

Asthma

ABSTRACTS

- Allen DB., Inhaled corticosteroid therapy for asthma in preschool children: growth issues.
- Armentia A., 2001. Early introduction of cereals into children's diets as a risk-factor for grass pollen asthma.
- Baker JC., 2000. Diet and asthma.
- Balachandran A., 2001. Drug therapy of childhood asthma.
- Bengtsson A., 2001. Thiols decrease cytokine levels and down-regulate the expression of CD30 on human allergen-specific T helper (Th) 0 and Th2 cells.
- Boushey HA Jr., Experiences with monoclonal antibody therapy for allergic asthma.
- Bremner P, 2002. Natural products as targeted modulators of the nuclear factor-kappaB pathway.
- Brown KM., 2001. Selenium, selenoproteins and human health: a review.
- Centanni S., 2001. The potential role of tocopherol in asthma and allergies: modification of the leukotriene pathway.
- Corradi M., 2001. Increased nitrosothiols in exhaled breath condensate in inflammatory airway diseases.
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- Hijazi N., 2000. Diet and childhood asthma in a society in transition: a study in urban and rural Saudi Arabia.
- Huang SL., 2001. Dietary factors associated with physician-diagnosed asthma and allergic rhinitis in teenagers: analyses of the first Nutrition and Health Survey in Taiwan.
- Huang SL., 2001. Dietary fats and asthma in teenagers: analyses of the first Nutrition and Health Survey in Taiwan (NAHSIT).
- Kalliomaki M., 2001. Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial.
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Inhaled corticosteroid therapy for asthma in preschool children: growth issues.

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Although inhaled corticosteroids (ICS) have emerged as the preventive treatment of choice for persistent asthma, few studies have been conducted in infants and very young children that assess the benefits and risks of ICS therapy, particularly with regard to growth. Oral glucocorticoids inhibit growth at multiple levels by blunting pulsatile growth hormone (GH) secretion, decreasing insulin-like growth factor-1 bioactivity, and directly inhibiting new collagen synthesis. Normal childhood growth can be divided conceptually into 3 phases according to primary growth-supporting factors: nutrition-dependent growth of infancy, GH-dependent childhood growth, and sex steroid/GH stimulation of pubertal growth. Susceptibility to glucocorticoid-induced growth suppression appears to increase during periods of transition from one phase to another, particularly in the immediate prepubertal years. Studies using ICS at varying dosages demonstrate the possibility of short-term growth suppression, but long-term studies suggest a negligible effect, if any, on final adult height or bone mineral density. Although certain speculations regarding the safety of ICS use in infants and very young children can be made based on these data, age-specific studies are needed to account for effects of differences in oral versus airway deposition and growth axis resiliency, which may occur in these patients.

Early introduction of cereals into children's diets as a risk-factor for grass pollen asthma.

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Clin Exp Allergy 2001 Aug;31(8):1250-5

BACKGROUND: The prevalence of asthma has increased from the 1950s to the 1990s. The relationship between diet and asthma is an area of controversy that has never been fully evaluated. Attempts at dietary prevention of asthma have produced conflicting results. We have recently identified allergens from cereals that show cross-reactivity with proteins in grass pollen. An early intake of cereals in the diet during early life might cause IgE sensitization to cereals. It is not known whether such sensitization predisposes the development of allergy to pollen.

METHODS: To test this hypothesis, a cross-sectional study and an observational case-control analysis of reviewed data were carried out on 16381 patients who had been admitted to our Allergy Unit between 1989 and 1999. All the patients underwent allergy tests to identify asthma risk-factors. All information in our data base was analysed using the SPSS computer system.

RESULTS: There has been an increase of 7.8% in incidences of allergic asthma and a 7.3% increase in asthma due to grass pollen in the last decade. Grass-pollen asthma was associated with sensitization to cereals. The early introduction of cereals in the diet of children was found to be a risk factor for grass-pollen asthma (OR = 5.95; 95% CI 3.89-9.10).

CONCLUSIONS: These findings document the progression of allergic asthma during a decade in a large sample of people who were influenced by similar environmental conditions and studied with the same diagnostic methods. This study represents the largest database of patients in which a common food is shown to be a risk factor for asthma.

Diet and asthma.

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Respir Med 2000 Oct;94(10):925-34

The role of food intolerance in asthma is well recognized, and where food avoidance measures are instituted considerable improvement in asthma symptoms and in reduction in drug therapy and hospital admissions can result. These benefits may have a greater impact in those patients with greater symptoms. However, the promise of such benefits should not result in an approach which ignores inhaled drug therapy, or in a dietary regime which is inappropriate in the face of mild symptoms. Whilst sub-optimal intake of dietary nutrients is also a recently recognized potential risk factor for asthma, available data are insufficient to implicate any as casual. A number of studies have sought to establish the role of the antioxidant vitamins, A, C and E and selenium, yet others of the elements sodium and magnesium. Sub-optimal nutrient intake may enhance asthmatic inflammation, consequently contributing to bronchial hyperreactivity. Prospective studies of supplementation therapy are needed to confirm this.

Drug therapy of childhood asthma

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Indian J Pediatr 2001 Sep;68 Suppl 4:S12-6

Drug therapy is used to prevent and control asthma, and also to reduce the frequency and severity of its exacerbations, and reverse airflow obstruction. Asthma medications are thus categorized into two general classes--bronchodilators (relievers) and anti-inflammatory drugs (preventers). Short acting beta2-agonists is the therapy of choice for relief of acute symptoms and prevention of exercise induced bronchospasm (EIB). Corticosteroids are the most potent and effective anti-inflammatory medication currently available. Inhaled form is used in the long-term control of asthma. Systemic corticosteroids are used to gain prompt control of the disease when initiating long-term therapy. Long acting bronchodilator used concomitantly with anti-inflammatory medications for long-term control of symptoms, especially nocturnal symptoms. Ipratropium bromide may provide some additive benefit to inhaled beta2-agonists in severe exacerbations. Sustained release theophylline is a mild to moderate bronchodilator used principally as adjuvant to inhaled corticosteroids for prevention of nocturnal asthma. Leukotriene modifiers may be considered as an alternative therapy to inhaled corticosteroids or cromolyn or nedocromil.

Thiols decrease cytokine levels and down-regulate the expression of CD30 on human allergen-specific T helper (Th) 0 and Th2 cells.

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Clin Exp Immunol 2001 Mar;123(3):350-60

The thiol antioxidant N-acetyl- L-cysteine (NAC), known as a precursor of glutathione (GSH), is used in AIDS treatment trials, as a chemoprotectant in cancer chemotherapy and in treatment of chronic bronchitis. In vitro, GSH and NAC are known to enhance T cell proliferation, production of IL-2 and up-regulation of the IL-2 receptor. The 120-kD CD30 surface antigen belongs to the tumour necrosis factor (TNF) receptor superfamily. It is expressed by activated T helper (Th) cells and its expression is sustained in Th2 cells. We have analysed the effect of GSH and NAC on the cytokine profile and CD30 expression on human allergen-specific T cell clones (TCC). TCC were stimulated with anti-CD3 antibodies in the presence of different concentrations of GSH and NAC. Both thiols caused a dose dependent down-regulation of IL-4, IL-5 and IFN-gamma levels in Th0 and Th2 clones, with the most

pronounced decrease of IL-4. Furthermore, the surface expression of CD30, and the levels of soluble CD30 (sCD30) in the culture supernatants were decreased. In contrast, the surface expression of CD28 or CD40 ligand (CD40L) was not significantly changed after treatment with 20 mM NAC. These results indicate that GSH and NAC favour a Th1 response by a preferential down-regulation of IL-4. In addition, the expression of CD30 was down regulated by GSH and NAC, suggesting that CD30 expression is dependent on IL-4, or modified by NAC. In the likely event that CD30 and its soluble counterpart prove to contribute to the pathogenesis in Th2 related diseases such as allergy, NAC may be considered as a future therapeutic agent in the treatment of these diseases.

Experiences with monoclonal antibody therapy for allergic asthma.

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J Allergy Clin Immunol 2001 Aug;108(2 Suppl):S77-83

Identification of the central role IgE plays in the pathogenesis of allergic diseases made it a key target for therapy. The first selective anti-IgE therapy, a unique humanized monoclonal anti-IgE antibody (omalizumab), binds with high affinity to the Fc(epsilon)RI receptor binding site on IgE, thereby reducing the amount of free IgE available to bind to Fc(epsilon)RI receptors on mast cells, basophils, and other cells. In addition, administration of omalizumab indirectly reduces Fc(epsilon)RI receptor density on cells involved in allergic responses. In two bronchoprovocation trials involving patients with mild allergic asthma, omalizumab attenuated both early- and late-phase allergic responses. Omalizumab was subsequently evaluated as a treatment for asthma in large, multicenter, randomized, double-blind phase II and III trials involving patients with moderate to severe asthma who required corticosteroid therapy. When added to treatment with oral or inhaled corticosteroids, omalizumab reduced symptoms and exacerbations, improved lung function and quality of life, and reduced the need for rescue medications. These benefits persisted even in the "corticosteroid reduction" phase of these trials, when omalizumab treatment was shown to allow patients to reduce or discontinue their inhaled and/or oral corticosteroids. These effects of omalizumab in improving asthma control, as well as its excellent safety profile, may ultimately make this agent a useful addition to the physician's armamentarium of treatments for asthma.

Natural products as targeted modulators of the nuclear factor-kappaB pathway.

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J Pharm Pharmacol 2002 Apr;54(4):453-72

The use of plant extracts to alleviate inflammatory diseases is centuries old and continues to this day. This review assesses the current understanding of the use of such plants and natural products isolated from them in terms of their action against the ubiquitous transcription factor, nuclear factor kappa B (NF-kappaB). As an activator of many pro-inflammatory cytokines and inflammatory processes the modulation of the NF-kappaB transduction pathway is a principal target to alleviate the symptoms of such diseases as arthritis, inflammatory bowel disease and asthma. Two pathways of NF-kappaB activation will first be summarised, leading to the IKK (IkkappaB kinase) complex, that subsequently initiates phosphorylation of the NF-kappaB inhibitory protein (IKB). Natural products and some extracts are reviewed and assessed for their activity and potency as NF-kappaB inhibitors. A large number of compounds are currently known as NF-kappaB modulators and include the isoprenoids, most notably kaurene diterpenoids and members of the sesquiterpene lactones class, several phenolics including curcumin and flavonoids such as silybin. Additional data on cellular toxicity are also highlighted as an exclusion principle for pursuing such compounds in clinical development. In addition, where enough data exists some conclusions on structure-activity relationship are provided.

