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ABSTRACTS

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Carnosine

Protective effects of carnosine against malondialdehyde-induced toxicity towards cultured rat brain endothelial cells.

Malondialdehyde (MDA) is a deleterious end-product of lipid peroxidation. The naturally-occurring dipeptide carnosine (beta-alanyl-L-histidine) is found in brain and innervated tissues at concentrations up to 20 mM. Recent studies have shown that carnosine can protect proteins against cross-linking mediated by aldehyde-containing sugars and glycolytic intermediates. Here we have investigated whether carnosine is protective against malondialdehyde-induced protein damage and cellular toxicity. The results show that carnosine can (1) protect cultured rat brain endothelial cells against MDA-induced toxicity and (2) inhibit MDA-induced protein modification (formation of cross-links and carbonyl groups).

Neurosci Lett 1997 Dec 5;238(3):135-8

The antihypertensive hydralazine is an efficient scavenger of acrolein.

Recent work indicates the highly toxic alpha,beta-unsaturated aldehyde acrolein is formed during the peroxidation of polyunsaturated lipids, raising the possibility that it functions as a 'toxicological second messenger' during oxidative cell injury. Acrolein reacts rapidly with proteins, forming adducts that retain carbonyl groups. Damage by this route may thus contribute to the burden of carbonylated proteins in tissues. This work evaluated several amine compounds with known aldehyde-scavenging properties for their ability to attenuate protein carbonylation by acrolein. The compounds tested were: (i) the glycooxidation inhibitors, aminoguanidine and carnosine; (ii) the antihypertensive, hydralazine; and (iii) the classic carbonyl reagent, methoxyamine. Each compound attenuated carbonylation of a model protein, bovine serum albumin, during reactions with acrolein at neutral pH and 37 degrees C. However, the most efficient agent was hydralazine, which strongly suppressed carbonylation under these conditions. Study of the rate of reaction between acrolein and the various amines in a protein-free buffered system buttressed these findings, since hydralazine reacted with acrolein at rates 2-3 times faster than its reaction with the other scavengers. Hydralazine also protected isolated mouse hepatocytes against cell killing by allyl alcohol, which undergoes in situ alcohol dehydrogenase-catalysed conversion to acrolein.

Redox Rep 2000;5(1):47-9

Carnosine reacts with a glycated protein.

Oxidation and glycation induce formation of carbonyl (CO) groups in proteins, a characteristic of cellular aging. The dipeptide carnosine (beta-alanyl-L-histidine) is often found in long-lived mammalian tissues at relatively high concentrations (up to 20 mM). Previous studies show that carnosine reacts with low-molecular-weight aldehydes and ketones. We examine here the ability of carnosine to react with ovalbumin CO groups generated by treatment of the protein with methylglyoxal (MG). Incubation of MG-treated protein with carnosine accelerated a slow decline in CO groups as measured by dinitrophenylhydrazine reactivity. Incubation of [(14)C]-carnosine with MG-treated ovalbumin resulted in a radiolabeled precipitate on addition of trichloroacetic acid (TCA); this was not observed with control, untreated protein. The presence of lysine or N-(alpha)-acetylglycyl-lysine methyl ester caused a decrease in the TCA-precipitable radiolabel. Carnosine also inhibited cross-linking of the MG-treated ovalbumin to lysine and normal, untreated alpha-crystallin. We conclude that carnosine can react with protein CO groups (termed "carnosinylation") and thereby modulate their deleterious interaction with other polypeptides. It is proposed that, should similar reactions occur intracellularly, then carnosine's known "anti-aging" actions might, at least partially, be explained by the dipeptide facilitating the inactivation/removal of deleterious proteins bearing carbonyl groups.

Free Radic Biol Med 2000 May 15;28(10):1564-70

Toxic effects of beta-amyloid(25-35) on immortalised rat brain endothelial cell: protection by carnosine, homocarnosine and beta-

alanine.

