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ABSTRACTS**Cinnamon****INTERACTIONS BETWEEN VOLATILE AND NONVOLATILE COFFEE COMPONENTS. 1. SCREENING OF NONVOLATILE COMPONENTS.**

This study is the first of two publications that investigate the phenomena of coffee nonvolatiles interacting with coffee volatile compounds. The purpose was to identify which coffee nonvolatile(s) are responsible for the interactions observed between nonvolatile coffee brew constituents and thiols, sulfides, pyrroles, and diketones. The overall interaction of these compounds with coffee brews prepared with green coffee beans roasted at three different roasting levels (light, medium, and dark), purified nonvolatiles, and medium roasted coffee brew fractions (1% solids after 1 or 24 h) was measured using a headspace solid-phase microextraction technique. The dark roasted coffee brew was slightly more reactive toward the selected compounds than the light roasted coffee brew. Selected pure coffee constituents, such as caffeine, trigonelline, arabinogalactans, chlorogenic acid, and caffeic acid, showed few interactions with the coffee volatiles. Upon fractionation of medium roasted coffee brew by solid-phase extraction, dialysis, size exclusion chromatography, or anion exchange chromatography, characterization of each fraction, evaluation of the interactions with the aromas, and correlation between the chemical composition of the fractions and the magnitude of the interactions, the following general conclusions were drawn. (1) Low molecular weight and positively charged melanoidins present significant interactions. (2) Strong correlations were shown between the melanoidin and protein/peptide content, on one hand, and the extent of interactions, on the other hand ($R = 0.83-0.98$, depending on the volatile compound). (3) Chlorogenic acids and carbohydrates play a secondary role, because only weak correlations with the interactions were found in complex matrixes.

J Agric Food Chem. 2005 Jun 1;53(11):4417-25

DIETARY POLYPHENOLS AND THE PREVENTION OF DISEASES.

Polyphenols are the most abundant antioxidants in the diet and are widespread constituents of fruits, vegetables, cereals, dry legumes, chocolate, and beverages, such as tea, coffee, or wine. Experimental studies on animals or cultured human cell lines support a role of polyphenols in the prevention of cardiovascular diseases, cancers, neurodegenerative diseases, diabetes, or osteoporosis. However, it is very difficult to predict from these results the effects of polyphenol intake on disease prevention in humans. One of the reasons is that these studies have often been conducted at doses or concentrations far beyond those documented in humans. The few clinical studies on biomarkers of oxidative stress, cardiovascular disease risk factors, and tumor or bone resorption biomarkers have often led to contradictory results. Epidemiological studies have repeatedly shown an inverse association between the risk of myocardial infarction and the consumption of tea and wine or the intake level of some particular flavonoids, but no clear associations have been found between cancer risk and polyphenol consumption. More human studies are needed to provide clear evidence of their health protective effects and to better evaluate the risks possibly resulting from too high a polyphenol consumption.

Crit Rev Food Sci Nutr. 2005;45(4):287-306

EFFECTS OF COFFEE CONSUMPTION ON OXIDATIVE SUSCEPTIBILITY OF LOW-DENSITY LIPOPROTEINS AND SERUM LIPID LEVELS IN HUMANS.

Since little is known about how coffee intake affects low-density lipoprotein (LDL) oxidative susceptibility and serum lipid levels, we conducted an in vivo study in 11 healthy male students of Wakayama Medical University aged between 20 and 31 years fed an average Japanese diet. On days 1-7 of the study, the subjects drank mineral water. On day 7, the subjects began drinking coffee, 24 g total per day, for one week. This was followed by a one week "washout period" during which mineral water was consumed. Fasting peripheral venous blood samples were taken at the end of each one-week period. LDL oxidation lag time was approximately 8% greater ($p < 0.01$) after the coffee drinking period than the other periods. Serum levels of total cholesterol and LDL-cholesterol (LDL-C) and malondialdehyde (MDA) as thiobarbituric acid reactive substances (TBARS) were significantly decreased after the coffee drinking period. Finally, regular coffee ingestion may favorably affect cardiovascular risk status by modestly reducing LDL oxidation susceptibility and decreasing LDL-cholesterol and MDA levels.

ISOLATION AND CHARACTERIZATION OF POLYPHENOL TYPE-A POLYMERS FROM CINNAMON WITH INSULIN-LIKE BIOLOGICAL ACTIVITY.