Selenium, selenoproteins and human health: a review.

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Public Health Nutr 2001 Apr;4(2B):593-9

Selenium is of fundamental importance to human health. It is an essential component of several major metabolic pathways, including thyroid hormone metabolism, antioxidant defence systems, and immune function. The decline in blood selenium concentration in the UK and other European Union countries has therefore several potential public health implications, particularly in relation to the chronic disease prevalence of the Western world such as cancer and cardiovascular disease. Ten years have elapsed since recommended dietary intakes of selenium were introduced on the basis of blood glutathione peroxidase activity. Since then 30 new selenoproteins have been identified, of which 15 have been purified to allow characterisation of their biological function. The long term health implications in relation to declining selenium intakes have not yet been thoroughly examined, yet the implicit importance of selenium to human health is recognised universally. Selenium is incorporated as selenocysteine at the active site of a wide range of selenoproteins. The four glutathione peroxidase enzymes (classical GPx1, gastrointestinal GPx2, plasma GPx3, phospholipid hydroperoxide GPx4) which represent a major class of functionally important selenoproteins, were the first to be

characterised. Thioredoxin reductase (TR) is a recently identified seleno-cysteine containing enzyme which catalyzes the NADPH dependent reduction of thioredoxin and therefore plays a regulatory role in its metabolic activity. Approximately 60% of Se in plasma is incorporated in selenoprotein P which contains 10 Se atoms per molecule as selenocysteine, and may serve as a transport protein for Se. However, selenoprotein-P is also expressed in many tissues which suggests that although it may facilitate whole body Se distribution, this may not be its sole function. A second major class of selenoproteins are the iodothyronine deiodinase enzymes which catalyse the 5'5-mono-deiodination of the prohormone thyroxine (T4) to the active thyroid hormone 3,3',5'-triiodothyronine (T3). Sperm capsule selenoprotein is localised in the mid-piece portion of spermatozoa where it stabilises the integrity of the sperm flagella. Se intake affects tissue concentrations of selenoprotein W which is reported to be necessary for muscle metabolism. It is of great concern that the health implications of the decline in Se status in the UK over the past two decades have not been systematically investigated. It is well recognised that dietary selenium is important for a healthy immune response. There is also evidence that Se has a protective effect against some forms of cancer; that it may enhance male fertility; decrease cardiovascular disease mortality, and regulate the inflammatory mediators in asthma. The potential influence of Se on these chronic diseases within the European population are important considerations when assessing Se requirement.

The potential role of tocopherol in asthma and allergies: modification of the leukotriene pathway.

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BioDrugs 2001;15(2):81-86

Metabolism of arachidonic acid via the 5-lipoxygenase (5-LO) pathway leads to the formation of hydroperoxyeicosatetraenoic acids (HPETEs) and leukotriene (LT) A₄. This unstable allylic epoxide can be further converted by secondary enzymes into LTB₄ and cysteinyl LTs. LTs represent a family of potent biologically active compounds synthesised by specific cell types and by transcellular biosynthetic mechanisms. Cysteinyl LTs are involved in the pathogenesis of asthma, and recent data indicate that individuals with asthma may have enhanced basal excretion of urinary LTE₄ compared with normal individuals. Tocopherol (vitamin E) and tocopherol acetate strongly inhibit potato 5-LO in an irreversible and noncompetitive way, and, by affecting the redox state of cells possessing 5-LO, they may influence the production of biologically active LTs. It has been reported that normal plasma levels of tocopherol may enhance the lipoxygenation of arachidonic acid, whereas higher tocopherol levels exert a suppressive effect that is consistent with its role as a hydroperoxide scavenger. Receptor-mediated activation of neutrophils in individuals with asthma results in the synthesis of LTs. This activation is inhibited by tocopherol in a concentration-dependent manner. Additional controlled studies are needed to assess the effect of tocopherol on leukotriene production in asthmatic individuals. The results of these studies may be useful in developing new therapeutic approaches in asthmatic/allergic patients.

Increased nitrosothiols in exhaled breath condensate in inflammatory airway diseases.

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Am J Respir Crit Care Med 2001 Mar;163(4):854-8

Nitrosothiols (RS-NOs) are formed by interaction of nitric oxide (NO) with glutathione and may limit the detrimental effect of NO. Because NO generation is increased in airway inflammation, we have measured RS-NOs in exhaled breath condensate in patients with asthma, cystic fibrosis, or chronic obstructive pulmonary disease (COPD). We also measured exhaled NO and nitrite (NO₂-) in the same subjects. RS-NOs were detectable in exhaled breath condensate of all subjects. RS-NOs were higher in subjects with severe asthma (0.81 ± 0.06 µM) when compared with normal control subjects (0.11 ± 0.02 µM, < 0.01) and with subjects with mild asthma (0.08 ± 0.01 µM, < 0.01). Elevated RS-NOs values were also found in patients with cystic fibrosis (0.35 ± 0.07 µM, < 0.01), in those with COPD (0.24 ± 0.04 µM, < 0.01) and in smokers (0.46 ± 0.09 µM, < 0.01). In current smokers there was a correlation (r = 0.8, < 0.05) between RS-NOs values and smoking history (pack/year). We also found elevated concentrations of NO₂- in patients with severe asthma, cystic fibrosis, or COPD, but not in smokers or patients with mild asthma. This suggests that exhaled NO₂- is less sensitive than exhaled RS-NOs. This study has shown that RS-NOs are detectable in exhaled breath condensate of healthy subjects and are increased in patients with inflammatory airway diseases. As RS-NOs concentrations in exhaled breath condensate vary in the different airway diseases and increase with the severity of asthma, their measurement may have clinical relevance as a noninvasive biomarker of nitrosative stress.

Dietary vitamin E, IgE concentrations, and atopy.

Fogarty A, Lewis S, Weiss S, Britton J.

Lancet 2000 Nov 4;356(9241):1573-1574

Vitamin E inhibits IgE responses to allergic stimuli in animals. We investigated the relation between dietary vitamin E intake and

serum IgE concentrations and atopy, measured as allergen skin sensitisation, in a random sample of 2633 adults. Higher concentrations of vitamin E intake were associated with lower serum IgE concentrations and a lower frequency of allergen sensitisation. These findings may explain the beneficial effect of dietary vitamin E on the incidence of asthma.

Anti-inflammatory effects of a stabilized lipid extract of *Perna canaliculus* (Lyprinol).

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Allerg Immunol (Paris) 2000 Sep;32(7):272-8

A lipid-rich extract, prepared by supercritical fluid (CO₂) extraction of freeze-dried stabilized NZ green-lipped mussel powder (Lyprinol) has shown significant anti-inflammatory (AI) activity when given to animals and humans. When treated p.o. with Lyprinol, Wistar and Dark Agouti rats developed neither adjuvant-induced polyarthritis or collagen(II)-induced auto-allergic arthritis. This was achieved with doses < NSAIDs, and 200 times < of other seed or fish oils. Lyprinol subfractions inhibited LTB₄ biosynthesis by PMN in vitro, and PGE₂ production by activated macrophages. Much of this AI activity was associated with omega-3 PUFAs and natural antioxidants [e.g. carotenoids]. In contrast to NSAIDs, Lyprinol is non-gastro toxic in disease-stressed rats at 300 mg/kg p.o., and does not affect platelet aggregation [human, rat]. Clinical studies, either controlled or randomized, have demonstrated very significant AI activity in patients with osteoarthritis (OA), rheumatoid arthritis (RA), asthma, and other inflammatory conditions. Lyprinol is a reproducible, stable source of bioactive lipids with much greater potency than plant/marine oils currently used as nutritional supplements to ameliorate signs of inflammation.

Diet and childhood asthma in a society in transition: a study in urban and rural Saudi Arabia.

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Thorax 2000 Sep;55(9):775-779

BACKGROUND: The causes of the worldwide increases in asthma and allergic diseases in childhood, which seem to relate to increasing prosperity, are unknown. We have previously hypothesised that a reduction in the antioxidant component of the diet is an important factor. An investigation was undertaken of dietary and other risk factors for asthma in Saudi Arabia where major lifestyle differences and prevalences of allergic disease are found in different communities.

METHODS: From a cross sectional study of 1444 children with a mean age of 12 (SD 1) years in Jeddah and a group of rural Saudi villages, we selected 114 cases with a history of asthma and wheeze in the last 12 months and 202 controls who had never complained of wheeze or asthma, as recorded on the ISAAC questionnaire. Risk factors for asthma and allergies (family history, social class, infections, immunisations, family size, and diet) were ascertained by questionnaire. Atopy was assessed by skin prick testing.

RESULTS: In univariate analyses, family history, atopy, and eating at fast food outlets were significant risk factors for wheezy illness, as were the lowest intakes of milk and vegetables and of fibre, vitamin E, calcium, magnesium, sodium, and potassium. These differences were present also in the urban children considered separately. Sex, family size, social class, infections, and parental smoking showed no relationship to risk. In multiple logistic regression analysis, urban residence, positive skin tests, family history of allergic disease, and the lowest intakes of vitamin E, magnesium and sodium related significantly and independently to risk. The lowest tertile of intake of vitamin E was associated with a threefold (95% CI 1.38 to 6.50) increase in risk when adjusted for the other factors. Intake of milk and vegetables both showed inverse linear relationships to being a case.

CONCLUSIONS: This study suggests that dietary factors during childhood are an important influence in determining the expression of wheezy illness, after allowing for urban/rural residence, sex, family history, and atopy. The findings are consistent with previous studies in adults and with the hypothesis that change in diet has been a determinant of the worldwide increases in asthma and allergies.

Dietary factors associated with physician-diagnosed asthma and allergic rhinitis in teenagers: analyses of the first Nutrition and Health Survey in Taiwan.

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Clin Exp Allergy 2001 Feb;31(2):259-64

The occurrence of asthma and allergy are related to lifestyle factors, and dietary pattern may be one of the contributing factors. To

examine the possible association between dietary intake and the prevalence of asthma and allergic rhinitis in teenagers. In a population-based cross-sectional survey, the relationship was sought between food frequency and physician-diagnosed asthma and allergic rhinitis in 1166 adolescents aged 13-17. The prevalence was 4.0% for asthma and 12.4% for rhinitis. Living in an urbanized area was a significant predictor of asthma and rhinitis. In univariate analysis, higher frequencies of oily fish, butcher's meat, liver and deep-fried foods were associated with asthma. Relevant food frequency variables were dichotomized at the 75th percentile for multivariate logistic regression analysis, which included adjustment for two levels of urbanization. Asthma was associated with intakes of liver (OR = 2.32, 95%CI 1.11-4.80), deep-fried foods (OR = 2.13, 95%CI 1.06-4.30) and butcher's meat (OR 1.84, 95%CI 0.89-3.80). In a similar analysis, allergic rhinitis was associated with liver (OR = 1.67, 95%CI 1.06-2.63). No protective effect was demonstrated for any of the food items examined. Protein-rich and fat-rich foods of animal origin were associated with a higher prevalence of asthma in teenagers.