The effect of a truncated form of the neurotoxin beta-amyloid peptide (A beta25-35) on rat brain vascular endothelial cells (RBE4 cells) was studied in cell culture. Toxic effects of the peptide were seen at 200 microg/ml A beta using a mitochondrial dehydrogenase activity (MTT) reduction assay, lactate dehydrogenase release and glucose consumption. Cell damage could be prevented completely at 200 microg/ml A beta and partially at 300 microg/ml A beta, by the dipeptide carnosine. Carnosine is a naturally occurring dipeptide found at high levels in brain tissue and innervated muscle of mammals including humans. Agents which share properties similar to carnosine, such as beta-alanine, homocarnosine, the anti-glycating agent aminoguanidine, and the antioxidant superoxide dismutase (SOD), also partially rescued cells, although not as effectively as carnosine. We postulate that the mechanism of carnosine protection lies in its anti-glycating and antioxidant activities, both of which are implicated in neuronal and endothelial cell damage during Alzheimer's disease. Carnosine may therefore be a useful therapeutic agent.

Neurosci Lett 1998 Feb 13;242(2):105-8

Hydrogen peroxide-mediated protein oxidation in young and old human MRC-5 fibroblasts.

It is suggested that the aging process is dependent on the action of free radicals. One of the highlights of age-related changes of cellular metabolism is the accumulation of oxidized proteins. The present investigation was undertaken to reveal the proliferation-related changes in the protein oxidation and proteasome activity during and after an acute oxidative stress. It could be demonstrated that the activity of the cytosolic proteasomal system declines during proliferative senescence of human MRC-5 fibroblasts and is not able to remove oxidized proteins in old cells efficiently. Whereas in young cells removal of oxidized proteins was accompanied by an increase in the overall protein turnover, this increase in protein turnover could not be seen in old MRC-5 fibroblasts. Therefore, our studies demonstrate that old fibroblasts are much more vulnerable to the accumulation of oxidized proteins after oxidative stress and are not able to remove these oxidized proteins as efficiently as young fibroblasts.

Arch Biochem Biophys 2000 Mar 1;375(1):50-4

Carnosine protects against excitotoxic cell death independently of effects on reactive oxygen species.

The role of carnosine, N-acetylcarnosine and homocarnosine as scavengers of reactive oxygen species and protectors against neuronal cell death secondary to excitotoxic concentrations of kainate and N-methyl-D-aspartate was studied using acutely dissociated cerebellar granule cell neurons and flow cytometry. We find that carnosine, N-acetylcarnosine and homocarnosine at physiological concentrations are all potent in suppressing fluorescence of 2',7'-dichlorofluorescein, which reacts with intracellularly generated reactive oxygen species. However, only carnosine in the same concentration range was effective in preventing apoptotic neuronal cell death, studied using a combination of the DNA binding dye, propidium iodide, and a fluorescent derivative of the phosphatidylserine-binding dye, Annexin-V. Our results indicate that carnosine and related compounds are effective scavengers of reactive oxygen species generated by activation of ionotropic glutamate receptors, but that this action does not prevent excitotoxic cell death. Some other process which is sensitive to carnosine but not the related compounds is a critical factor in cell death. These observations indicate that at least in this system reactive oxygen species generation is not a major contributor to excitotoxic neuronal cell death.

Neuroscience 1999;94(2):571-7

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COX-2 Inhibitors

n-3 fatty acids specifically modulate catabolic factors involved in articular cartilage degradation.

This study describes specific molecular mechanisms by which supplementation with n-3 fatty acids (i.e. those present in fish oils) can modulate the expression and activity of degradative and inflammatory factors that cause cartilage destruction during arthritis. Our data show that incorporation of n-3 fatty acids (but not other polyunsaturated or saturated fatty acids) into articular cartilage chondrocyte membranes results in a dose-dependent reduction in: (i) the expression and activity of proteoglycan degrading enzymes (aggrecanases) and (ii) the expression of inflammation-inducible cytokines (interleukin (IL)-1 α and tumor necrosis factor (TNF)- α) and cyclooxygenase (COX-2), but not the constitutively expressed cyclooxygenase COX-1. These findings provide evidence that n-3 fatty acid supplementation can specifically affect regulatory mechanisms involved in chondrocyte gene transcription and thus further advocate a beneficial role for dietary fish oil supplementation in alleviation of several of the physiological parameters that cause and propagate

J Biol Chem 2000 Jan 14;275(2):721-4

n-3 polyunsaturated fatty acids and cytokine production in health and disease.