The causes and control of type 2 diabetes mellitus are not clear, but there is strong evidence that dietary factors are involved in its regulation and prevention. We have shown that extracts from cinnamon enhance the activity of insulin. The objective of this study was to isolate and characterize insulin-enhancing complexes from cinnamon that may be involved in the alleviation or possible prevention and control of glucose intolerance and diabetes. Water-soluble polyphenol polymers from cinnamon that increase insulin-dependent in vitro glucose metabolism roughly 20-fold and display antioxidant activity were isolated and characterized by nuclear magnetic resonance and mass spectroscopy. The polymers were composed of monomeric units with a molecular mass of 288. Two trimers with a molecular mass of 864 and a tetramer with a mass of 1,152 were isolated. Their protonated molecular masses indicated that they are A type doubly linked procyanidin oligomers of the catechins and/or epicatechins. These polyphenolic polymers found in cinnamon may function as antioxidants, potentiate insulin action, and may be beneficial in the control of glucose intolerance and diabetes.

J Agric Food Chem. 2004 Jan 14;52(1):65-70

CINNAMON EXTRACT (TRADITIONAL HERB) POTENTIATES IN VIVO INSULIN-REGULATED GLUCOSE UTILIZATION VIA ENHANCING INSULIN SIGNALING IN RATS.

Cinnamon has been shown to potentiate the insulin effect through upregulation of the glucose uptake in cultured adipocytes. In the present study, we evaluated the effect of the cinnamon extract on the insulin action in awaked rats by the euglycemic clamp and further analyzed possible changes in insulin signaling occurred in skeletal muscle. The rats were divided into saline and cinnamon extract (30 and 300 mg/kg BW-doses: C30 and C300) oral administration groups. After 3-weeks, cinnamon extract treated rats showed a significantly higher glucose infusion rate (GIR) at 3 mU/kg per min insulin infusions compared with controls (118 and 146% of controls for C30 and C300, respectively). At 30 mU/kg per min insulin infusions, the GIR in C300 rats was increased 17% over controls. There were no significant differences in insulin receptor (IR)-beta, IR substrate (IRS)-1, and phosphatidylinositol (PI) 3-kinase protein content between C300 rats and controls. However, the skeletal muscle insulin-stimulated IR-beta and the IRS-1 tyrosine phosphorylation levels in C300 rats were 18 and 33% higher, respectively, added to 41% higher IRS-1/PI 3-kinase association. These results suggest that the cinnamon extract would improve insulin action via increasing glucose uptake in vivo, at least in part through enhancing the insulin-signaling pathway in skeletal muscle.

Diabetes Res Clin Pract. 2003 Dec;62(3):139-48

CARDIOVASCULAR EFFECTS OF COFFEE: IS IT A RISK FACTOR?

Intake of coffee, one of the most common beverages worldwide, is often reported as a cardiovascular risk factor; however, definitive data are lacking. Acute intake of coffee or beverages containing caffeine can increase blood pressure, heart minute volumes, and cardiac index, as well as activate the sympathetic nervous system in nonhabitual coffee drinkers. Interestingly, this is not observed in habitual coffee drinkers. Restriction of coffee or caffeinated beverages is no longer indicated in the seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) guidelines for the treatment of hypertension. In fact, no clear association between coffee and the risk of hypertension, myocardial infarction, or other cardiovascular diseases has been demonstrated. In contrast to early studies, recent research indicates that habitual moderate coffee intake does not represent a health hazard and may even be associated with beneficial effects on cardiovascular health.

Prog Cardiovasc Nurs. 2005 Spring;20(2):65-9

COFFEE CONSUMPTION AND RISK FOR TYPE 2 DIABETES MELLITUS.

BACKGROUND: In small, short-term studies, acute administration of caffeine decreases insulin sensitivity and impairs glucose tolerance. **OBJECTIVE:** To examine the long-term relationship between consumption of coffee and other caffeinated beverages and incidence of type 2 diabetes mellitus. **DESIGN:** Prospective cohort study. **SETTING:** The Nurses' Health Study and Health Professionals' Follow-up Study. **PARTICIPANTS:** The authors followed 41 934 men from 1986 to 1998 and 84,276 women from 1980 to 1998. These participants did not have diabetes, cancer, or cardiovascular disease at baseline. **MEASUREMENTS:** Coffee consumption was assessed every 2 to 4 years through validated questionnaires. **RESULTS:** The authors documented 1,333 new cases of type 2 diabetes in men and 4,085 new cases in women. The authors found an inverse association between coffee intake and type 2 diabetes after adjustment for age, body mass index, and other risk factors. The multivariate relative risks for diabetes according to regular coffee consumption categories (0, <1, 1 to 3, 4 to 5, or > or =6 cups per day) in men were 1.00, 0.98, 0.93, 0.71, and 0.46 (95% CI, 0.26 to 0.82; P = 0.007 for trend), respectively. The corresponding multivariate relative risks in women were 1.00, 1.16, 0.99, 0.70, and 0.71 (CI, 0.56 to 0.89; P < 0.001 for trend), respectively. For decaffeinated coffee, the