Dietary fats and asthma in teenagers: analyses of the first Nutrition and Health Survey in Taiwan (NAHSIT).

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Clin Exp Allergy 2001 Dec;31(12):1875-80

BACKGROUND: The occurrence of asthma may be associated with dietary factors.

OBJECTIVE: To examine the association between nutrient intake and physician-diagnosed asthma and allergic rhinitis.

METHODS: A stratified, multiple-staged sampling design was used to select study areas, in which household interviews were carried out to gather information on health status and 24-h food recall. Data from 1166 adolescents, 13-17 years of age, were analysed.

RESULTS: In univariate analysis, total calorie and energy-adjusted fat intake were associated with the prevalence of asthma, whereas vitamin A and vitamin C intake showed negative association with asthma. Multivariate logistic regression was used to adjust for sex and levels of urbanization; intake of saturated fats was associated with increased risk (OR = 2.02 for an increase of one SD, 95%CI 1.40-2.90), while monounsaturated fats were inversely related to asthma (OR = 0.65 for an increase of one SD, 95% CI 0.43-0.99). Vitamin C intake in the lowest quartile was associated with elevated risk for asthma with marginal significance (OR = 1.81, 95%CI 0.88-3.71, P = 0.10). None of the nutritional factors was associated with allergic rhinitis.

CONCLUSION: Results from this cross-sectional survey suggest that saturated and monounsaturated fats may have different effects on airway inflammation.

Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial.

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Lancet 2001 Apr 7;357(9262):1076-9

BACKGROUND: Reversal of the progressive increase in frequency of atopic disease would be an important breakthrough for health care and wellbeing in western societies. In the hygiene hypothesis this increase is attributed to reduced microbial exposure in early life. Probiotics are cultures of potentially beneficial bacteria of the healthy gut microflora. We assessed the effect on atopic disease of Lactobacillus GG (which is safe at an early age and effective in treatment of allergic inflammation and food allergy).

METHODS: In a double-blind, randomised placebo-controlled trial we gave Lactobacillus GG prenatally to mothers who had at least one first-degree relative (or partner) with atopic eczema, allergic rhinitis, or asthma, and postnatally for 6 months to their infants. Chronic recurring atopic eczema, which is the main sign of atopic disease in the first years of life, was the primary endpoint.

FINDINGS: Atopic eczema was diagnosed in 46 of 132 (35%) children aged 2 years. Asthma was diagnosed in six of these children and allergic rhinitis in one. The frequency of atopic eczema in the probiotic group was half that of the placebo group (15/64 [23%] vs 31/68 [46%]; relative risk 0.51 [95% CI 0.32-0.84]). The number needed to treat was 4.5 (95% CI 2.6-15.6).

INTERPRETATIONS: Lactobacillus GG was effective in prevention of early atopic disease in children at high risk. Thus, gut microflora might be a hitherto unexplored source of natural immunomodulators and probiotics, for prevention of atopic disease.

Dietary fatty acids and allergy.

Ann Med 1999 Aug;31(4):282-7

The increase in the prevalence of atopic diseases has recently been linked to altered consumption of polyunsaturated fatty acids (PUFAs). As typical Western diets contain almost 10 times more linoleic acid (18:2 omega-6) than alpha-linolenic acid (18:3 omega-3), it is the metabolism of the former that predominates. Subsequently produced arachidonic acid-derived eicosanoids alter the balance of T-helper cells type 1 and type 2 thus favouring the production of immunoglobulin (Ig)E. In atopic subjects, the impact of this excessive eicosanoid production may be further strengthened as a result of changes in cyclic nucleotide metabolism exacerbated by substrate availability. Dietary omega-3 fatty acids can have marked influence on both specific and nonspecific immune responses in modifying eicosanoid production and replacing omega-6 fatty acids in cell membranes. Therefore, it is concluded that careful manipulation of dietary PUFAs may play a key role in the successful management of inflammation associated with atopic diseases.

An analysis of therapeutic effect of drug acupoint application in 209 cases of allergic asthma.

Lai X, Li Y, Fan Z, Zhang J, Liu B. Guanzhou University of Traditional Chinese Medicine and Pharmacy, Guangdong Province 510407.

J Tradit Chin Med 2001 Jun;21(2):122-6

Both therapies of traditional crude herb moxibustion and drug acupoint application were used in 209 cases of allergic asthma to compare their long-term and short-term therapeutic effects and to analyze the relationship between clinic therapeutic effects of both therapies and differential types of the disease. The results showed that the short-term total effective rate in the group of drug acupoint application was higher than that in the group of traditional crude herb moxibustion, the therapeutic effects of drug acupoint application being closely related to differential types. Analysis also shows the best short-term therapeutic effect was in the type of heat in the lung while the poorest effect in the type of deficiency of the kidney-yang.

Effects of ginkgo leave concentrated oral liquor in treating asthma. [Article in Chinese]

Li MH, Zhang HL, Yang BY Qingdao Hospital of Integrated Traditional and Western Medicine, Shandong.

Chung Kuo Chung Hsi I Chieh Ho Tsa Chih 1997 Apr;17(4):216-8 Zhongguo Zhong Xi Yi Jie He Za Zhi. 1997 Apr;17(4):216-8.

OBJECTIVE: To determine the effects of Ginkgo leave concentrated oral liquor (GLC) on airway inflammation.

METHODS: Airway hyperreactivity and clinical symptoms and pulmonary functions of asthma patients were determined.

RESULTS: In contrast to placebo group, GLC significantly reduced airway hyperreactivity (< 0.05) and improved clinical symptoms (< 0.05), pulmonary functions (< 0.05) of the asthmatic patients.

CONCLUSION: GLC is an effective drug of anti airway inflammation.

From asthma to AirBeat: community-driven monitoring of fine particles and black carbon in Roxbury, Massachusetts.

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Environ Health Perspect 2002 Apr;110 Suppl 2:297-301

Asthma is an ongoing environmental justice concern in Roxbury, an urban neighborhood of Boston, Massachusetts. Residents, especially local youth, were the first to investigate the potential links between high asthma rates and air pollution, particularly from diesel buses and trucks. A youth-led march for clean air and community air monitoring projects drew governmental and media attention to these problems. In 1998, a collaboration of environmental justice, government, and research groups came together to develop a real-time air pollution monitoring system known as AirBeat. This community-based participatory research project was designed to answer community questions about whether there are pollution "hot spots" in Roxbury and the degree to which diesel emissions are contributing to health problems. AirBeat measures and reports levels of PM_{2.5} (particulate matter with a mass median aerodynamic diameter \leq to 2.5 microm), ozone, and black carbon on an hourly basis. These data are accessible via a website, telephone hotline, and a flag warning system. AirBeat is successful because community residents and organizations participate as equal partners with an equitable share of funding. The project also promotes a community sense of ownership and

pride. Dozens of youth have developed leadership and scientific skills. The media have extensively covered the project as a community victory. The data support the claim that Dudley Square in Roxbury is a hot spot for air pollution. This information is now being used to advocate for alternative fuel transit buses and other clean air measures. Finally, this project has strengthened community partnerships with research and governmental institutions.

In vitro effects of Ginkgolide B on lymphocyte activation in atopic asthma: comparison with cyclosporin A.

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Jpn J Pharmacol 2000 Jul;83(3):241-5

The effects of Ginkgolide B (BN52021) on in vitro activation responses of human peripheral blood mononuclear cells (PBMC) from asthmatic patients was measured using 2-channel flow cytometric analysis of activation-associated cell surface antigens or ELISA assays for cytokines known to be expressed by PBMC during T1 or T2 immunological activation. BN52021 is an anti-inflammatory extract of Ginkgo biloba and has been used therapeutically. It is a known inhibitor of platelet activating factor (PAF), which is important in the pathogenesis of asthma, and may synergise with cyclosporin A (CyA) to inhibit pathogenic immune activation in asthmatics. We compared the inhibitory effects of BN52021 and CyA (1 microM each) on activation of PBMC of asthmatic patients stimulated by phorbol myristate acetate and calcium ionophore. Inhibition of production of the cytokines IL-4 and IL-5 by BN52021 was insignificant compared to CyA. However, BN52021 significantly reversed the increase in activation-associated CD45RA expression, with a trend towards decreased expression of HLA-DR. Lymphocyte activation markers were not significantly altered by CyA. Since they appear to have differing effects on activated cells, the anti-inflammatory effects of CyA and BN52021 in atopic asthma is potentially additive. The present approach may be useful for preliminary evaluation of novel therapeutic modalities for asthma treatment.

Viruses in asthma.

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Br Med Bull 2002;61:29-43

Current evidence suggests that the overall load of infectious agents, including respiratory viruses, encountered early in life is an important factor influencing maturation of the immune system from a type 2 bias at birth towards predominantly type 1 responses, thus avoiding atopic diseases. The 'hygiene hypothesis' proposes that the relatively sterile environment present in industrialised Western countries has contributed to the recent epidemic of asthma and atopy. Whether specific infections are of greater or lesser protective value is an important question if strategies are to be derived to mimic the beneficial effects of childhood infection whilst avoiding morbidity and potential mortality of the natural pathogens. Infection by respiratory viruses is a major trigger of wheezing in infants and of exacerbations of asthma in older children. Viruses are detected in up to 85% of such episodes. Rhinovirus is common in all age groups; respiratory syncytial virus (RSV) is most important in infants and young children. Knowledge of the immunopathogenetic mechanisms of virus infection in the asthmatic airway will lead to the development of new treatments for virus-induced asthma.

The etiologies, pathophysiology, and alternative complementary treatment of asthma.