Arachidonic-acid-derived eicosanoids modulate the production of pro-inflammatory and immunoregulatory cytokines. Overproduction of these cytokines is associated with both septic shock and chronic inflammatory diseases. The n-3 polyunsaturated fatty acids (PUFAs) eicosapentaenoic acid (EPA) and docosahexaenoic acid, which are found in fish oils, suppress the production of arachidonic-acid-derived eicosanoids and EPA is a substrate for the synthesis of an alternative family of eicosanoids. Thus, dietary fats which are rich in n-3 PUFAs have the potential to alter cytokine production. Animal studies have provided a great deal of evidence that feeding plant or fish oils rich in n-3 PUFAs does alter the ex vivo production of tumour necrosis factor (TNF), interleukin 1 (IL-1), IL-6 and IL-2, but many contradictory observations have been made; it is most likely that the discrepancies in the literature result from differences in the cell types and experimental protocols used. Human studies provide more consistent data: several studies have shown that supplementation of the diet of healthy volunteers results in reduced ex vivo production of IL-1, IL-6, TNF and IL-2 by peripheral blood mononuclear cells. Similar findings have been made in patients with rheumatoid arthritis and multiple sclerosis. Animal studies indicate that dietary fish oil reduces the response to endotoxin and to pro-inflammatory cytokines, resulting in increased survival; such diets have been beneficial in some models of bacterial challenge, chronic inflammation and auto-immunity. These beneficial effects of dietary n-3 PUFAs may be of use as a therapy for acute and chronic inflammation and for disorders which involve an inappropriately activated immune response.

Ann Nutr Metab 1997;41(4):203-34

Differential regulation of prostaglandin E2 and thromboxane A2 production in human monocytes: implications for the use of cyclooxygenase inhibitors.

There is an autocrine relationship between eicosanoid and cytokine synthesis, with the ratio of prostaglandin E2 (PGE2)/thromboxane A2 (TXA2) being one of the determinants of the level of cytokine synthesis. In monocytes, cyclooxygenase type 1 (COX-1) activity appears to favor TXA2 production and COX-2 activity appears to favor PGE2 production. This has led to speculation regarding possible linkage of COX isozymes with PGE and TXA synthase. We have studied the kinetics of PGE2 and TXA2 synthesis under conditions that rely on COX-1 or -2 activity. With small amounts of endogenously generated prostaglandin H2 (PGH2), TXA2 synthesis was greater than PGE2. With greater amounts of endogenously generated PGH2, PGE2 synthesis was greater than TXA2. Also, TXA synthase was saturated at lower substrate concentrations than PGE synthase. This pattern was observed irrespective of whether PGH2 was produced by COX-1 or COX-2 or whether it was added directly. Furthermore, the inhibition of eicosanoid production by the action of nonsteroidal anti-inflammatory drugs or by the prevention of COX-2 induction with the p38 mitogen-activated protein kinase inhibitor SKF86002 was greater for PGE2 than for TXA2. It is proposed that different kinetics of PGE synthase and TXA synthase account for the patterns of production of these eicosanoids in monocytes under a variety of experimental conditions. These properties provide an alternative explanation to notional linkage or compartmentalization of COX-1 or -2 with the respective terminal synthases and that therapeutically induced changes in eicosanoid ratios toward predominance of TXA2 may have unwanted effects in long-term anti-inflammatory and anti-arthritic therapy.

Proinflammatory cytokines detectable in synovial fluids from patients with temporomandibular disorders.