multivariate relative risks comparing persons who drank 4 cups or more per day with nondrinkers were 0.74 (CI, 0.48 to 1.12) for men and 0.85 (CI, 0.61 to 1.17) for women. Total caffeine intake from coffee and other sources was associated with a statistically significantly lower risk for diabetes in both men and women. CONCLUSIONS: These data suggest that long-term coffee consumption is associated with a statistically significantly lower risk for type 2 diabetes.

Ann Intern Med. 2004 Jan 6;140(1):1-8

REDUCED INSULINOTROPIC EFFECT OF GASTRIC INHIBITORY POLYPEPTIDE IN FIRST-DEGREE RELATIVES OF PATIENTS WITH TYPE 2 DIABETES.

In patients with type 2 diabetes, gastric inhibitory polypeptide (GIP) has lost much of its insulinotropic activity. Whether this is similar in first-degree relatives of patients with type 2 diabetes is unknown. A total of 21 first-degree relatives, 10 patients with type 2 diabetes, and 10 control subjects (normal oral glucose tolerance) were examined. During a hyperglycemic "clamp" (140 mg/dl for 120 min), synthetic human GIP (2 pmol. kg(-1). min(-1)) was infused intravenously (30-90 min). With exogenous GIP, patients with type 2 diabetes responded with a lower increment (Delta) in insulin (P = 0.0003) and C-peptide concentrations (P < 0.0001) than control subjects. The GIP effects in first-degree relatives were diminished compared with control subjects (Delta insulin: P = 0.04; Delta C-peptide: P = 0.016) but significantly higher than in patients with type 2 diabetes (P < or = 0.05). The responses over the time course were below the 95% CI derived from control subjects in 7 (insulin) and 11 (C-peptide) of 21 first-degree relatives of patients with type 2 diabetes. In conclusion, a reduced insulinotropic activity of GIP is typical for a substantial subgroup of normoglycemic first-degree relatives of patients with type 2 diabetes, pointing to an early, possibly genetic defect.

Diabetes. 2001 Nov;50(11):2497-504

COFFEE CONSUMPTION AND RISK OF TYPE 2 DIABETES MELLITUS AMONG MIDDLE-AGED FINNISH MEN AND WOMEN.

CONTEXT: Only a few studies of coffee consumption and diabetes mellitus (DM) have been reported, even though coffee is the most consumed beverage in the world. OBJECTIVE: To determine the relationship between coffee consumption and the incidence of type 2 DM among Finnish individuals, who have the highest coffee consumption in the world. DESIGN, SETTING, AND PARTICIPANTS: A prospective study from combined surveys conducted in 1982, 1987, and 1992 of 6,974 Finnish men and 7,655 women aged 35 to 64 years without history of stroke, coronary heart disease, or DM at baseline, with 175 682 person-years of follow-up. Coffee consumption and other study parameters were determined at baseline using standardized measurements. MAIN OUTCOME MEASURES: Hazard ratios (HRs) for the incidence of type 2 DM were estimated for different levels of daily coffee consumption. RESULTS: During a mean follow-up of 12 years, there were 381 incident cases of type 2 DM. After adjustment for confounding factors (age, study year, body mass index, systolic blood pressure, education, occupational, commuting and leisure-time physical activity, alcohol and tea consumption, and smoking), the HRs of DM associated with the amount of coffee consumed daily (0-2, 3-4, 5-6, 7-9, > or =10 cups) were 1.00, 0.71 (95% confidence interval [CI], 0.48-1.05), 0.39 (95% CI, 0.25-0.60), 0.39 (95% CI, 0.20-0.74), and 0.21 (95% CI, 0.06-0.69) (P for trend<.001) in women, and 1.00, 0.73 (95% CI, 0.47-1.13), 0.70 (95% CI, 0.45-1.05), 0.67 (95% CI, 0.40-1.12), and 0.45 (95% CI, 0.25-0.81) (P for trend =.12) in men, respectively. In both sexes combined, the multivariate-adjusted inverse association was significant (P for trend <.001) and persisted when stratified by younger and older than 50 years; smokers and never smokers; healthy weight, overweight, and obese participants; alcohol drinker and nondrinker; and participants drinking filtered and nonfiltered coffee. CONCLUSION: Coffee drinking has a graded inverse association with the risk of type 2 DM; however, the reasons for this risk reduction associated with coffee remain unclear.

