GSH)] was significantly increased when patients performed exercise for a short period of time until exhaustion. Their resting blood GSSG/GSH was 0.039 +/- 0.008 (SD) (n = 5), whereas after exercise it increased to 0.085 +/- 0.019, P < 0.01. Glutathione oxidation associated with exercise was partially prevented by oxygen therapy (resting value: 0.037 +/- 0.014, n = 5; after exercise: 0.047 +/- 0.016, n = 5, P < 0.01). We conclude that light exercise causes an oxidation of glutathione in COPD patients, which can be partially prevented by oxygen therapy.

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