OBJECTIVE: To measure the levels of the proinflammatory cytokines, interleukin (IL)-1 beta, IL-6, tumor necrosis factor- (TNF) alpha, IL-8, and interferon- (IFN) gamma in synovial fluid samples taken from patients with temporomandibular disorders (TMD). **STUDY DESIGN:** We studied 6 asymptomatic volunteers and 51 patients with TMD. The IL-1 beta, IL-6, TNF-alpha, IL-8, and IFN-gamma levels in temporomandibular joint synovial fluid were measured using enzyme-linked immunosorbent assay. **RESULTS:** Measurable level of at least one cytokine in the synovial fluid was found in 40 (64.5%) of 62 joints in the patients: IL-1 beta and IFN-gamma were each detected in 18 (29.0%) of 62 joints; IL-6 in 13 (21.0%) of 62 joints; IL-8 in 11 (19.3%) of 57 joints; and TNF-alpha in only 5 (8.1%) of 62 joints. None of these cytokines was detectable in the synovial fluid in the control group. Furthermore, there was a strong correlation between the detection of IL-1 beta and pain in the joint area. **CONCLUSIONS:** These data clearly demonstrate increased levels of several proinflammatory cytokines in certain patients with TMD and suggest that these cytokines may play a role in the pathogenesis of synovitis and degenerative changes of the cartilaginous tissue and bone of the temporomandibular joint.

Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998 Feb;85(2):135-41

Plant extracts from stinging nettle (*Urtica dioica*), an antirheumatic remedy, inhibit the proinflammatory transcription factor NF-kappaB.

Activation of transcription factor NF-kappaB is elevated in several chronic inflammatory diseases and is responsible for the enhanced expression of many proinflammatory gene products. Extracts from leaves of stinging nettle (*Urtica dioica*) are used as antiinflammatory remedies in rheumatoid arthritis. Standardized preparations of these extracts (IDS23) suppress cytokine production, but their mode of action remains unclear. Here we demonstrate that treatment of different cells with IDS23 potently inhibits NF-kappaB activation. An inhibitory effect was observed in response to several stimuli, suggesting that IDS23 suppressed a common NF-kappaB pathway. Inhibition of NF-kappaB activation by IDS23 was not mediated by a direct modification of DNA binding, but rather by preventing degradation of its inhibitory subunit I kappa B-alpha. Our results suggests that part of the antiinflammatory effect of *Urtica* extract may be ascribed to its inhibitory effect on NF-kappaB activation.

FEBS Lett 1999 Jan 8;442(1):89-94

Inhibition of prostaglandin and leukotriene biosynthesis by gingerols and diarylheptanoids.

The rhizomes of *Zingiber officinale* (ginger) and *Alpinia officinarum* contain potent inhibitors against prostaglandin biosynthesizing enzyme (PG synthetase). Gingerols and diarylheptanoids were identified as active compounds. Their possible mechanism of action which was deduced from the structures of active compounds indicated that the inhibitors would also be active against arachidonate 5-lipoxygenase, an enzyme of leukotriene (LT) biosynthesis. This was verified by testing their inhibitory effects on 5-lipoxygenase prepared from RBL-1 cells. A diarylheptanoid with catechol group was the most active compound against 5-lipoxygenase, while yakuchinone A was the most active against PG synthetase.

Chem Pharm Bull (Tokyo) 1992 Feb;40(2):387-91

Inhibition of human neutrophil 5-lipoxygenase activity by gingerdione, shogaol, capsaicin and related pungent compounds.

A series of structurally related pungent natural products including capsaicin, gingerol, and gingerdione among others were evaluated and found to be potent inhibitors of 5-HETE biosynthesis in intact human leukocytes, with IC50 values of 100 and 15 microM for capsaicin and gingerdione, respectively. Several compounds within this series were also found to inhibit PGE2 formation, with the most potent being gingerdione (IC50 = 18 microM). These and other data indicate that members of the capsaicin/gingerol family of pungent compounds can act as dual inhibitors of arachidonic acid metabolism, which could account in part for the antiinflammatory and analgesic properties of compounds within this group.