JAMA. 2004 Mar 10;291(10):1213-9

COFFEE CONSUMPTION AND RISK OF TYPE 2 DIABETES MELLITUS.

Coffee is a major source of caffeine, which has been shown to acutely reduce sensitivity to insulin, but also has potentially beneficial effects. We prospectively investigated the association between coffee consumption and risk of clinical type 2 diabetes in a population-based cohort of 17,111 Dutch men and women aged 30-60 years. During 125,774 person years of follow-up, 306 new cases of type 2 diabetes were reported. After adjustment for potential confounders, individuals who drank at least seven cups of coffee a day were 0.50 (95% CI 0.35-0.72, p=0.0002) times as likely as those who drank two cups or fewer a day to develop type 2 diabetes. Coffee consumption was associated with a substantially lower risk of clinical type 2 diabetes.

Lancet. 2002 Nov 9;360(9344):1477-8

ABSTRACTS

Metabolic Syndrome

A PERSPECTIVE ON THE CURRENT STRATEGIES FOR THE TREATMENT OF OBESITY.

The prevalence in obesity has increased dramatically over the past 30 years, more than double in the United States alone. Obesity is associated with an increased risk for type 2 diabetes mellitus, dyslipidemia, hypertension, biliary disease, obstructive sleep apnea, and certain types of cancer. The pathophysiology of obesity is complex, involving behavioral, environmental, and genetic factors. Current treatment options include behavior modification and lifestyle changes which incorporate weight-reducing diets and physical activity, FDA approved long-term anti-obesity pharmacological agents sibutramine and orlistat, non-FDA approved over-the-counter (OTC) supplements and nutraceuticals, and, when appropriate, bariatric surgery. Without adequate prevention and treatment of obesity, government agencies have suggested that the direct and indirect costs associated with obesity may overwhelm the healthcare system. This brief review explores the current data available on treatments for the obese patient including the relative merits of different types of macronutrient composition (e.g., low carbohydrate vs. high carbohydrate diets) of weight-reducing diets, the value of resistance/ strength training in physical activity programs designed for the obese patient, the safety and efficacy associated with OTC supplements and nutraceuticals for weight reduction (e.g., Ephedra, conjugated linoleic acid (CLA), Garcinia cambogia/ hydroxycitric acid (HCA), chromium, pyruvate), the safety and efficacy of FDA-approved long-term obesity treatments sibutramine and orlistat, and bariatric surgery.

Curr Drug Targets CNS Neurol Disord. 2004 Oct;3(5):341-56

THE NUTRITIONAL PHENOTYPE IN THE AGE OF METABOLOMICS.

The concept of the nutritional phenotype is proposed as a defined and integrated set of genetic, proteomic, metabolomic, functional, and behavioral factors that, when measured, form the basis for assessment of human nutritional status. The nutritional phenotype integrates the effects of diet on disease/wellness and is the quantitative indication of the paths by which genes and environment exert their effects on health. Advances in technology and in fundamental biological knowledge make it possible to define and measure the nutritional phenotype accurately in a cross section of individuals with various states of health and disease. This growing base of data and knowledge could serve as a resource for all scientific disciplines involved in human health. Nutritional sciences should be a prime mover in making key decisions that include: what environmental inputs (in addition to diet) are needed; what genes/proteins/metabolites should be measured; what end-point phenotypes should be included; and what informatics tools are available to ask nutritionally relevant questions. Nutrition should be the major discipline establishing how the elements of the nutritional phenotype vary as a function of diet. Nutritional sciences should also be instrumental in linking the elements that are responsive to diet with the functional outcomes in organisms that derive from them. As the first step in this initiative, a prioritized list of genomic, proteomic, and metabolomic as well as functional and behavioral measures that defines a practically useful subset of the nutritional phenotype for use in clinical and epidemiological investigations must be developed. From this list, analytic platforms must then be identified that are capable of delivering highly quantitative data on these endpoints. This conceptualization of a nutritional phenotype provides a concrete form and substance to the recognized future of nutritional sciences as a field addressing diet, integrated metabolism, and health.