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Altern Med Rev 2001 Feb;6(1):20-47

A chronic inflammatory disorder of the respiratory airways, asthma is characterized by bronchial airway inflammation resulting in increased mucus production and airway hyper-responsiveness. The resultant symptomatology includes episodes of wheezing, coughing, and shortness of breath. Asthma is a multifactorial disease process with genetic, allergic, environmental, infectious, emotional, and nutritional components. The underlying pathophysiology of asthma is airway inflammation. The underlying process driving and maintaining the asthmatic inflammatory process appears to be an abnormal or inadequately regulated CD4+ T-cell immune response. The T-helper 2 (Th2) subset produces cytokines including interleukin-4 (IL-4), IL-5, IL-6, IL-9, IL-10, and IL-13, which stimulate the growth, differentiation, and recruitment of mast cells, basophils, eosinophils, and B-cells, all of which are involved in humoral immunity, inflammation, and the allergic response. In asthma, this arm of the immune response is overactive, while Th1 activity, generally corresponding more to cell-mediated immunity, is dampened. It is not yet known why asthmatics have this out-of-balance immune activity, but genetics, viruses, fungi, heavy metals, nutrition, and pollution all can be contributors. A plant lipid preparation containing sterols and sterolins has been shown to dampen Th2 activity. Antioxidant nutrients, especially vitamins C and E, selenium, and zinc appear to be necessary in asthma treatment. Vitamins B6 and B12 also may be helpful. Omega-3 fatty acids from fish, the flavonoid quercetin, and botanicals Tylophora asthmatica, Boswellia serrata and Petasites hybridus address the inflammatory component. Physical modalities, including yoga, massage, biofeedback, acupuncture, and

chiropractic can also be of help.

Self-reported asthma prevalence among adults?

MMWR. Morb. Mortal. Wkly. Rep. 2001 Aug 17; 50(32): 682-6.

United States, 2000.

The effect of air pollution on inner-city children with asthma.

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Eur Respir J 2002 Apr;19(4):699-705

The effect of daily ambient air pollution was examined within a cohort of 846 asthmatic children residing in eight urban areas of the USA, using data from the National Cooperative Inner-City Asthma Study. Daily air pollution concentrations were extracted from the Aerometric Information Retrieval System database from the Environment Protection Agency in the USA. Mixed linear models and generalized estimating equation models were used to evaluate the effects of several air pollutants (ozone, sulphur dioxide (SO₂), nitrogen dioxide (NO₂) and particles with a 50% cut-off aerodynamic diameter of 10 microm (PM₁₀) on peak expiratory flow rate (PEFR) and symptoms in 846 children with a history of asthma (ages 4-9 yrs). None of the pollutants were associated with evening PEFR or symptom reports. Only ozone was associated with declines in morning % PEFR (0.59% decline (95% confidence interval (CI) 0.13-1.05%) per interquartile range (IQR) increase in 5-day average ozone). In single pollutant models, each pollutant was associated with an increased incidence of morning symptoms: (odds ratio (OR)=1.16 (95% CI 1.02-1.30) per IQR increase in 4-day average ozone, OR=1.32 (95% CI 1.03-1.70) per IQR increase in 2-day average SO₂, OR=1.48 (95% CI 1.02-2.16) per IQR increase in 6-day average NO₂ and OR=1.26 (95% CI 1.0-1.59) per IQR increase in 2-day average PM₁₀. This longitudinal analysis supports previous time-series findings that at levels below current USA air-quality standards, summer-air pollution is significantly related to symptoms and decreased pulmonary function among children with asthma.

Prevalence of mood disorders and relationship to asthma severity in patients at an inner-city asthma clinic.

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Ann Allergy Asthma Immunol 2001 Aug;87(2):129-33

BACKGROUND: Depressive symptoms are associated with noncompliance and even sudden death in asthma patients. Some studies suggest that low-income, minority, inner-city asthma patients may be at high risk for asthma-related morbidity and mortality in which depression may be a risk factor. Minimal data are available on the prevalence of depression and other mood disorders in asthma patients.

OBJECTIVE: In this pilot study, we examined the prevalence of depression and the association between depression and measures of asthma severity in patients at an inner-city asthma clinic.

METHODS: Mood disorders were diagnosed using a diagnostic interview given to patients (N = 44) at asthma clinic visits. Inhaled steroid dose, FEV1 percentage, and asthma severity were also obtained.

RESULTS: Eighteen patients (41%) had a lifetime mood disorder but only seven of these patients received pharmacotherapy. Patients with a past mood disorder had significantly higher FEV1 percentage predicted values (P = 0.03) than those without a mood disorder. Trends toward less severe asthma (P = 0.13) and lower inhaled steroid dose (P = 0.13) in patients with a mood disorder history were also found.

CONCLUSIONS: The data suggest that mood disorders are common, but often unrecognized and untreated in asthma patients. The data also suggest that mood disorders are not necessarily associated with more severe asthma, at least in the population studied.

Reduction of exercise-induced asthma oxidative stress by lycopene, a natural antioxidant.

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BACKGROUND: Lycopene has previously been shown to have high antioxidative activity. In view of the controversy regarding the beneficial effect of antioxidants on asthma, the acute effects of lycopene (LYC-O-MATO) on airway hyperreactivity were assessed in patients with exercise-induced asthma (EIA).

METHODS: Twenty patients with EIA participated in our study to verify the antioxidative effects. The test was based on the following sequence: measurement of baseline pulmonary function, 7-min exercise session on a motorized treadmill, 8-min rest and again measurement of pulmonary function, 1-week, oral, randomly administered, double-blind supplementation of placebo or 30 mg/day of lycopene (LYC-O-MATO), measurement of pulmonary function at rest, 7-min exercise session, and 8-min rest and again measurement of pulmonary function. A 4-week washout interval was allowed between each protocol.

RESULTS: All patients given placebo showed significant postexercise reduction of more than 15% in their forced expiratory volume in 1 s (FEV₁). After receiving a daily dose of 30 mg of lycopene for 1 week, 11 (55%) patients were significantly protected against EIA. Serum analyses of the patients by high-pressure liquid chromatography detected in the lycopene-supplemented patients an elevated level of lycopene compared to the placebo group, with no change in retinol, tocopherols, or in the other carotenoids.

CONCLUSIONS: Our results indicate that a daily dose of lycopene exerts a protective effect against EIA in some patients, most probably through an *in vivo* antioxidative effect.

Breastfeeding and asthma in children: findings from a West Australian study.

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Breastfeed Rev. 2000 Mar;8(1):5-11

The primary aim was to determine whether there was an inverse association between the duration of exclusive breastfeeding and the development of traits associated with asthma in children at age six years. A prospective cohort study of children from Western Australia was enrolled prior to birth and followed to age six. Two thousand, nine hundred and seventy-nine children were recruited through antenatal clinics at the major tertiary obstetric hospital in Perth. Unconditional logistic regression was used to model the association between duration of exclusive breastfeeding and outcomes related to asthma or atopy at age six allowing for a number of important confounders. These included gender, gestational age, smoking in pregnancy and early child care. After adjustment for confounders, the introduction of milk other than breastmilk before four months of age was a significant (< 0.05) risk factor for all asthma-related outcomes in six-year-old children: (i) doctor diagnosed asthma odds ratio inverted question mark OR inverted question mark = 1.25 (95% CI 1.02-1.54); (ii) wheeze three or more times since the age of one year OR 1.42 (1.15-1.76); (iii) wheeze in the last twelve months OR 1.28 (1.02-1.76); (iv) sleep disturbance due to wheeze within the last twelve months OR 1.41 (1.04-1.90); (v) age at doctor diagnosis (hazard ratio inverted question mark HR inverted question mark 1.22 inverted question mark 1.03-1.43 inverted question mark); (vi) age at first wheeze (HR 1.36 inverted question mark 1.17-1.59 inverted question mark) and; (vii) positive reaction to common aeroallergens OR 1.27 (1.01-1.59). There is a substantial reduction in risk of childhood asthma as assessed at age six years, if exclusive breastfeeding is continued for at least the first four months of life. These findings are important for our understanding of the aetiology of and for the potential prevention of asthma in children.

The function of allergy: immunological defense against toxins.

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Q Rev Biol 1991 Mar;66(1):23-62

This paper proposes that the mammalian immune response known as "allergy" evolved as a last line of defense against the extensive array of toxic substances that exist in the environment in the form of secondary plant compounds and venoms. Whereas nonimmunological defenses typically can target only classes of toxins, the immune system is uniquely capable of the fine-tuning required to target selectively the specific molecular configurations of individual toxins. Toxic substances are commonly allergenic. The pharmacological chemicals released by the body's mast cells during an IgE antibody-mediated allergic response typically cause vomiting diarrhea, coughing, tearing, sneezing, or scratching, which help to expel from the body the toxic substance that triggered the response; individuals frequently develop aversions to substances that have triggered such responses. A strong allergic response often includes a decrease in blood pressure, which slows the rate at which toxins circulate to target organs. The immune system identifies as toxic the following kinds of substances: (1) those low-molecular-weight substances that bind covalently to serum proteins (e.g., many plant toxins); (2) nontoxic proteins that act as carriers of toxins with low molecular weights (e.g., plant proteins associated with plant toxins); (3) specific substances of high molecular weight that harmed individuals in ancestral mammalian populations for a span of time that was significant from the standpoint of natural selection (e.g., the toxic proteins of bee venom. Substances that bind covalently to serum proteins generally are acutely toxic, and because many of these substances also bind covalently to the DNA of target cells, they are potentially mutagenic and carcinogenic as well. Thus, by protecting against

acute toxicity, allergy may also defend against mutagens and carcinogens. The toxic hypothesis explains the main phenomena of allergy; why IgE-mediated allergies usually occur within minutes of exposure to an allergen and why they are often so severe; why the manifestations of allergy include vomiting, diarrhea, coughing, sneezing, scratching, tearing, and a drop in blood pressure; why covalent binding of low-molecular-weight substances to serum proteins frequently causes allergy; why allergies occur to many foods, pollens, venoms, metals, and drugs; why allergic cross-reactivity occurs to foods and pollen from unrelated botanical families; why allergy appears to be so capricious and variable; and why allergy is more prevalent in industrial societies than it is in foraging societies. This hypothesis also has implications for the diagnosis, prevention, and treatment of allergy.

Features of asthma in the elderly.

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J Asthma 2001 Aug;38(5):377-89

Asthma has been considered a rare disease in the elderly, but recent studies have shown that it is as common in the elderly as in the middle-aged population. Diagnosis of asthma is often overlooked in older patients, leading to undertreatment. Spirometry, determination of expiratory flow lability, and histamine challenge tests are tools that are as useful for the evaluation of elderly asthmatics as they are for younger patients. Asthma is more severe in the elderly, especially in long-standing asthmatics. Treatment of asthma in the elderly should follow the same stepwise guidelines that are recommended for all age groups, though it will require more intense monitoring. An aggressive treatment approach to mild and moderate asthma in young people is the best hope of changing the future trends of asthma in the elderly.

Dietary phytoestrogens have anti-inflammatory activity in a guinea pig model of asthma.