Prostaglandins Leukot Med 1986 Oct;24(2-3):195-8

Efficacy and safety of glucosamine sulfate versus ibuprofen in patients with knee osteoarthritis.

A double-blind therapeutic investigation was performed on 178 Chinese patients suffering from osteoarthritis of the knee randomized into two groups, one treated for 4 weeks with glucosamine sulfate (GS, CAS 29031-19-4, Viartil-S) at the daily dose of 1,500 mg and the other with ibuprofen (IBU, CAS 15687-27-1) at the daily dose of 1,200 mg. Knee pain at rest, at movement and at pressure, knee swelling, improvement and therapeutic utility as well as adverse events and drop-outs were recorded after 2 and 4 weeks of treatment. The variables were recorded also after 2 weeks of treatment discontinuation in order to appreciate the remnant

therapeutic effect. Both GS and IBU significantly reduced the symptoms of osteoarthritis with the trend of GS to be more effective. After 2 weeks of drug discontinuation there was a remnant therapeutic effect in both groups, with the trend to be more pronounced in the GS group. GS was significantly better tolerated than IBU, as shown by the adverse drug reactions (6% in the patients of the GS group and 16% in the IBU group-- $p = 0.02$) and by the drug-related drop-outs (0% of the patients in the GS group and 10% in the IBU group-- $p = 0.0017$). The better tolerability of GS is explained by its mode of action, because GS specifically curbs the pathogenic mechanisms of osteoarthritis and does not inhibit the cyclo-oxygenases as the non-steroidal anti-inflammatory drugs (NSAIDs) do, with the consequent anti-inflammatory analgesic activities but also with the several adverse reactions due to this not targeted effect. The present study confirms that GS is a selective drug for osteoarthritis, as effective on the symptoms of the disease as NSAIDs but significantly better tolerated. For these properties GS seems particularly indicated in the long-term treatments needed in osteoarthritis.

Arzneimittelforschung 1998 May;48(5):469-74

Selective Inhibition of Cyclooxygenase-2 by C-Phycocyanin, a Biliprotein from *Spirulina platensis*.

We report data from two related assay systems (isolated enzyme assays and whole blood assays) that C-phycocyanin a biliprotein from *Spirulina platensis* is a selective inhibitor of cyclooxygenase-2 (COX-2) with a very low IC(50) COX-2/IC(50) COX-1 ratio (0.04). The extent of inhibition depends on the period of preincubation of phycocyanin with COX-2, but without any effect on the period of preincubation with COX-1. The IC(50) value obtained for the inhibition of COX-2 by phycocyanin is much lower (180 nM) as compared to those of celecoxib (255 nM) and rofecoxib (401 nM), the well-known selective COX-2 inhibitors. In the human whole blood assay, phycocyanin very efficiently inhibited COX-2 with an IC(50) value of 80 nM. Reduced phycocyanin and phycocyanobilin, the chromophore of phycocyanin are poor inhibitors of COX-2 without COX-2 selectivity. This suggests that apoprotein in phycocyanin plays a key role in the selective inhibition of COX-2. The present study points out that the hepatoprotective, anti-inflammatory, and anti-arthritic properties of phycocyanin reported in the literature may be due, in part, to its selective COX-2 inhibitory property, although its ability to efficiently scavenge free radicals and effectively inhibit lipid peroxidation may also be involved.

Biochem Biophys Res Commun 2000 Nov 2;277(3):599-603

Selective inhibition of cyclooxygenase-2 suppresses growth and induces apoptosis in human esophageal adenocarcinoma cells.