J Nutr. 2005 Jul;135(7):1613-6

DOES C-REACTIVE PROTEIN IDENTIFY A SUBCLINICAL METABOLIC DISEASE IN HEALTHY SUBJECTS?

BACKGROUND: Highly sensitive C-reactive protein (hs-CRP) levels are significant predictors of subsequent diabetes and metabolic syndrome (MS). Owing to the strong correlations between components of the MS and obesity with hs-CRP levels, previous studies about the associations of hs-CRP with insulin resistance might have been confounded by the inclusion of overweight or dysmetabolic subjects. **DESIGN:** Our aim was to evaluate the associations between hs-CRP levels and fasting insulin and insulin resistance (evaluated by the Homeostasis Model Assessment: HOMA IR) in a subgroup of subjects with normal body mass index (BMI) and without any metabolic abnormalities. Out of a cohort of 1,658 middle-aged subjects, representative of the local sanitary districts of the province of Asti (north-western Italy) enrolled for metabolic screening: 241 (14.5%) showed normal BMI, glucose tolerance, blood pressure and waist values and no dyslipidaemia. **RESULTS:** In this subgroup of subjects, those with hs-CRP levels ≥ 3 mg L⁻¹ showed significantly higher median insulin and HOMA-IR values (respectively: 20.4 vs. 6.0 pmol L⁻¹, and 0.8 vs. 0.2 microU mL⁻¹ x mmol L⁻¹). In a multiple regression model, insulin and insulin resistance remained significantly and independently related to hs-CRP levels, after adjustments for age, sex, BMI, waist, alcohol consumption, level of physical activity and smoking habits. Very few individuals within lower fasting insulin quartiles showed hs-CRP values ≥ 3 mg L⁻¹ when compared with approximately 60% of those within the highest quartile. **CONCLUSIONS:** The novel finding is that a state of low-grade systemic inflammation is present in normal BMI subjects who

ENDOGENOUS SEX HORMONES AND METABOLIC SYNDROME IN AGING MEN.

BACKGROUND: Sex hormone levels in men change during aging. These changes may be associated with insulin sensitivity and the metabolic syndrome. **METHODS:** We studied the association between endogenous sex hormones and characteristics of the metabolic syndrome in 400 independently living men between 40 and 80 yr of age in a cross-sectional study. Serum concentrations of lipids, glucose, insulin, total testosterone (TT), SHBG, estradiol (E2), and dehydroepiandrosterone sulfate (DHEA-S) were measured. Bioavailable testosterone (BT) was calculated using TT and SHBG. Body height, weight, waist-hip circumference, blood pressure, and physical activity were assessed. Smoking and alcohol consumption was estimated from self-report. The metabolic syndrome was defined according to the National Cholesterol Education Program definition, and insulin sensitivity was calculated by use of the quantitative insulin sensitivity check index. **RESULTS:** Multiple logistic regression analyses showed an inverse relationship according to 1 sd increase for circulating TT [odds ratio (OR) = 0.43; 95% confidence interval (CI), 0.32-0.59], BT (OR = 0.62; 95% CI, 0.46-0.83), SHBG (OR = 0.46; 95% CI, 0.33-0.64), and DHEA-S (OR = 0.76; 95% CI, 0.56-1.02) with the metabolic syndrome. Each sd increase in E2 levels was not significantly associated with the metabolic syndrome (OR = 1.16; 95% CI, 0.92-1.45). Linear regression analyses showed that higher TT, BT, and SHBG levels were related to higher insulin sensitivity; beta-coefficients (95% CI) were 0.011 (0.008-0.015), 0.005 (0.001-0.009), and 0.013 (0.010-0.017), respectively, whereas no effects were found for DHEA-S and E2. Estimates were adjusted for age, smoking, alcohol consumption, and physical activity score. Further adjustment for insulin levels and body composition measurements attenuated the estimates, and the associations were similar in the group free of cardiovascular disease and diabetes. **CONCLUSIONS:** Higher testosterone and SHBG levels in aging males are independently associated with a higher insulin sensitivity and a reduced risk of the metabolic syndrome, independent of insulin levels and body composition measurements, suggesting that these hormones may protect against the development of metabolic syndrome.

GREEN COFFEE BEAN EXTRACT IMPROVES HUMAN VASOREACTIVITY.