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Proc Soc Exp Biol Med 2000 Apr;223(4):372-8

Phytoestrogens are a normal constituent of soy protein and have been shown to have anti-inflammatory activity in various in vitro and in vivo models. The present study was designed to determine if a diet enriched in the phytoestrogen isoflavones, genistin and daidzin, would alter the antigen-induced cellular infiltration, particularly eosinophilia, characteristic of a guinea pig model of asthma. Throughout the duration of the study, guinea pigs were maintained on a control diet (standard guinea pig chow) or the same diet enriched in isoflavones. The animals were placed on the diet 2 weeks prior to active sensitization with ovalbumin (OA). Three weeks after sensitization, animals were challenged with OA aerosol. The cellular infiltration into the lung and protein and red blood cells (RBC) in the bronchoalveolar lavage fluid (BAL) were determined 17 hr later. In animals maintained on the control diet, OA aerosol challenge resulted in the expected increase in eosinophils in both the BAL and the lung tissue, an increase in neutrophils in the BAL, and an increase in protein and the number of RBC in the BAL. In contrast, in animals maintained on the isoflavone diet, the OA-induced eosinophilia in the lung tissue was significantly attenuated. In addition, OA challenge caused a greater increase in BAL protein in animals maintained on the isoflavone diet compared with animals on the control diet. Our results indicated that a diet enriched in isoflavones results in reduced antigen-induced eosinophilia in the lung in the guinea pig model of asthma. However, this beneficial anti-inflammatory effect of dietary phytoestrogens is accompanied by a potentially detrimental increase in antigen-induced leakage of protein into the airspace.

A review of the French maritime pine bark extract (Pycnogenol), a herbal medication with a diverse clinical pharmacology.

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Int J Clin Pharmacol Ther 2002 Apr;40(4):158-68

OBJECTIVES: An increasing body of evidence indicates that Pycnogenol (PYC), a standardized extract of French maritime pine bark, has favorable pharmacological properties. This is a review of studies with both PYC and components of the preparation, that have helped to elucidate target sites and possible mechanisms for activity in men.

METHODS: Studies appearing in peer reviewed literature, as well as results presented at international meetings not yet available as published papers, are included in this review. Additional data from published sources in German and French languages that are not widely available are also included.

RESULTS: Chemical identification studies showed that PYC is primarily composed of procyanidins and phenolic acids.

Procyanidins are biopolymers of catechin and epicatechin subunits which are recognized as important constituents in human nutrition. PYC contains a wide variety of procyanidins that range from the monomeric catechin and taxifolin to oligomers with 7 or more flavonoid subunits. The phenolic acids are derivatives of benzoic and cinnamic acids. The ferulic acid and taxifolin components are rapidly absorbed and excreted as glucuronides or sulphates in men, whereas procyanidins are absorbed slowly and metabolized to valerolactones which are excreted as glucuronides. PYC has low acute and chronic toxicity with mild unwanted effects occurring in a small percentage of patients following oral administration. Clinical studies indicate that PYC is effective in the treatment of chronic venous insufficiency and retinal micro-hemorrhages. PYC protects against oxidative stress in several cell systems by doubling the intracellular synthesis of anti-oxidative enzymes and by acting as a potent scavenger of free radicals. Other anti-oxidant effects involve a role in the regeneration and protection of vitamin C and E. Anti-inflammatory activity has been demonstrated in vitro and in vivo in animals. Protection against UV-radiation-induced erythema was found in a clinical study following oral intake of PYC. In asthma patients symptom scores and circulating leukotrienes are reduced and lung function is improved. Immunomodulation has been observed in both animal models as well as in patients with Lupus erythematosus. PYC antagonizes the vasoconstriction caused by epinephrine and norepinephrine by increasing the activity of endothelial nitric oxide synthase. Dilation of the small blood vessels has been observed in patients with cardiovascular disease, whereas in smokers, PYC prevents smoking-induced platelet aggregation and reduces the concentration of thromboxane. The ability to inhibit angiotensin-converting enzyme is associated with a mild antihypertensive effect. PYC relieves premenstrual symptoms, including abdominal pain and this action may be associated with the spasmolytic action of some phenolic acids. An improvement in cognitive function has been observed in controlled animal experiments and these findings support anecdotal reports of improvement in ADHD patients taking PYC supplements.

CONCLUSIONS: There is much evidence showing that PYC has beneficial effects on physiological functions. Results from ongoing clinical research are required to confirm and extend previous observations.

Breastfeeding and asthma among Brazilian children.

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J Asthma 2000;37(7):575-83

We examined the association of breastfeeding and the presence of chronic respiratory symptoms among 5,182 Brazilian schoolchildren 7-14 years of age who were participants in the International Study on Asthma and Allergies in Childhood (ISAAC). The prevalence of medically diagnosed asthma and current wheeze were respectively 4.6% (95% confidence interval [CI] 4.0%-5.2%) and 11.9% (95% CI 11.0%-12.8%). Ninety percent of the mothers in our study population had breastfed their child. After adjusting for potential confounding factors, we found that children who had not been breastfed were more likely to have a medical diagnosis of asthma (odds ratio [OR] = 1.51, 95% CI 1.00-2.51), experience current wheeze (OR = 1.29, 95% CI 0.96-1.74), and wheeze after exercise (OR = 1.51, 95% CI 1.01-2.27) than children who had been breastfed for more than 6 months. This effect was only present among children with no family history of asthma (OR = 1.54, 95% CI 0.90-2.42 for medical diagnosis of asthma; OR = 1.27, 95% CI 0.93-1.75 for current wheezing; and OR = 1.74, 95% CI 1.12-2.6 for wheeze after exercise). We conclude that the low prevalence of asthma and wheeze observed in our population may be partly related to the high level of breastfeeding.

Antioxidants and protein carbonyls in bronchoalveolar lavage fluid of children: normal data.

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Pediatr Res 2001 Feb;49(2):155-61

Antioxidant-oxidant imbalances in bronchoalveolar lavage fluid (BAL) are thought to contribute to oxidative stress in respiratory disease. However, normal reference ranges for BAL antioxidants and oxidized proteins in children are not available. In this study, we recruited 124 children attending for elective surgery for a noninflammatory condition; 83 were nonasthmatic, nonatopic (N) and 41 were nonasthmatic, atopic (NA). A nonbronchoscopic lavage was performed and ascorbate, uric acid, alpha-tocopherol, and protein carbonyl (as a measure of oxidative damage) concentrations were determined in BAL fluid. The 95% reference range was 0.112-1.897 micromol/L for ascorbate, 0.149-2.163 micromol/L for urate, 0.0029-0.066 micromol/L for alpha-tocopherol, and 0.280-4.529 nmol/mg for protein carbonyls in BAL fluid. Age, gender, and exposure to environmental tobacco smoke did not affect the concentration of ascorbate, urate, alpha-tocopherol, or protein carbonyls. However, in multiple linear regression analyses, the type of home heating (glass-fronted fires or oil-fired central heating) was found to influence ascorbate and urate concentrations in the BAL fluid (ss-coefficient for ascorbate: 0.445, $p = 0.031$; for urate: 0.114, $p = 0.001$). There was no significant difference between the N and NA group in BAL fluid concentrations of ascorbate, urate, or protein carbonyls. The alpha-tocopherol concentration was significantly increased in the NA group ($p = 0.037$). Uric acid and alpha-tocopherol concentrations in BAL fluid and serum were not correlated. Intriguingly, serum and BAL ascorbate concentrations were significantly correlated ($r = 0.297$, $p = 0.018$, $n = 63$), which may offer an explanation for why supplementing the diet with vitamin C can improve asthma symptoms. Further studies will

investigate the role of BAL antioxidant concentrations in children with inflammatory respiratory diseases.

Diet, infection and wheezy illness: lessons from adults.

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Pediatr Allergy Immunol 2000;11 Suppl 13:37-40

An increase in asthma and atopic disease has been recorded in many countries where society has become more prosperous. We have investigated two possible explanations: a reduction in childhood infections and a change in diet. In a cohort of people followed up since 1964, originally selected as a random sample of primary school children, we have investigated the relevance of family size and the common childhood infectious diseases to development of eczema, hay fever and asthma. Although membership of a large family reduced risks of hay fever and eczema (but not asthma), this was not explained by the infections the child had suffered. Indeed, the more infections the child had had, the greater the likelihood of asthma, although measles gave a modest measure of protection. We have investigated dietary factors in two separate studies. In the first, we have shown the risks of bronchial hyper-reactivity are increased seven-fold among those with the lowest intake of vitamin C, while the lowest intake of saturated fats gave a 10-fold protection. In the second, we have shown that the risk of adult-onset wheezy illness is increased five-fold by the lowest intake of vitamin E and doubled by the lowest intake of vitamin C. These results were supported by direct measurements of the vitamins and triglycerides in plasma. We have proposed that changes in the diet of pregnant women may have reflected those observed in the population as a whole and that these may have resulted in the birth of cohorts of children predisposed to atopy and asthma. The direct test of this is to study the diet and nutritional status of a large cohort of pregnant women and to follow their offspring forward. This is our current research.

Dietary antioxidants and asthma in adults: population-based case-control study.

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Am J Respir Crit Care Med 2001 Nov 15;164(10 Pt 1):1823-8

A protective role for dietary antioxidants in asthma has been proposed. However, epidemiological evidence to implicate antioxidant vitamins is weak, and data on the role of flavonoid-rich foods and antioxidant trace elements are lacking. We carried out a population-based case-control study in South London, UK, to investigate whether asthma is less common and less severe in adults who consume more dietary antioxidants. Participants were aged 16-50 yr and registered with 40 general practices. Asthma was defined by positive responses to a standard screening questionnaire in 1996, and complete information about usual diet was obtained by food frequency questionnaire from 607 cases and 864 controls in 1997. After controlling for potential confounding factors and total energy intake, apple consumption was negatively associated with asthma (odds ratio [OR] per increase in frequency group 0.89 [95% confidence interval [CI]: 0.82 to 0.97]; $p = 0.006$). Intake of selenium was also negatively associated with asthma (OR per quintile increase 0.84 [0.75 to 0.94]; $p = 0.002$). Red wine intake was negatively associated with asthma severity. The associations between apple and red wine consumption and asthma may indicate a protective effect of flavonoids. The findings for dietary selenium could have implications for health policy in Britain where intake has been declining.

Dietary antioxidants and ozone-induced bronchial hyperresponsiveness in adults with asthma.