Adenocarcinoma in Barrett's esophagus has been increasing in incidence at a rapid rate for more than two decades. Cyclooxygenase (COX)-2 appears to play an important role in gastrointestinal carcinogenesis, and COX-2 overexpression has been demonstrated both in esophageal adenocarcinomas and in the metaplastic epithelium of Barrett's esophagus. The aim of our study was to determine whether selective inhibition of COX-2 by NS-398 would alter the rates of cell growth and apoptosis in human Barrett's-associated esophageal adenocarcinoma cell lines. COX-1 and COX-2 expression in adenocarcinoma cell lines was determined using reverse transcription-PCR and Western blotting for mRNA and protein, respectively. Esophageal adenocarcinoma cell lines were treated with various concentrations of NS-398 (selective for COX-2 inhibition) and flurbiprofen (selective for COX-1 inhibition). Cell growth was compared in flurbiprofen-treated and untreated tumor cell lines; cell growth and apoptosis were compared in NS-398-treated and untreated tumor cell lines. COX-2 mRNA and protein were detected in two of three cell lines (SEG-1 and FLO); the third cell line, BIC-1, did not express COX-2 mRNA or protein under basal conditions or after stimulation with phorbol 12-myristate 13-acetate. Treatment with COX-1-selective concentrations of flurbiprofen did not affect cell growth in any of the three tumor cell lines. In contrast, treatment with COX-2-selective concentrations of NS-398 significantly suppressed cell growth and increased apoptosis in the cell lines that expressed COX-2 (SEG-1 and FLO), but not in the cell line that did not express COX-2 (BIC-1). We conclude that the administration of a selective inhibitor of COX-2 significantly decreases cell growth and increases apoptosis in Barrett's-associated adenocarcinoma tumor cells that express COX-2. These observations suggest a potential role for selective COX-2 inhibitors in the prevention and treatment of esophageal adenocarcinoma for patients with Barrett's esophagus.

Cancer Res 2000 Oct 15;60(20):5767-72

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Child Health

Vitamin A status in children with pneumonia.

OBJECTIVE: To assess vitamin A status in children with pneumonia. **INTERVENTIONS:** Thirty-four hospitalised patients with pneumonia were randomly allocated into two groups: the study group, besides the routine treatment, received a high dose of aqueous retinyl palmitate oral solution; the control group received only the routine treatment. **METHODS:** The concentrations of plasma vitamin A and carotenoids were determined by colorimetric method. Retinol binding protein (RBP) was determined by the radial immunodiffusion technique. **RESULTS:** After 1 week of treatment there was a statistically significant ($P < 0.05$) increase in the levels (mean \pm s.e.) of vitamin A (study group: 14.1 \pm 1.6 to 26.5 \pm 5.8 micrograms/dl; control group: 16.1 \pm 3.3 to 24.1 \pm 2.3 micrograms/dl) and RBP (study group: 0.8 \pm 0.2 to 2.2 \pm 0.6 mg/dl; control group: 0.6 \pm 0.2 to 3.0 \pm 0.5 mg/dl) in both groups as compared to the baseline. On day 7 of treatment when the average levels of vitamin A (26.5 \pm 5.8 and 24.1 \pm 2.3 micrograms/dl) were compared, there was no statistically significant difference between the groups. **CONCLUSION:** This study suggests that low levels of circulating plasma vitamin A in child with pneumonia may be a consequence of acute phase of infectious disease.

Eur J Clin Nutr 1995 May;49(5):379-84

Signs of impaired cognitive function in adolescents with marginal cobalamin status.

BACKGROUND: Lack of cobalamin may lead to neurologic disorders, which have been reported in strict vegetarians. **OBJECTIVE:** The objective of this study was to investigate whether cognitive functioning is affected in adolescents (aged 10-16 y) with marginal cobalamin status as a result of being fed a macrobiotic diet up to an average age of 6 y. **DESIGN:** Data on dietary intake, psychological test performance, and biochemical variables of cobalamin status were collected from 48 adolescents who consumed macrobiotic (vegan type) diets up to the age of 6 y, subsequently followed by lactovegetarian or omnivorous diets, and from 24 subjects (aged 10-18 y) who were fed omnivorous diets from birth onward. Thirty-one subjects from the previously macrobiotic group were cobalamin deficient according to their plasma methylmalonic acid concentrations. Seventeen previously macrobiotic subjects and all control subjects had normal cobalamin status. **RESULTS:** The control subjects performed better on most psychological tests than did macrobiotic subjects with low or normal cobalamin status. A significant relation between test score and cobalamin deficiency ($P = 0.01$) was observed for a test measuring fluid intelligence (correlation coefficient: -0.28; 95% CI: -0.48, -0.08). This effect became more pronounced ($P = 0.003$) within the subgroup of macrobiotic subjects (correlation coefficient: -0.38; 95% CI: -0.62, -0.14). **CONCLUSION:** Our data suggest that cobalamin deficiency, in the absence of hematologic signs, may lead to impaired cognitive performance in adolescents.