Our previous study revealed the antihypertensive effects of green coffee bean extract (GCE) ingestion in spontaneously hypertensive rats. We suggested that this antihypertensive action was due to the fact that GCE contains chlorogenic acid (CQA) as a major phenolic compound, and CQA in turn contains ferulic acid as a metabolic component that acts on nitric oxide (NO) derived from the vascular endothelium. In this study, the effects of GCE on blood vessels were evaluated in healthy males. The subjects were 20 healthy males with reduced vasodilation responses measured by strain gauge plethysmograms (SPG) to ischemic reactive hyperemia. Of the 20 subjects, 10 (mean age, 37.2 years) ingested a test drink containing GCE (CQA: 140 mg/day), and the other 10 (mean age, 34.8 years) ingested a placebo drink for 4 months. During the ingestion period, SPG, pulse wave velocity (PWV), and serum biochemical parameters were measured, and acceleration plethysmograms (APG) were taken. The reactive hyperemia ratio (RHR) in the test drink group began to increase after ingestion for 1 month and was significantly higher ($p < 0.05$) than that in the placebo group after ingestion for 3 months and 4 months. In addition, after ingestion for 4 months, the test drink group showed a significant decrease ($p < 0.01$) in the plasma total homocysteine level compared with the pre-ingestion level. However, there were no significant differences in PWV or APG between the test drink group and the placebo drink group. The improvement in RHR after ingestion of a drink containing GCE suggested an improvement in vasoreactivity by this component.

A CHLOROGENIC ACID-INDUCED INCREASE IN GLP-1 PRODUCTION MAY MEDIATE THE IMPACT OF HEAVY COFFEE CONSUMPTION ON DIABETES RISK.

Recent prospective epidemiology links heavy coffee consumption to a substantial reduction in risk for type 2 diabetes. Yet there is no evidence that coffee improves insulin sensitivity and, at least in acute studies, caffeine has a negative impact in this regard. Thus, it is reasonable to suspect that coffee influences the risk for beta cell "failure" that precipitates diabetes in subjects who are already insulin resistant. Indeed, there is recent evidence that coffee increases production of the incretin hormone glucagon-like peptide-1 (GLP-1), possibly owing to an inhibitory effect of chlorogenic acid (CGA -- the chief polyphenol in coffee) on glucose absorption. GLP-1 acts on beta cells, via cAMP-dependent mechanisms, to promote the synthesis and activity of the transcription factor IDX-1, crucial for maintaining the responsiveness of beta cells to an increase in plasma glucose. Conversely, the "glucolipotoxicity" thought to initiate and sustain beta cell dysfunction in diabetics can suppress expression of this transcription factor. The increased production of GLP-1 associated with frequent coffee consumption could thus be expected to counteract the adverse impact of chronic free fatty acid overexposure on beta cell function in overweight insulin resistant subjects. CGA's putative impact on glucose absorption may reflect the ability of this compound to inhibit glucose-6-phosphate translocase 1, now known to play a role in intestinal glucose transport. Delayed glucose absorption may itself protect beta cells

by limiting postprandial hyperglycemia -- though, owing to countervailing effects of caffeine on plasma glucose, and a paucity of relevant research studies, it is still unclear whether coffee ingestion blunts the postprandial rise in plasma glucose. More generally, diets high in "lente carbohydrate", or administration of nutraceuticals/pharmaceuticals which slow the absorption of dietary carbohydrate, should help preserve efficient beta cell function by boosting GLP-1 production, as well as by blunting the glucotoxic impact of postprandial hyperglycemia on beta cell function.

Med Hypotheses. 2005;64(4):848-53

COFFEE ACUTELY MODIFIES GASTROINTESTINAL HORMONE SECRETION AND GLUCOSE TOLERANCE IN HUMANS: GLYCEMIC EFFECTS OF CHLOROGENIC ACID AND CAFFEINE.