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Arch Environ Health 2001 May-Jun;56(3):242-9

Ozone exposure aggravates asthma, as has been demonstrated in both controlled exposures and epidemiologic studies. In the current double-blind crossover study, the authors evaluated the effects of dietary antioxidants (i.e., 400 IU vitamin E/500 mg vitamin C) on ozone-induced bronchial hyperresponsiveness in adult subjects with asthma. Seventeen subjects were exposed to 0.12 ppm of ozone or to air for 45 min during intermittent moderate exercise. Bronchial hyperresponsiveness was assessed with 10-min sulfur dioxide (i.e., 0.10 ppm and 0.25 ppm) inhalation challenges. Subjects who were given dietary antioxidants responded less severely to sulfur dioxide challenge than subjects given a placebo (i.e., forced expiratory volume in the 1st sec: -1.2% vs. 4.4%, respectively; peak flow: +2.2% vs. -3.0%, respectively; and mid-forced expiratory flow: +2.0% vs. -4.3%, respectively). Effects were more pronounced when subjects were grouped by response to sulfur dioxide at the screening visit. The results suggest that dietary supplementation with vitamins E and C benefits asthmatic adults who are exposed to air pollutants.

Relation of body mass index to asthma and atopy in children: the National Health and Nutrition Examination Study III.

Thorax 2001 Nov;56(11):835-8

BACKGROUND: An increase in the prevalence of obesity and asthma over recent decades has been reported in affluent societies. Both overweight and obesity have been shown to be inversely related to having been breastfed, which is also a potential protective factor against childhood atopic diseases. The aim of this analysis was to explore the relation of body mass index (BMI) to asthma and atopy in a large representative sample of the United States population.

METHODS: Children aged 4-17 years were included in the NHANES III survey. Prevalences of atopic diseases and potential confounding factors such as exposure to environmental tobacco smoke, birth weight, breast feeding, and household size were assessed using structured interviews with parents. Height and weight were measured, and BMI was calculated as kg/m² and transformed into Z scores. Children underwent skin prick tests for atopy to a battery of food and inhalant allergens.

RESULTS: The prevalence of asthma (8.7% v 9.3% v 10.3% v 14.9%, p=0.0001) and atopy (48.6% v 50.5% v 53.0% v 53.2%, p=0.05) rose significantly with increasing quartiles of BMI. After adjustment for confounders, a significant positive association between BMI and asthma remained (adjusted OR 1.77, 95% confidence interval 1.44 to 2.19 between the highest and lowest quartiles of BMI), whereas no independent relation between BMI and atopy was evident. No effect modification by sex or ethnic group was seen.

CONCLUSIONS: The effects of increased BMI on asthma may be mediated by mechanical properties of the respiratory system associated with obesity or by upregulation of inflammatory mechanisms rather than by allergic eosinophilic inflammation of the airway epithelium.

Serum and red blood cell antioxidant status in patients with bronchial asthma.

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Can Respir J 2000 Nov-Dec;7(6):476-80

Levels of vitamin C, ceruloplasmin, transferrin and albumin in serum, and glutathione in red blood cells were investigated in 40 patients with asthma to determine whether their antioxidant status was different from healthy subjects. Serum vitamin C and albumin levels were lower in the patient group (36.91±12.50 microM and 46.2±3.0 g/L, respectively) than in 43 healthy volunteers (53.38±13.06 microM and 48.8±2.1 g/L, < 0.001 and < 0.05, respectively). However, erythrocyte glutathione and serum ceruloplasmin levels were higher in the patient group (0.59±0.11 mol/mol hemoglobin and 442±73 micromol/L, respectively) than in controls (0.49±0.09 mol/mol hemoglobin and 308±47 micromol/L, < 0.001 and < 0.001, respectively). No difference was observed in transferrin levels between the groups. The results suggest that reactive oxygen species may be a contributing factor in patients with asthma, causing changes in serum vitamin C, ceruloplasmin and erythrocyte glutathione levels.

Consumption of hypoallergenic flour prevents gluten-induced airway inflammation in Brown Norway rats.

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Biosci Biotechnol Biochem 2001 Aug;65(8):1729-35

Brown Norway rats were immunized with gluten, and then fed a diet containing hypoallergenic flour or an amino acid mixture. The rats were then made to inhale a solubilized gluten to induce gluten-specific bronchial asthma. The antibody levels in the serum of rats were measured by ELISA, and cell counts were done on cytospin preparations of bronchoalveolar lavage fluid. Body weight was decreased after allergen challenge in rats fed the amino acid mixture but not in rats fed the hypoallergenic flour. Antibody levels in the serum were significantly lower in rats fed hypoallergenic flour than in those fed the amino acid mixture. Differential cell counts in the bronchoalveolar lavage fluid showed that the numbers of eosinophils, lymphocytes, and neutrophils were significantly lower in rats fed the hypoallergenic flour than in those fed the amino acid mixture. These results suggest that hypoallergenic flour actively suppresses the allergic reactions, probably by inducing oral tolerance.

Reduced levels of glutathione S-transferases in patch test reactions to dithranol and sodium lauryl sulphate as demonstrated by quantitative immunocytochemistry: evidence for oxidative stress in acute irritant contact dermatitis.

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There is increasing evidence that oxidative stress plays a role in the pathogenesis of acute irritant contact dermatitis. As part of ongoing studies into the effect of irritant chemicals on the anti-oxidant enzyme systems in the skin, we have examined the changing levels of two classes of glutathione S-transferase in patch test reactions to dithranol and sodium lauryl sulphate, using quantitative immunocytochemistry. Although no changes were evident after 6 hrs, significant reductions in the density of staining for glutathione S-transferase alpha were seen with both irritants after 48 hrs and 96 hrs. Glutathione S-transferase pi levels were reduced to a lesser degree, reaching significance for dithranol at the 96 hrs time point only, and for sodium lauryl sulphate at 48 hrs only. The results support the hypothesis that oxidative stress plays a role in chemically-induced inflammation, not only in the case of irritants such as dithranol which are known to directly generate reactive oxygen species, but also with chemicals not generally associated with free radical generation.

SUGGESTED READING

Cytokine-directed therapies for asthma.

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J Allergy Clin Immunol 2001 Aug;108(2 Suppl):S72-6

Increasing knowledge of the pathophysiologic roles of various cytokines in atopic diseases has provided the basis for the development of novel therapies. Strategic approaches for cytokine inhibition include the blocking of transcription factors that lead to their expression, blockade after their release, cytokine receptor antagonism, and the inhibition of signaling pathways that are activated after cytokine-receptor binding. The proinflammatory cytokines IL-5, IL-4, IL-13, and TNF-alpha are among the therapeutic targets. Results with a humanized anti-IL-5 have been disappointing. Although successful in markedly reducing circulating eosinophils and in preventing eosinophil accumulation in airways, the humanized anti-IL-5 was unable to affect early or late responses to allergen or to reduce airway reactivity to methacholine challenge in patients with asthma. On the other hand, a soluble IL-4 receptor antagonist has shown clinical benefits for patients with moderate asthma who require daily inhaled corticosteroids. Agents that target IL-13 and TNF-alpha remain to be evaluated in asthmatic inflammation. The use of cytokines with anti-inflammatory effects may also have therapeutic value. The evaluation of such agents in human beings, including IL-10, IL-12, and IFN-gamma, is at a preliminary stage, but so far results have not been encouraging.

Using homeopathy for treating childhood asthma: understanding a family's choice.

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J Pediatr Nurs 2001 Aug;16(4):269-76

The incidence and severity of asthma are increasing despite concerted efforts in comprehensive management. Families may be expected to look to complementary or alternative therapies (CAM) for help in treating persistent childhood asthma. One such therapy is homeopathy, a system of medicine that uses specially prepared, highly dilute substances to induce the body's self-healing in a comprehensive manner. This article describes the contrasting experiences for a family who undergoes specialty consultations with an allergist and with a homeopath. The style of the interview and the diagnostic tools used vary, as well as the basic philosophies and goals. The advantages and limitations, as well as the regulatory framework of homeopathy are explained, as evidenced by the literature. For nurses and other clinicians caring for children and families who use nonconventional therapies, the clinical implications are that these professionals need to become knowledgeable about the various alternative therapies which can complement conventional care. Families who wish to try homeopathy along with conventional care need to have open lines of communication and cooperation between their providers, both conventional and homeopathic. The care of childhood asthma may prove to benefit from clinical trials in homeopathy. Copyright 2001 by W.B. Saunders Company

Anti-remodelling drugs for the treatment of asthma: requirement for animal models of airway wall remodelling.

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Clin Exp Pharmacol Physiol 2001 Aug;28(8):619-29

1. Airway wall remodelling (AWR), the structural change induced by acute and chronic inflammation in the airways, may be one of the most significant and difficult to reverse components of progressive asthma. 2. The mechanisms underlying the development of AWR are not known. Studies of only the most superficial wall structures of large airways can be conducted in living humans

because of the degree of invasiveness required to measure airway structural changes. These studies reveal that currently available agents do not fully prevent or reverse AWR. Thus, animal models of asthma pathology may be used to assess the contribution of particular mediators and cells to the development of remodelling and may also prove to be useful in the initial screening of potential anti-remodelling agents. 3. Airway hyperresponsiveness and AWR stimulated by chronic antigen challenge in previously disease-free animals is the most popular of the currently used models of remodelling. Other animal models include the use of specially bred strains with intrinsic airway hyperresponsiveness or animals that have a naturally occurring asthma-like disease, such as cats with feline asthma or horses with heaves. The further development of animal models of AWR will facilitate the development of novel anti-asthma therapies.

[Atopy with recurrent wheezy bronchitis in children]. [Article in Polish]

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Pneumonol Alergol Pol 2001;69(1-2):73-83

Childhood asthma and wheezy bronchitis are the most frequent chronic diseases of childhood. Unfortunately their clinical symptoms are similar--which makes it difficult to distinguish between the two, and therefore decide on proper treatment of patients. The aim of the study was to establish the parameters leading to right diagnosis. The study was performed in 50 children aged 3-7 years with recurrent wheezy bronchitis. All patients underwent allergological examinations (skin tests with inhaled allergens, personal and family history and serum total and specific IgE levels). 42 of them were tested for ventilatory parameters with bronchodilatation test. Three features of atopy were found in 21 (42%) patients, two features in 7 (14%) patients. In 31 (62%) children at least one feature of atopy was shown. 7 (17%) of the examined children had significant bronchodilatation after salbutamol inhalation. Finally in 24 (48%) of children suffering from wheezy bronchitis, bronchial asthma was diagnosed. The diagnosis was confirmed by antiasthmatic treatment with cromones or inhaled corticosteroids. In great majority (88%) of patients bronchial asthma was atopic. In 23% wheezy bronchitis children not diagnosed with bronchial asthma features of atopy were observed. They are of bronchial asthma risk group.