Am J Clin Nutr 2000 Sep;72(3):762-9

The relation of overweight to cardiovascular risk factors among children and adolescents: the Bogalusa Heart Study.

BACKGROUND: Although overweight and obesity in childhood are related to dyslipidemia, hyperinsulinemia, and hypertension, most studies have examined levels of these risk factors individually or have used internal cutpoints (eg, quintiles) to classify overweight and risk factors. **OBJECTIVE:** We used cutpoints derived from several national studies to examine the relation of overweight (Quetelet index, >95 th percentile) to adverse risk factor levels and risk factor clustering. **DESIGN:** The sample consisted of 9167 5- to 17-year-olds examined in seven cross-sectional studies conducted by the Bogalusa Heart Study between 1973 and 1994. **RESULTS:** About 11% of examined schoolchildren were considered overweight. Although adverse lipid, insulin, and blood pressure levels did not vary substantially with the Quetelet index at levels <85 th percentile, risk factor prevalences increased greatly at higher levels of the Quetelet index. Overweight schoolchildren were 2.4 times as likely as children with a Quetelet index <85 th percentile to have an elevated level of total cholesterol. Odds ratios for other associations were 2.4 (diastolic blood pressure), 3.0 (low-density lipoprotein cholesterol), 3.4 (high-density lipoprotein cholesterol), 4.5 (systolic blood pressure), 7.1 (triglycerides), and 12.6 (fasting insulin). Several of these associations differed between whites and blacks, and by age. Of the 813 overweight schoolchildren, 475 (58%) were found to have at least one risk factor. Furthermore, the use of overweight as a screening tool could identify 50% of schoolchildren who had two or more risk factors. **CONCLUSIONS:** Because overweight is associated with various risk factors even among young children, it is possible that the successful prevention and treatment of obesity in childhood could reduce the adult incidence of cardiovascular disease.

Attention Deficit/Hyperactivity disorder (ADHD) in children: rationale for its integrative management.

Attention Deficit/Hyperactivity Disorder (ADHD) is the most common behavioral disorder in children. ADHD is characterized by attention deficit, impulsivity, and sometimes overactivity ("hyperactivity"). The diagnosis is empirical, with no objective confirmation available to date from laboratory measures. ADHD begins in childhood and often persists into adulthood. The exact etiology is unknown; genetics plays a role, but major etiologic contributors also include adverse responses to food additives, intolerances to foods, sensitivities to environmental chemicals, molds, and fungi, and exposures to neurodevelopmental toxins such as heavy metals and organohalide pollutants. Thyroid hypofunction may be a common denominator linking toxic insults with ADHD symptomatology. Abnormalities in the frontostriatal brain circuitry and possible hypofunctioning of dopaminergic pathways are apparent in ADHD, and are consistent with the benefits obtained in some instances by the use of methylphenidate (Ritalin) and other potent psychostimulants. Mounting controversy over the widespread use of methylphenidate and possible life-threatening effects from its long-term use make it imperative that alternative modalities be implemented for ADHD management. Nutrient deficiencies are common in ADHD; supplementation with minerals, the B vitamins (added in singly), omega-3 and omega-6 essential fatty acids, flavonoids, and the essential phospholipid phosphatidylserine (PS) can ameliorate ADHD symptoms. When individually managed with supplementation, dietary modification, detoxification, correction of intestinal dysbiosis, and other features of a wholistic/integrative program of management, the ADHD subject can lead a normal and productive life.

Altern Med Rev. 2000 Oct;5(5):402-428.

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