BACKGROUND: Accumulating evidence suggests that certain dietary polyphenols have biological effects in the small intestine that alter the pattern of glucose uptake. Their effects, however, on glucose tolerance in humans are unknown. **OBJECTIVE:** The objective was to investigate whether chlorogenic acids in coffee modulate glucose uptake and gastrointestinal hormone and insulin secretion in humans. **DESIGN:** In a 3-way, randomized, crossover study, 9 healthy fasted volunteers consumed 25 g glucose in either 400 mL water (control) or 400 mL caffeinated or decaffeinated coffee (equivalent to 2.5 mmol chlorogenic acid/L). Blood samples were taken frequently over the following 3 h. **RESULTS:** Glucose and insulin concentrations tended to be higher in the first 30 min after caffeinated coffee consumption than after consumption of decaffeinated coffee or the control ($P < 0.05$ for total and incremental area under the curve for glucose and insulin). Glucose-dependent insulinotropic polypeptide secretion decreased throughout the experimental period ($P < 0.005$), and glucagon-like peptide 1 secretion increased 0-120 min postprandially ($P < 0.01$) after decaffeinated coffee consumption compared with the control. Glucose and insulin profiles were consistent with the known metabolic effects of caffeine. However, the gastrointestinal hormone profiles were consistent with delayed intestinal glucose absorption. **CONCLUSIONS:** Differences in plasma glucose, insulin, and gastrointestinal hormone profiles further confirm the potent biological action of caffeine and suggest that chlorogenic acid might have an antagonistic effect on glucose transport. Therefore, a novel function of some dietary phenols in humans may be to attenuate intestinal glucose absorption rates and shift the site of glucose absorption to more distal parts of the intestine.

Am J Clin Nutr. 2003 Oct;78(4):728-33

THE METABOLIC SYNDROME.

The metabolic syndrome is a common metabolic disorder that results from the increasing prevalence of obesity. The disorder is defined in various ways, but in the near future a new definition(s) will be applicable worldwide. The pathophysiology seems to be largely attributable to insulin resistance with excessive flux of fatty acids implicated. A proinflammatory state probably contributes to the syndrome. The increased risk for type 2 diabetes and cardiovascular disease demands therapeutic attention for those at high risk. The fundamental approach is weight reduction and increased physical activity; however, drug treatment could be appropriate for diabetes and cardiovascular disease risk reduction.

Lancet. 2005 Apr 16-22;365(9468):1415-28

VITAMINS FOR CHRONIC DISEASE PREVENTION IN ADULTS: SCIENTIFIC REVIEW.

CONTEXT: Although vitamin deficiency is encountered infrequently in developed countries, inadequate intake of several vitamins is associated with chronic disease. **OBJECTIVE:** To review the clinically important vitamins with regard to their biological effects, food sources, deficiency syndromes, potential for toxicity, and relationship to chronic disease. **DATA SOURCES AND STUDY SELECTION:** We searched MEDLINE for English-language articles about vitamins in relation to chronic diseases and their references published from 1966 through January 11, 2002. **DATA EXTRACTION:** We reviewed articles jointly for the most clinically important information, emphasizing randomized trials where available. **DATA SYNTHESIS:** Our review of 9 vitamins showed that elderly people, vegans, alcohol-dependent individuals, and patients with malabsorption are at higher risk of inadequate intake or absorption of several vitamins. Excessive doses of vitamin A during early pregnancy and fat-soluble vitamins taken anytime may result in adverse outcomes. Inadequate folate status is associated with neural tube defect and some cancers. Folate and vitamins B(6) and B(12) are required for homocysteine metabolism and are associated with coronary heart disease risk. Vitamin E and lycopene may decrease the risk of prostate cancer. Vitamin D is associated with decreased occurrence of fractures when taken with calcium. **CONCLUSIONS:** Some groups of patients are at higher risk for vitamin deficiency and suboptimal vitamin status. Many physicians may be unaware of common food sources of vitamins or unsure which vitamins they should recommend for their patients. Vitamin excess is possible with supplementation, particularly for fat-soluble vitamins. Inadequate intake of several vitamins has been linked to chronic diseases, including coronary heart disease, cancer, and osteoporosis

JAMA. 2002 Jun 19;287(23):3116-26

ABSTRACTS

Migraine

NONPHARMACOLOGIC TREATMENT OF MIGRAINE.

Nonpharmacologic treatment of migraine is often used by patients and can provide interesting options for physicians. Knowledge about the evidence and its absence is important. Avoidance of trigger factors can help, if individualized. Behavioral approaches, such as relaxation techniques, biofeedback, and cognitive-behavioral therapy, require far more specialist time or technical devices, but are supported by some evidence, which is mostly old. The same is true for hypnosis. A new approach in migraine prevention is aerobic exercise, which is associated with positive side effects. Whether it will take a strong role, similar to the treatment of depression, remains to be seen. There is no convincing evidence for the efficacy of spinal manipulation. Hyperbaric oxygen may be an effective, but rarely practical prophylactic measure. The evidence pertaining to the efficacy of acupuncture is controversial because of methodologic difficulties, but an ongoing large German study may provide valuable evidence in the near future. Nutritional supplements acting on mitochondrial metabolism, such as magnesium, riboflavin, and coenzyme Q10, were shown to be effective in small, randomized, controlled trials. More studies on the different therapeutic interventions are needed, using modern diagnostic standards and state-of-the-art trial methodology.