A novel 11 beta-hydroxysteroid dehydrogenase inhibitor contained in saiboku-to, a herbal remedy for steroid-dependent bronchial asthma.

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J Pharm Pharmacol 1994 Apr;46(4):305-9

To identify the inhibitor of prednisolone metabolism contained in Saiboku-To, we conducted in-vitro experiments of 11 beta-hydroxysteroid dehydrogenase (11 beta-HSD), using rat liver homogenate and cortisol as a typical substrate. We studied the effects of ten herbal constituents on 11 beta-HSD. Five herbal extracts showed inhibitory activity with *Glycyrrhiza glabra* < *Perillae frutescens* & *Zizyphus vulgaris* & *Magnolia officinalis* & *Scutellaria baicalensis*. This suggests that unknown 11 beta-HSD inhibitors are contained in four herbs other than *G. glabra* which contains a known inhibitor, glycyrrhizin (and glycyrrhetic acid). Seven chemical constituents which have been identified as the major urinary products of Saiboku-To in healthy and asthmatic subjects were studied; magnolol derived from *M. officinalis* showed the most potent inhibition of the enzyme (IC₅₀, 1.8 x 10⁻⁴ M). Although this activity was less than that of glycyrrhizin, the inhibition mechanism (non-competitive) was different from a known competitive mechanism. These results suggest that magnolol might contribute to the inhibitory effects of Saiboku-To on prednisolone metabolism through inhibition of 11 beta-HSD.

Understanding the pathogenesis of allergic asthma using mouse models.

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Ann Allergy Asthma Immunol 2001 Aug;87(2):96-109; quiz 110,

OBJECTIVE: This paper reviews the current views of the pathogenesis of airway eosinophilic inflammation and airway hyperresponsiveness (AHR) in allergic asthma based on mouse models of the disease. The reader will also encounter new treatment strategies that have arisen as this knowledge is applied in practice.

DATA SOURCES: MEDLINE searches were conducted with key words asthma, mouse model, and murine. Additional articles were identified from references in articles and book chapters.

STUDY SELECTION: Original research papers and review articles from peer-reviewed journals were chosen.

RESULTS: Although the mouse model does not replicate human asthma exactly, the lessons learned about the pathogenesis of allergic airway inflammation and AHR are generally applicable in humans. Type 2 T helper lymphocytes (Th2) orchestrate the inflammation and are crucial for the development of AHR. Cells and molecules involved in T cell activation (dendritic cells, T cell receptor, major histocompatibility complex molecule, and costimulatory molecules) are also vital. Besides these, no other cell or molecule could be shown to be indispensable for the establishment of the model under all experimental conditions. There are at least three pathways that lead to AHR. One is dependent on immunoglobulin E and mast cells, one on eosinophils and interleukin-5 (IL-5), and one on IL-13. Eosinophils are probably the most important effector cells of AHR. Radical methods to treat asthma have been tested in the animal model, including modifying the polarity of lymphocyte response and antagonizing IL-5.

CONCLUSIONS: AHR, the hallmark of asthma, is attributable to airway inflammation ultimately mediated by helper T cells via three pathways, at least. The mouse model is also a valuable testing ground for new therapies of asthma.

Family history and the risk of early-onset persistent, early-onset transient, and late-onset asthma.

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Epidemiology 2001 Sep;12(5):577-83

Family history of asthma and allergies strongly influences asthma risk in children, but the association may differ for early-onset persistent, early-onset transient, and late-onset asthma. We analyzed the relation between family history and these types of asthma using cross-sectional data from a school-based study of 5,046 Southern California children. Parental and/or sibling history of asthma and allergy were generally more strongly associated with early-onset persistent asthma compared with early-onset transient or late-onset asthma. For children with two asthmatic parents relative to those with none, the prevalence ratio for early-onset persistent asthma was 12.1 [95% confidence interval (CI) = 7.91-18.7] compared with 7.51 (95% CI = 2.62-21.5) for early-onset transient asthma and 5.38 (95% CI = 3.40-8.50) for late-onset asthma. Maternal smoking in pregnancy was predominantly related to the risk of early-onset persistent asthma in the presence of parental history of allergy and asthma, and the joint effects were more than additive (interaction contrast ratio = 3.10, 95% CI = 1.45-4.75). Our results confirm earlier data that parental history of asthma and allergy is most strongly associated with early-onset persistent asthma and suggest that among genetically predisposed children, an early-life environmental exposure, maternal smoking during pregnancy, favors the development of early-onset asthma that persists into later early childhood.

Antioxidant nutrients: current dietary recommendations and research update.

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J Am Pharm Assoc (Wash) 2000 Nov-Dec;40(6):785-99

OBJECTIVE: To review the importance of antioxidant nutrients in the maintenance of health and the prevention and treatment of disease, with a focus on data pertaining to vitamin C, vitamin E, selenium, and carotenoids. A secondary objective was to discuss the new Dietary Reference Intakes released by the Institute of Medicine (IOM) for these nutrients.

DATA SOURCES: IOM reports on the use of antioxidant vitamins were reviewed for nutrient recommendations. In addition, a

MEDLINE search was performed to identify recent research and review articles on the topic, which were analyzed to identify key research findings in the area.

DATA SYNTHESIS: The review discusses the biologic processes of oxidation reactions and antioxidants in biologic systems, provides an overview of information on selected antioxidant nutrients, and explores their role in the prevention and treatment of cancer, cardiovascular disease, ocular disorders, and respiratory disorders.

CONCLUSION: There appear to be significant health benefits from dietary antioxidants, as can be found in fruits and vegetables. Some prospective assessment of the effect of supplemental antioxidants also suggests benefit, especially for vitamin E; however, there are conflicting results in this area. Overall, it appears that antioxidant nutrients, especially those from food sources, have important roles in preventing pathogenic processes related to cancer, cardiovascular disease, macular degeneration, cataracts, and asthma, and may enhance immune function.

Why do asthmatic subjects respond so strongly to inhaled adenosine?

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Bronchospasm induced by adenosine is blocked by representatives of all the major classes of drugs used in the treatment of asthma. Understanding the mechanism of this bronchospasm may help understand the way these drugs work. Clinical studies have suggested involvement of neural pathways, mast-like cells and mediators such as histamine, serotonin and lipoxygenase products. There is a strong link between responsiveness to adenosine and eosinophilia. In different animal models A1, A2b and A3 adenosine receptor subclasses have all been implicated in inducing bronchospasm. whilst occupation of the A2a receptor generally has no, or the opposite effect. At least two different mechanisms, both involving neural pathways, exist. One, involving the adenosine A1 receptor, functions in mast cell depleted animals; the other requires interaction with a population of mast-like cells activated over A2b or A3 receptors. Not only histamine but also serotonin and lipoxygenase products released from the mast-like cells are potential mediators. In animal models good reactivity to adenosine receptor agonists is generally only found when the animals are first sensitized and exposed to allergen in ways likely to induce an allergic inflammation. An exception is the BDE rat, which reacts to adenosine receptor agonists such as APNEA or NECA even without allergen exposure. This rat strain does however show evidence of spontaneous eosinophilic inflammation in the lung even without immunization. As mast cells both release adenosine and respond to adenosine, adenosine provides a non-specific method of amplifying specific signals resulting from IgE/antigen interaction. This mechanism may not only have a pathological significance in asthma; it may be part of a normal bodily defense response that in asthmatic subjects is inappropriately activated.

Inhibitory effect of baicalein, a flavonoid in Scutellaria Root, on eotaxin production by human dermal fibroblasts.

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Planta Med 2001 Mar;67(2):132-5

Eotaxin is an eosinophil-specific chemokine associated with the recruitment of eosinophils to sites of allergic inflammation. "Saiboku-to" (Formula magnoliae et bupleuri) is a kampo herbal medicine used for the treatment of bronchial asthma in Japan. In this study, we investigated the effects of Scutellaria Root, a major herb in Saiboku-to and its components such as baicalein and baicalin on eotaxin production by IL-4 plus TNF-alpha-stimulated human fibroblasts. An extract of Scutellaria Root markedly inhibited eotaxin production. Four major flavonoids from Scutellaria Root were found to show inhibitory activity on eotaxin production at a concentration of 10 micrograms/ml in the order of baicalein & oroxylin A & baicalin & skullcapflavon II. The inhibitory effect of baicalein was expressed in a dose-dependent manner, and almost 50% inhibition was observed at 1.8 micrograms/ml. Furthermore, baicalein prevented human eotaxin mRNA expression in IL-4 plus TNF-alpha-stimulated human fibroblasts. These results help explain the pharmacological efficacy of Scutellaria Root in the treatment of bronchial asthma since it would suppress eotaxin associated recruitment of eosinophils.

Maternal asthma, infant feeding, and the risk of asthma in childhood.

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J Allergy Clin Immunol 2002 Jul;110(1):65-7

Controversy surrounds the issue of whether children with asthmatic mothers should be breast-fed. The aim of this study was to investigate whether maternal asthma status alters the association between asthma and breast-feeding. In a cohort study of 2602 West Australian children enrolled before birth and followed prospectively, we collected data on method of infant feeding, maternal asthma (as reported by parental questionnaire), atopy (as measured by skin prick test), and current asthma (defined as a physician's diagnosis of asthma and wheeze in the last year) at 6 years of age. The risk of childhood asthma increased if exclusive breast-feeding was stopped (other milk was introduced) before 4 months (odds ratio, 1.28; 95% CI, 1.01-1.62; P =.038), and this risk was not altered by atopy or maternal asthma status. After adjusting for covariates, exclusive breast-feeding for less than 4 months was a significant risk factor for current asthma (odds ratio, 1.35; 95% CI, 1.00-1.82; P =.049). There was no formal statistical interaction between breast-feeding and maternal asthma status (P =.970). In this study maternal asthma status did not modify the association between asthma and breast-feeding duration. We recommend that infants with or without a maternal history of asthma be exclusively breast-fed for 4 months and beyond.

The effects of respiratory infections, atopy, and breastfeeding on childhood asthma.

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Eur Respir J 2002 May;19(5):899-905

The objectives of the present study were to quantify the association of atopy and respiratory infections with asthma, and exclusive breastfeeding with respiratory illness, atopy and asthma in children. A cohort study of 2,602 children enrolled prior to birth and followed prospectively, provided data on respiratory illness, the method of feeding in the first year of life, as reported on a prospective diary card, and current asthma at the age of 6 yrs (defined as doctor-diagnosed asthma with wheeze in the last year or cough without a cold, and currently taking either preventer or reliever asthma medication), as reported by parental questionnaire. Atopy was defined by a positive skin-prick test assessed at the age of 6 yrs. Wheezing lower respiratory illness (LRI) in the first year of life, particularly multiple episodes of wheezing LRI, increased the risk for current asthma in both nonatopic (odds ratio (OR) 4.10, $p=0.0005$) and atopic children (OR 9.00, $p=0.0005$), but did not increase the risk for atopy. In contrast, up to three upper respiratory tract infections demonstrated a negative association and four or more a positive risk for current asthma in unadjusted ($p=0.006$) and adjusted ($p=0.057$) analysis. Following adjustment, exclusive breastfeeding for < 4 months was associated with an increased risk for current asthma (OR 1.36, 95% confidence interval 1.00-1.85, $p=0.047$). Wheezing lower respiratory illness in the first year of life and atopy are independently associated with increased risk for current asthma at the age of 6 yrs, suggesting that their effects are mediated via different causal pathways and that these risk factors are multiplicative when they operate concomitantly within individual children. Exclusive breastfeeding protects against asthma via effects on both these pathways, as well as through other as yet undefined mechanisms

Dietary micronutrients/antioxidants and their relationship with bronchial asthma severity.

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Allergy 2001 Jan;56(1):43-9

BACKGROUND: Because little is known about micronutrient/antioxidant intake and asthma severity, we investigated dietary intake and plasma/serum levels of micronutrients/antioxidants in a group of asthma patients with various degrees of severity, and compared the results with healthy subjects.

METHODS: A case control study was carried out on 118 asthma patients and 121 healthy subjects. The severity of the disease was classified by division of patients into four groups. Normal dietary micronutrient/antioxidant intake was estimated from a food frequency questionnaire. Plasma/serum levels of vitamins C, E, and A, selenium, magnesium, zinc, and platelet glutathione peroxidase (GSH-Px) activity were also determined.

RESULTS: No differences in daily micronutrient/antioxidant intake were seen between patients and healthy subjects. The severity of the disease showed no significant relationship with micronutrient/antioxidant intake. There were no differences in plasma/serum levels in any of the micronutrients/antioxidants between healthy subjects and asthmatics. Nor were any differences found between asthma groups in severity in the biochemical measures, except in platelet GSH-Px activity, which was significantly lower in the most severe groups.

CONCLUSIONS: In this study, we found no evidence of any association between micronutrient/antioxidant intake or plasma/serum levels of micronutrients/antioxidants and asthma. Reduction of platelet GSH-Px activity in the most severe patients suggests that these patients have a diminished capacity to restore part of the antioxidant defences.

[CD4+ T cell activation and IL-5 production in atopic and nonatopic asthmatics]. [Article in Chinese]

Quan B, Tang C, Wang D. 202nd Hospital, PLA, Shenyang 110003.

Zhonghua Jie He He Hu Xi Za Zhi 1998 Oct;21(10):604-6

OBJECTIVE: To understand the reasons and roles of CD4+ T cell activation and IL-5 production in atopic and asthmatic patients.

METHOD: Bronchoalveolar lavage(BAL) cells and peripheral blood mononuclear cells (PBMC) from 12 atopic and 10 nonatopic asthmatics, 9 atopic nonasthmatics, and 10 normal controls were cultured with or without house dust mite(HDM), CD4+ T cell activation, and IL-5 production were assessed.

RESULT: The percentage of CD4+, CD25+ in unstimulated PBMC cultures were not significantly different in the four groups, but it increased following HDM stimulation in both PBMC and BAL cultures in two atopic groups(< 0.01). The percentage of CD4+, CD25+ in unstimulated BAL cell culture increased in two asthmatic groups (< 0.05 , < 0.01). The levels of spontaneous IL-5 released from both BALF cells and PBMC in two asthmatic groups were higher than those in AN and N (< 0.05 , < 0.01). A significant elevation in IL-5 release following HDM stimulation in PBMC and BALF cells was observed in the both asthmatic and atopic groups; but the value in AA was higher than that in NAA, and it was also higher in BALF cells than in PBMC.

CONCLUSION: The allergen stimulation is important reasons for CD4+ T cell activation and IL-5 production in atopics. CD4+ T cell activation and IL-5 production are common feature in atopic and nonatopic asthma, it correlates with both asthmatic and atopic status.

New insights into the role of cytokines in asthma.

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J Clin Pathol 2001 Aug;54(8):577-89

Asthma is a triad of intermittent airway obstruction, bronchial smooth muscle cell hyperreactivity to bronchoconstrictors, and chronic bronchial inflammation. From an aetiological standpoint, asthma is a heterogeneous disease, but often appears as a form of immediate hypersensitivity. Many patients with asthma have other manifestations of atopy, such as rhinitis or eczema. Even among non-atopic patients with asthma, the pathophysiology of airway constriction is similar, raising the hypothesis that alternative mechanisms of mast cell degranulation may underlie the disease. The primary inflammatory lesion of asthma consists of accumulation of CD4(+) T helper type 2 (TH2) lymphocytes and eosinophils in the airway mucosa. TH2 cells orchestrate the asthmatic inflammation through the secretion of a series of cytokines, particularly interleukin 4 (IL-4), IL-13, IL-5, and IL-9. IL-4 is the major factor regulating IgE production by B cells, and is required for optimal TH2 differentiation. However, blocking IL-4 is not sufficient to inhibit the development of asthma in experimental models. In contrast, inhibition of IL-13, another TH2 cytokine whose signal transduction pathway overlaps with that of IL-4, completely blocks airway hyperreactivity in mouse asthma models. IL-5 is a key factor for eosinophilia and could therefore be responsible for some of the tissue damage seen in chronic asthma. IL-9 has pleiotropic activities on allergic mediators such as mast cells, eosinophils, B cells and epithelial cells, and might be a good target for therapeutic interventions. Finally, chemokines, which can be produced by many cell types from inflamed lungs, play a major role in recruiting the mediators of asthmatic inflammation. Genetic studies have demonstrated that multiple genes are involved in asthma. Several genome wide screens point to chromosome 5q31-33 as a major susceptibility locus for asthma and high IgE values. This region includes a cluster of cytokine genes, and genes encoding IL-3, IL-4, IL-5, IL-9, IL-13, granulocyte macrophage colony stimulating factor, and the beta chain of IL-12. Interestingly, for some of these cytokines, a linkage was also established between asthma and their receptor. Another susceptibility locus has been mapped on chromosome 12 in a region that contains other potential candidate cytokine genes, including the gene encoding interferon gamma, the prototypical TH1 cytokine with inhibitory activities for TH2 lymphocytes. Taken together, both experimental and genetic studies point to TH2 cytokines, such as IL-4, IL-13, IL-5, and IL-9, as important targets for therapeutic applications in patients with asthma.

Prospective study of the patient-level cost of asthma care in children.

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Pediatr Pulmonol 2001 Aug;32(2):101-8

Our objective was to assess the cost of asthma care at the patient level in children from the perspectives of society, the Ontario Ministry of Health, and the patient. In this longitudinal evaluation, health service use data and costs were collected during telephone interviews at 1, 3, and 6 months with parents of 339 Ontario children with asthma. Direct costs were respiratory-related visits to healthcare providers, emergency rooms, hospital admissions, pulmonary function tests, prescription medications, devices, and out-of-pocket expenses. Indirect costs were parents' absences from work/usual activities and travel and waiting time. Hospital admissions accounted for 43%, medications for 31%, and parent productivity losses for 12% of total costs from a societal perspective. Statistically significant predictors of higher total costs were worse symptoms, younger age group, and season of participation. Adjusted annual societal costs per patient in 1995 Canadian dollars varied from \$1,122 in children aged 4-14 years to \$1,386 in children under 4 years of age. From the Ministry of Health perspective, adjusted annual costs per patient were \$663 in children over 4 years and \$904 in younger children. Adjusted annual costs from the patient perspective were \$132 in children over 4 years and \$129 in children under 4 years. The rising incidence of pediatric asthma demands that greater attention be paid to the delivery of optimal care to this segment of the population. Appropriate methods must be used to analyze healthcare costs and the use of services in the midst of widespread healthcare reform. The quality of clinical and health policy decision-making may be enhanced by cost-of-illness estimates that are comprehensive, precise, and expressed from multiple perspectives. Copyright 2001 Wiley-Liss, Inc.

Proinflammatory cytokines (IL-17, IL-6, IL-18 and IL-12) and Th cytokines (IFN-gamma, IL-4, IL-10 and IL-13) in patients with allergic asthma.

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Allergen-reactive T helper type-2 (Th2) cells and proinflammatory cytokines have been suggested to play an important role in the induction and maintenance of the inflammatory cascade in allergic asthma. We compared the plasma concentrations of novel proinflammatory cytokines IL-17 and IL-18, other proinflammatory cytokines IL-6 and IL-12, Th2 cytokines IL-10 and IL-13, and intracellular interferon-gamma (IFN-gamma) and IL-4 in Th cells of 41 allergic asthmatics and 30 sex- and age-matched health control subjects. Plasma cytokines were measured by enzyme-linked immunosorbent assay. Intracellular cytokines were quantified by flow cytometry. Plasma IL-18, IL-12, IL-10, IL-13 concentrations were significantly higher in allergic asthmatic patients than normal control subjects (IL-18: median 228.35 versus 138.72 pg/ml, < 0.001 ; IL-12: 0.00 versus 0.00 pg/ml, $P = 0.001$; IL-10: 2.51 versus 0.05 pg/ml, < 0.034 ; IL-13: 119.38 versus 17.89 pg/ml, < 0.001). Allergic asthmatic patients showed higher plasma IL-17 and IL-6 concentrations than normal controls (22.40 versus 11.86 pg/ml and 3.42 versus 0.61 pg/ml, respectively), although the differences were not statistically significant ($P = 0.077$ and 0.053 , respectively). The percentage of IFN-gamma-producing Th cells was significantly higher in normal control subjects than asthmatic patients (23.46 versus 5.72%, < 0.001) but the percentage of IL-4 producing Th cells did not differ (0.72 versus 0.79%, < 0.05). Consequently, the Th1/Th2 cell ratio was significantly higher in normal subjects than asthmatic patients (29.6 versus 8.38%, < 0.001). We propose that allergic asthma is characterized by an elevation of both proinflammatory and Th2 cytokines. The significantly lower ratio of Th1/Th2 cells confirms a predominance of Th2 cells response in allergic asthma.

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