Curr Pain Headache Rep. 2005 Jun;9(3):202-5

TREATMENT STRATEGIES IN MIGRAINE PATIENTS.

The goal of migraine treatment is to alleviate the symptoms of acute attacks and improve patients' quality of life. Therapeutic options and strategies principally rely on three types of approach: correction of causative factors; acute treatment of attacks; and prophylaxis. The quality of evidence supporting efficacy, personal experience, tolerability and safety profiles must guide the choice of a particular medication; nonetheless, we ought to keep in mind that therapeutic options should also be customized to target the individual patient, both in terms of personal characteristics and underlying comorbidities. Also, the framework of information the patient is given represents an essential component of migraine management, along with his/her active involvement in the therapeutic program and schedule.

Neurol Sci. 2004 Oct;25 Suppl 3:S242-3

DIAGNOSIS AND MANAGEMENT OF MIGRAINE HEADACHES.

Migraine headaches afflict approximately 6% of men and 18% of women in the United States, and cost billions of dollars each year in lost productivity, absenteeism, and direct medical expenditures. Despite its prevalence and the availability of therapeutic options, many patients do not seek treatment, and among those who do, a significant portion are misdiagnosed. Correct diagnosis can be made by identifying the historic and physical examination finding that distinguish primary headache disorders from secondary headache disorders, as well as the key clinical features that distinguish migraine headaches from other types. Once diagnosis is made, improper or inadequate management of headache pain, related symptoms such as nausea, and the possible aggravating side-effects of pharmacologic therapies represent further obstacles to effective therapy. Dissatisfaction with migraine therapy on the basis of these factors is common. Among abortive therapy options there are delivery methods available which may avoid aggravating symptom such as nausea. Recommended pharmacologic agents include non-steroidal anti-inflammatory drugs, intranasal butorphanol, ergotamine and its derivatives, and the triptans. Indications for prophylactic in addition to abortive therapy include the occurrence of headaches that require abortive therapy more than twice a week, that do not respond well to abortive therapy, and which are particularly severe. Research is ongoing in the pathophysiology of migraines, evaluation of nonpharmacologic treatment modalities, assessment of new drug therapies, and validation of headache guidelines.

South Med J. 2004 Nov;97(11):1069-77

CHALLENGING OR DIFFICULT HEADACHE PATIENTS.

This article addresses interesting and enigmatic presentations of headache from a diagnostic and treatment perspective. The emphasis is on migraineurs and other headache patients who represent a significant burden for the primary care provider. In particular, the author focuses on undiagnosed migraine, menstrual migraine, migraine in pregnancy, intractable migraine and status migrainosus, transformed migraine, hemiplegic migraine, basilar migraine, "triptan syndrome," sudden onset of severe headache, post-traumatic headache, and headache in elderly patients.

MIGRAINE HEADACHES: NUTRITIONAL, BOTANICAL, AND OTHER ALTERNATIVE APPROACHES.

Migraine headaches are an increasingly common health problem with a wide range of potential etiological factors. Stress, food allergies, neuroendocrine imbalances, and nutritional deficiencies all may contribute to migraine attacks. Many nutritional and botanical therapies aim to reduce migraine incidence by decreasing platelet aggregation and preventing the release of vasoactive neurotransmitters, and avoiding triggering foods. This article reviews much of the research on nutritional, botanical, dietary, and other alternative approaches to the treatment and prevention of migraines.

Altern Med Rev. 1999 Apr;4(2):86-95

ETIOLOGY AND PATHOGENESIS OF CLUSTER HEADACHE.

This last decade has seen remarkable progress made toward unraveling the mystery of primary headache disorders like migraine and cluster. The vascular theory has been superseded by recognition that neurovascular phenomena seem to be the permissive and triggering factors in migraine and cluster headache. This understanding has been achieved through new imaging modalities such as positron emission tomography and functional magnetic resonance imaging. Prior to these imaging techniques it was impossible to study the primary headache disorders because these had no structural basis. There is now an increasing body of evidence that the brain is involved primarily in cluster and migraine and that vessel dilatation is an epiphenomenon.

Curr Pain Headache Rep. 2002 Feb;6(1):71-5

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